Original research

Short-term association among meteorological variation, outdoor air pollution and acute bronchiolitis in children in a subtropical setting

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ABSTRACT

Objectives To examine the association among acute bronchiolitis-related hospitalisation in children, meteorological variation and outdoor air pollution.

Methods We obtained the daily counts of acute bronchiolitis-related admission of children≤2 years old from all public hospitals, meteorological data and outdoor air pollutants' concentrations between 1 January 2008 and 31 December 2017 in Hong Kong. We used quasi-Poisson generalised additive models together with distributed lag non-linear models to estimate the associations of interest adjusted for confounders.

Results A total of 29 688 admissions were included in the analysis. Increased adjusted relative risk (ARR) of acute bronchiolitis-related hospitalisation was associated with high temperature (ambient temperature and apparent temperature) and was marginally associated with high vapour pressure, a proxy for absolute humidity. High concentration of NO_2 was associated with elevated risk of acute bronchiolitis admission; the risk of bronchiolitis hospitalisation increased statistically significantly with cumulative NO_2 exposure over the range 66.2–119.6 µg/m^3. For PM_{10}, the significant effect observed at high concentrations appears to be immediate but not long lasting. For SO_2, ARR increased as the concentration approached the 75th percentile and then decreased though the association was insignificant.

Conclusions Acute bronchiolitis-related hospitalisation among children was associated with temperature and exposure to NO_2 and PM_{10} at different lag times, suggesting a need to adopt sustainable clean air policies, especially to target pollutants produced by motor vehicles, to protect young children's health.

Key messages

What is the key question?

- Are meteorological variation and outdoor air pollution associated with acute bronchiolitis-related hospitalisation in children?

What is the bottom line?

- Acute bronchiolitis-related hospitalisation among children was associated with temperature and exposure to NO_2 and PM_{10} at different lag times.

Why read on?

- This is one of the very few studies that explored the association of interest in a subtropical setting.

INTRODUCTION

Acute bronchiolitis is typically caused by viral infection. Respiratory syncytial virus (RSV) is the most common pathogen in childhood respiratory tract infection, especially among those ≤2 years old.[1–3] Clinical signs and symptoms of acute bronchiolitis include cough, tachypnoea, hyperinflation of lungs, chest retraction, inspiratory crackles and expiratory wheeze.[2 3]

Acute bronchiolitis causes significant morbidity and mortality among infants and young children worldwide.[1] It is the most common cause of lower respiratory tract infection (LTRI)-related hospitalisation.[1–3] In the USA, acute bronchiolitis is the leading cause of hospitalisation among infants ≤1 year old.[4] Nearly all children would be infected at least once by the time they reached the age of 2 years, and an estimated 2%–3% of all children would be hospitalised with acute bronchiolitis during their first year of life.[2 3 5 6] In temperate regions, the annual epidemics usually last from November all the way till April with a peak observed in January or February.[5 6] Similar patterns could be seen in European countries where the average RSV season commences in the beginning of December, peaks in early February and ends in early April.[7]

In Hong Kong, acute bronchiolitis is one of the major causes of hospital admissions among infants under the age of one. Up to 5% of total paediatric discharge from all hospitals under the Hong Kong Hospital Authority are attributed to this condition.[8] In a single hospital study, the estimated incidence of bronchiolitis hospitalisation was 21 per 1000 among children ≤2 years old with 86% of them having been infected with RSV.[9] Different from the USA and Europe, Hong Kong is located within the subtropical region where RSV season remains ill-defined but usually overlaps with the rainy season (ie, from March to September).[3 8]

Global surveillance suggested that the seasonal periodicity of RSV infection is related to climatic factors.[10] Meteorological conditions including ambient temperature, rainfall and humidity were reported to be associated with RSV activity,[6 10–12] while altitude, wind speed, dew point and ultraviolet B radiance were reported to be associated

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with bronchiolitis.[11 12] On the other hand, air pollutants such as primary traffic pollutants, ozone (O_3), fine suspended particulates ($PM_{2.5}$) and environmental nitrogen dioxide (NO_2), as well as living close to major roadways have been reported to be associated with exacerbation of respiratory infections in young children.[13 14]

Hong Kong is a densely populated cosmopolitan city in southern China with hot and humid summers, and mild and dry winters. According to the 2016 Population By-census, Hong Kong had a population of 7.34 million.[15] Motor vehicles are the main source of air pollutants in Hong Kong. According to the air quality guideline of the WHO, 8 hours daily mean of O_3 should not exceed 100 $\mu g/m^3$, while annual mean level of respirable suspended particulates (PM_{10}) and NO_2 should not exceed 20 $\mu g/m^3$ and 40 $\mu g/m^3$, respectively.[16] Unfortunately, in Hong Kong, the highest 8 hours mean concentration recorded for O_3 was 305 $\mu g/m^3$ and the highest annual mean concentrations recorded for PM_{10} and NO_2 were 46 $\mu g/m^3$ and 97 $\mu g/m^3$, respectively, in 2017, all of which exceeded the WHO's guideline limits.[17]

Previous studies suggested that acute bronchiolitis-related hospitalisation in children is associated with meteorological variation but its association with outdoor air pollution has not been well explored.[6 9–14 18 19]Furthermore, only limited studies have been conducted in subtropical regions, most of which yielded inconsistent results.[8 9 18 19] Therefore, in this study, we aim to evaluate the possible short-term association among acute bronchiolitis-related hospitalisation in children, meteorological variation and outdoor air pollution in Hong Kong.

METHODS

Study design

This is a retrospective time-series study to assess the short-term impacts of meteorological variation and outdoor air pollution on acute bronchiolitis-related hospitalisation among young children. We obtained the daily counts of acute bronchiolitis-related admission of children≤2 years old from a total of 12 public hospitals with acute paediatric inpatient services, daily meteorological data and daily outdoor air pollutants' concentrations between 1 January 2008 and 31 December 2017.

Hospital admission data

In Hong Kong, paediatric care services are provided by both the public and private sectors. Approximately, 71% of all hospitalisations in 2016 occurred in public hospitals.[20] The retrospective data of admissions of children ≤2 years old to all public hospitals for acute bronchiolitis (International Classification of Diseases 9th version (ICD-9): 466.1 in principal and secondary diagnosis) from 1 January 2008 to 31 December 2017 were extracted for statistical modelling. Data on influenza-associated hospital admission (ICD-9: 487.0, 487.1, 487.8) were also collected.

Meteorological data

Daily meteorological records measured at a single central monitoring station run by the Hong Kong Observatory were obtained for the study period, including mean ambient temperature (°C), mean relative humidity (RH%) and total rainfall (mm), from the open-access data available on their website (https://www.hko.gov.hk/cis/climat_e.htm). Actual vapour pressure (hPa), a proxy for absolute humidity well adopted in many environmental studies[21 22] was then derived using Teten's formula[23]:

$$e = \frac{RH}{100} \times 6.105 \times exp\left(\frac{17.27 \times TEMP}{237.7 + TEMP}\right)$$

where e, RH and TEMP denote actual vapour pressure, relative humidity and ambient temperature, respectively. Apparent temperature (°C) was derived using the following formula[24]:

$$\begin{aligned} \textit{Apparent temperature} \quad &= 1.04 \times TEMP + 0.2 \\ &\times e - 0.65 \times WIND - 2.7 \end{aligned}$$

where TEMP and e are as defined above and WIND denotes wind speed (m/s).

Ambient air pollutants data

Daily average levels of air pollutants measured at 13 general air monitoring stations (Central/Western, Eastern, Kwai Chung, Kwun Tong, Sham Shui Po, Shatin, Tai Po, Tap Mun, Tseng Kwan O, Tsuen Wan, Tuen Mun, Tung Chung and Yuen Long), including nitrogen dioxide (NO_2), sulphur dioxide (SO_2), ozone (O_3) and particulate matters (PM_{10}), were retrieved from the official website of the Environmental Protection Department of Hong Kong (https://cd.epic.epd.gov.hk/EPICDI/air/station/?lang=en). Data from Tap Mun station were excluded because it is situated in a remote area with very low population density, thus, might not represent the exposure of the general population. Data from the remaining 12 general air monitoring stations were averaged for downstream analysis.

Statistical analyses

Descriptive statistics were used to describe the demographic characteristics of the patients. A quasi-Poisson generalised additive model was used in conjunction with the distributed lag non-linear models (DLNMs) to assess the potentially lagged non-linear short-term associations between acute bronchiolitis-related hospitalisation of young children, meteorological variation and outdoor air pollution. In the DLNM, cross-basis is a bidimensional functional space created by combining two preselected sets of basis functions, which specify the relationships in the dimensions of an independent variable and lags, respectively. Algebraically, the cross-basis function of an independent variable X at time t with a maximum lag of L can be expressed in the following form:

$$cb\left(X,\ t,\ L\right) = \sum_{j=1}^{v_x}\sum_{k=1}^{v_\mathfrak{l}} \boldsymbol{r}_{tj.}^T \boldsymbol{c}_{.k}\eta_{jk}$$

where $\boldsymbol{r}_{tj.}$ is an $\left(L+1\right) \times 1$ vector representing the jth basis variable of X across the (L+1) lags, $\boldsymbol{c}_{.k}$ is an $\left(L+1\right) \times 1$ vector obtained by transforming the lag vector $\mathfrak{l} = \left[0,\ 1, \ldots, L\right]$ using the kth basis function in the lag dimension, v_x and $v_\mathfrak{l}$ are the dimensions of the basis functions of $\boldsymbol{x}_t$ and respectively, and η_{jk} is the unknown regression coefficient.[25]

The form of the primary model is as follows:

$$\begin{gathered} log\left[E\left(Y_t\right)\right] = \ + cb\left(TEMP,\ t,\ L\right) + \ cb\left(RH,\ t,\ L\right) + \\ cb\left(factor\left(RAINFALL\right),\ t,\ L\right) + \\ cb\left(NO_2,\ t,\ L\right) + \ cb\left(\log\left(PM_{10}\right),\ t,\ L\right) + \\ cb\left(O_3,\ t,\ L\right) + \ cb\left(\log\left(SO_2\right),\ t,\ L\right) + \\ cb\left(factor\left(HOLIDAY\right),\ t,\ L\right) + \ ns\left(DOS_t,\ df = 7\ per\ year\right) + \\ factor\left(DOW_t\right) + s\left(\sqrt{FLU_t},\ k = 7\right) \end{gathered}$$

where $E(Y_t)$ is the daily expected count of acute bronchiolitis admissions on day t; TEMP, RH, RAINFALL denote ambient temperature, relative humidity, and total rainfall, respectively; DOS_t and DOW_t denote day of study and day of week on day t respectively; α is the overall intercept; *factor*(.) is a set of indicator functions for any categorical independent variable, and *s*(.) denotes a smoothing spline function with maximum basis dimension *k*. In this study, natural cubic spline functions (*ns*) with 2 and 3 knots placed at equally spaced intervals were chosen as the basis function of the meteorological parameters (except for rainfall) and pollutants, respectively, which is equivalent to 3 and 4 degrees of freedom (*df*) respectively; whereas an *ns* function with 2 knots placed at logarithmically equal intervals, which is equivalent to 4 *df*, was selected as the basis function of lag. DOS was modelled using an *ns* function with 7 *df* per year. The incubation period for acute bronchiolitis is usually 5–7 days and disease period is usually 1–2 weeks[5]; hence, the maximum lags for independent variables were assumed to be 21 days. Total rainfall was categorised into three groups, namely 0 mm, 0 to 38.8 mm (the 95th percentile) and >38.8 mm, so as to better examine the effect of extreme rainfall and reduce the influence of outliers.[26] SO_2 and PM_{10} were log transformed to reduce skewness and the influence of outliers. An indicator variable HOLIDAY which denotes whether a specific day was a holiday, DOS, DOW and the square root of the number of influenza-associated hospital admission on the same day (FLU) were included in the model for confounder control. To further assess the adjusted effect of absolute humidity and apparent temperature on the daily counts of acute bronchiolitis admissions, two secondary models with vapour pressure in place of ambient temperature and relative humidity, and apparent temperature in place of ambient temperature were fitted due to high correlations between these meteorological variables (online supplemental appendix section A).

All results were reported in terms of overall cumulative adjusted relative risks (ARR), which accumulated the ARRs over the lag period of 21 days, along with the corresponding 95% CI, and ARR plots by lag at selected percentiles, at which the adjusted risks at a specific lag and percentile were compared with that at the reference value on the concurrent day. The reference values for rainfall and all pollutants were 0 mm and their corresponding 5th percentile, respectively, whereas the medians were chosen as the reference values for ambient temperature, apparent temperature, relative humidity and vapour pressure.

Model diagnostics and sensitivity analysis

Adjusted R^2 and residual plots were used to assess the goodness of fit of the final models. Partial autocorrelation function (PACF) plots were used to assess partial autocorrelation of residuals, with absolute values of pacfs <0.1 at the first 30 lag days regarded as adequate fit.[27] Sensitivity analyses were conducted to assess the robustness of the final results to the initial model choices. To be specific, changes in the overall cumulative ARRs induced by the alternation of the *df*s of the basis functions for meteorological parameters (2 and 4 except for rainfall), pollutants (3 and 5), and lag dimensions (3 and 5), as well as that of *ns* function for DOS (6 and 8 per year) were examined. The cut-off values for categorising total rainfall were also altered (online supplemental appendix section B).

All statistical analyses were performed using R V.3.6.0. (R Development Core Team, 2018: https://www.rproject.org/) and the raw outputs were listed in online supplemental appendix section E.

RESULTS

A total of 31 523 admissions from 2008 to 2017 were retrieved from the database, out of which 1835 were elective admission, and thus, were excluded in the analysis. Among the remaining 29 688 admissions, 66% were infants ≤12 months, 4% were preterm babies (<37 weeks), 68% were male and 99% were Asian. The median (IQR) length of stay was 3 days (2–4 days). 21.5% of cases were admitted more than once with acute bronchiolitis. During the study period, a total number of 10 deaths were recorded, corresponding to a mortality rate of 0.04% (table 1). The major causes of these deaths were respiratory failure and multiple organ failure. Each hospital applies different practices based on different priorities. Some hospitals might not examine nasopharyngeal aspirates (NPA) for pathogens since the results would not affect their medical management. From the available NPA results, RSV was the most common pathogen causing acute bronchiolitis in infants.

During the study period, the median (IQR) number of daily acute bronchiolitis admission was 8 (5–10) (table 2). The median (IQR) mean daily ambient temperature and mean relative humidity were 24.8°C (19.2°C–28.2°C) and 79% (74%–86%), respectively. According to the results, acute bronchiolitis was shown to exhibit seasonal pattern, with a major peak in spring (February–April) which could attain >400 cases per month, and a minor peak in late summer (September–October) having around 250 cases per month (figure 1).

Figure 2A–D show the overall cumulative ARRs and percentile-specific (5th, 25th, 75th and 95th percentiles) ARRs of acute bronchiolitis-related hospitalisation among children≤2 years old. The patterns of the overall cumulative ARR for ambient temperature and apparent temperature were similar, which showed an overall increasing trend (figure 2A,B). For ambient temperature, when the median (24.8°C) was taken as reference, the overall cumulative ARRs at the 5th, 25th, 75th and 95th percentiles were 0.990 (95% CI 0.721 to 1.361), 1.048 (95% CI 0.846 to 1.298), 1.034 (95% CI 0.904 to 1.182), and 1.108 (95% CI 0.871 to 1.409), respectively; whereas for apparent temperature, when the median (23.6°C) was taken as reference, resulted ARRs at the four percentiles were 1.005 (95% CI 0.761 to 1.326), 1.044 (95% CI 0.873 to 1.247), 1.112 (95% CI 0.962 to 1.286), and 1.323 (95% CI 1.011 to 1.731), respectively. It was found that, at the 75th and 95th percentiles of both ambient temperature and apparent temperature, the ARRs were statistically significant since lag 16–17 days.

For relative humidity (figure 2C), the overall cumulative ARR was comparatively higher when relative humidity was low compared with when it was high. When the median relative humidity (79.0%) was taken as reference, the overall cumulative ARRs at the 5th, 25th, 75th and 95th percentiles were 1.012 (95% CI 0.828 to 1.236), 0.987 (95% CI 0.901 to 1.080), 1.034 (95% CI 0.936 to 1.143) and 1.087 (95% CI 0.836 to 1.414), respectively. A delayed effect of high relative humidity (95th percentile) on the admission was evident: the estimated ARR was <1 from the concurrent day up to lag 4 days and was >1 afterwards.

The adjusted association between vapour pressure and the risk of acute bronchiolitis-related hospitalisation looked like a combination of the association of ambient temperature and that of relative humidity (figure 2D). Although the association appeared to be flattened U-shape, the risks were relatively higher at the higher end. Using median (24.7 hPa) as the reference value, the overall cumulative ARRs at the 5th, 25th, 75th and 95th percentiles were 1.056 (95% CI 0.851 to 1.311), 1.019 (95% CI 0.884 to 1.173), 1.070 (95% CI 0.903 to 1.267) and 1.125 (95% CI 0.864 to 1.466), respectively. While at the 5th percentile, the risk was relatively lower from the concurrent day to lag 3 days and was relatively higher up to lag 17 days. At moderately high (75th percentile) and very high (95th

Table 1 Characteristics of the 29 688 patient episodes

Variable	N (%)
Admission	29 688
Emergency	
Admission age, months	
Mean (SD)	10.6 (6.6)
0–6 moths	10 247 (34.5%)
7–12 moths	9224 (31.1%)
13–18 moths	6116 (20.6%)
19–24 moths	4101 (13.8%)
Gestation age	
Preterm (<37 weeks)	1145 (3.9%)
Full term (≥37 weeks)	28 543 (96.1%)
Gender	
Male	20 147 (67.9%)
Female	9541 (32.1%)
Race	
Asian	26 418 (89.0%)
Non-Asian	452 (1.5%)
Unknown	2818 (9.5%)
Principal diagnosis	
Acute bronchiolitis	27 009 (91.0%)
Pneumonia	837 (2.8%)
Acute respiratory disease	392 (1.3%)
Gastroenteritis	314 (1.1%)
Croup	281 (0.9%)
Influenza	199 (0.7%)
Febrile convulsions	130 (0.4%)
Others for example, infection disease	526 (1.8%)
Length of hospitalisation (days)	
Mean (SD)	3.7 (12.6)
1	4815 (16.2%)
2	8312 (28.0%)
3	6180 (20.8%)
4	3760 (12.7%)
5	2301 (7.8%)
6	1532 (5.2%)
7	942 (3.2%)
>7	1846 (6.2%)
Unplanned readmission*	6383 (21.5%)
Death episode	10/23 305 (0.04%)
Viral agents	
Respiratory syncytial virus	9695/22 011 (44.0%)
Parainfluenzae	636/9607 (6.6%)
Metapneumovirus	424/6098 (7.0%)
Adenovirus	403/21 276 (1.9%)
Influenza A	71/6937 (1.0%)
Influenza B	18/6901 (0.3%)

*Unplanned readmission is defined as any unscheduled emergency admissions due to acute bronchiolitis.

percentile) vapour pressures, the association was more complicated. The estimated ARR was >1 from lag 1 to 5 or 6 days as well as lag 15 days onwards, and was statistically significant since lag 18 days.

Total rainfall did not show a statistically significant relationship with the risk of hospitalisation adjusted for other variables in the model (figure 3). Nevertheless, there was apparently a harvesting effect at extreme rainfall (>38.8 mm), at which the risk was relatively higher during the first few lag days. We have tested the robustness of different cut-off values for categorising total rainfall and our results were not sensitive to the variation (online supplemental appendix section B).

The overall cumulative effects and percentile-specific (25th, 50th, 75th and 95th percentiles) effects of the air pollutants on acute bronchiolitis-related hospitalisation among children≤2 years old are shown in figure 4A–D. High concentrations of NO_2 were associated with elevated risks of acute bronchiolitis admission. In particular, the overall cumulative risk of bronchiolitis hospitalisation increased significantly when NO_2 was between 66.2 and 119.6 µg/m^3. The overall cumulative ARRs at the 25th, 50th, 75th and 95th percentiles were 1.013 (95% CI 0.849 to 1.208), 1.038 (95% CI 0.831 to 1.297), 1.237 (95% CI 0.961 to 1.592) and 1.643 (95% CI 1.155 to 2.338), respectively. At high concentration of NO_2, the estimated risk was statistically significantly higher after a lag of 2 weeks.

At very high concentrations of PM_{10}, the estimated overall cumulative adjusted risks tended to be higher than that at their corresponding 5th percentile despite statistical insignificance. For PM_{10}, the overall cumulative ARRs at the 25th, 50th, 75th and 95th percentiles were 1.084 (95% CI 0.916 to 1.282), 0.962 (95% CI 0.730 to 1.267), 0.793 (95% CI 0.572 to 1.099) and 0.756 (95% CI 0.522 to 1.094), respectively, and its effect appears to be immediate but not long lasting: the risk on the concurrent day was significantly higher at all percentile levels than if the exposure level had been the fifth percentile. The ARRs on the concurrent day at the four percentiles were 1.046 (95% CI 1.009 to 1.083), 1.056 (95% CI 1.005 to 1.110), 1.063 (95% CI 1.001 to 1.128) and 1.072 (95% CI 1.000 to 1.150), respectively.

For O_3, the overall cumulative ARRs at the 25th, 50th, 75th and 95th percentiles were 0.838 (95% CI 0.703 to 1.001), 0.934 (95% CI 0.751 to 1.162), 0.965 (95% CI 0.758 to 1.230) and 0.962 (95% CI 0.711 to 1.301), respectively, except for the 25th percentile the risk tended to be higher during lag 1–7 days and was lower afterwards.

For SO_2, the estimated ARR was above 1 when log(SO_2) was between 1.65 and 3.35, which was equivalent to the interval 5.21–28.5 µg/m^3 in the original scale. The overall cumulative ARRs at the 25th, 50th, 75th and 95th percentiles were 1.083 (95% CI 0.916 to 1.279), 1.179 (95% CI 0.952 to 1.460), 1.234 (95% CI 0.955 to 1.596) and 1.065 (95% CI 0.740 to 1.534), respectively. The patterns of ARR by lag at the four selected percentiles were similar. The estimated ARR was greater than 1 across lag 1–15 days.

Concerning model diagnostics, the adjusted R^2 of the primary model was 47.4%, and that of the two secondary models with apparent temperature and vapour pressure were 48.0% and 47.2%, respectively. The absolute values of PACFs of the residuals for the first 30 lags were all <0.1. In the sensitivity analyses, reducing the annual number of df for calendar time from 7 to 6 had the largest effect on the results (online supplemental appendix section C and D).

Table 2 Summary statistics of daily acute bronchiolitis hospital admissions, meteorological conditions and air pollutant concentrations in Hong Kong during 2008 to 2017

	Minimum	5th percentile	25th percentile	Median	75th percentile	95th percentile	Maximum
Daily numbers of admissions due to acute bronchiolitis	0.0	3.0	5.0	8.0	10.0	15.0	27.0
Temperature (°C)	4.9	14.1	19.2	24.8	28.2	30.1	32.4
Apparent temperature (°C)	−7.3	8.9	16	23.6	29.2	32.4	35.1
Relative humidity (%)	29.0	59.0	74.0	79.0	86.0	94.0	99.0
Total rainfall (mm)	0.0	0.0	0.0	0.0	1.9	38.8	307.1
Vapour pressure (hPa)	4.4	10.6	17.3	24.7	31.3	33.5	35.5
NO_2 (μg/m^2)	12.6	29.0	39.6	49.4	62.5	86.5	163.6
O_3 (μg/m^2)	4.7	12.6	20.8	35.0	55.0	85.2	149.1
SO_2 (μg/m^2)	3.1	5.2	7.3	10.2	14.9	26.3	73.3
PM_{10} (μg/m^2)	7.6	15.0	23.9	37.6	57.4	87.7	572.9

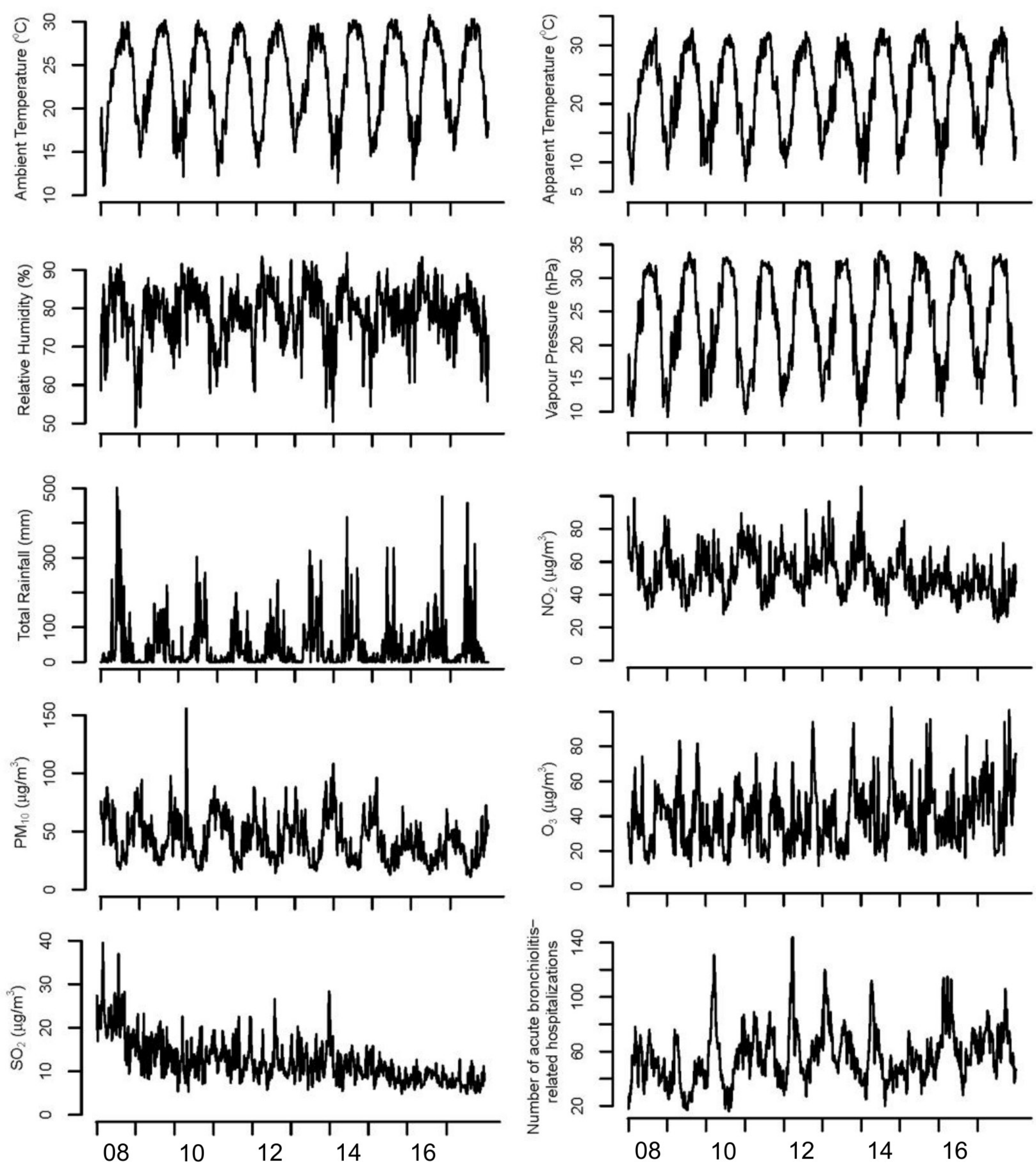

Figure 1 Seasonal variation in the weekly numbers of acute bronchiolitis-related admissions, meteorological parameters (monthly average ambient temperature, apparent temperature, relative humidity, vapour pressure and total rainfall), and air pollution level (monthly average nitrogen dioxide (NO_2), ozone (O_3), sulphur dioxide (SO_2), and PM_{10}) in Hong Kong during 2008 to 2017.

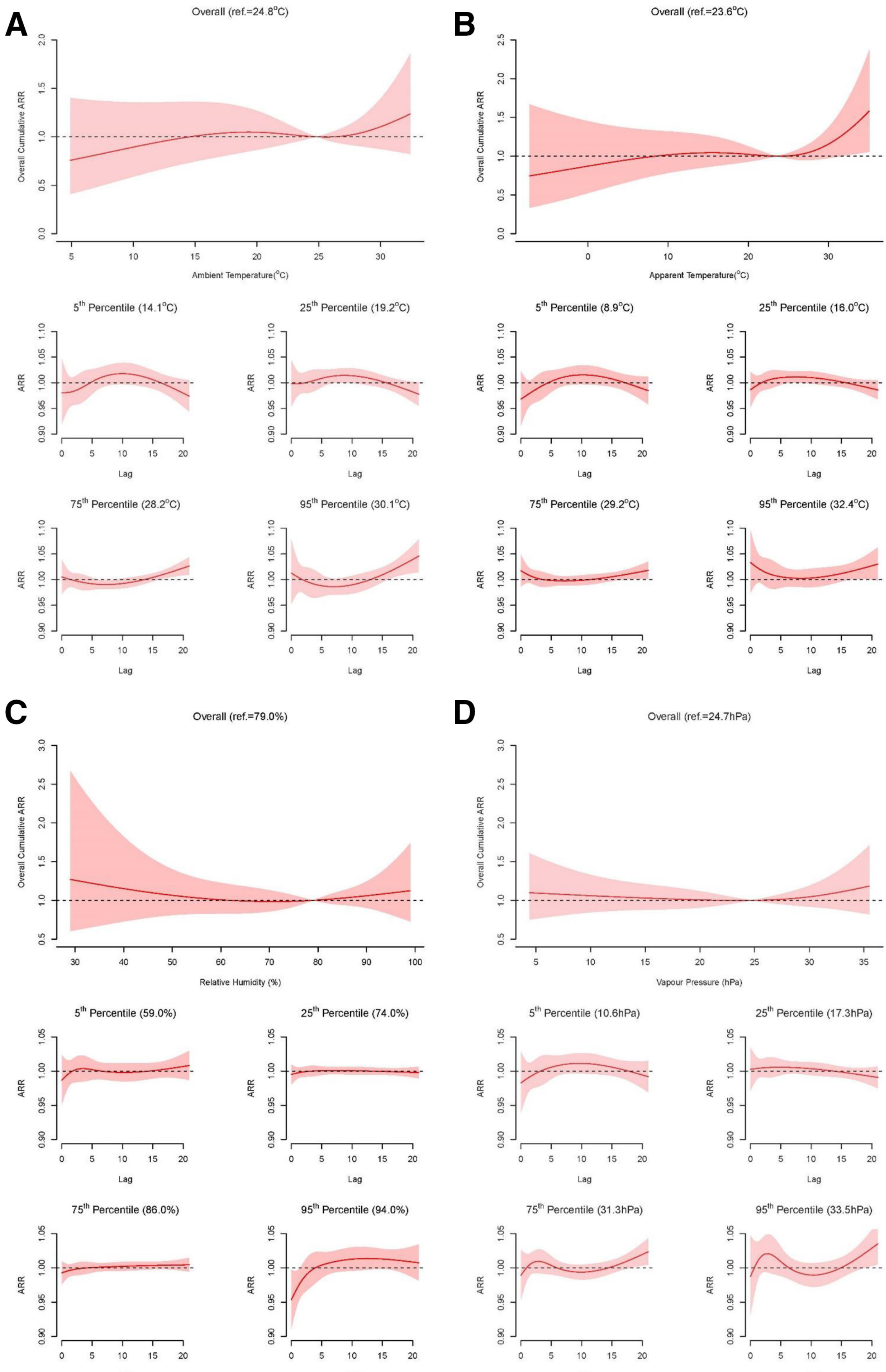

Figure 2 Overall cumulative adjusted relative risk along lags and adjusted relative risk by lag at selected percentiles against different meteorological variables. The reference values for (A) ambient temperature, (B) apparent temperature, (C) relative humidity and (D) vapour pressure for comparison were their corresponding median.

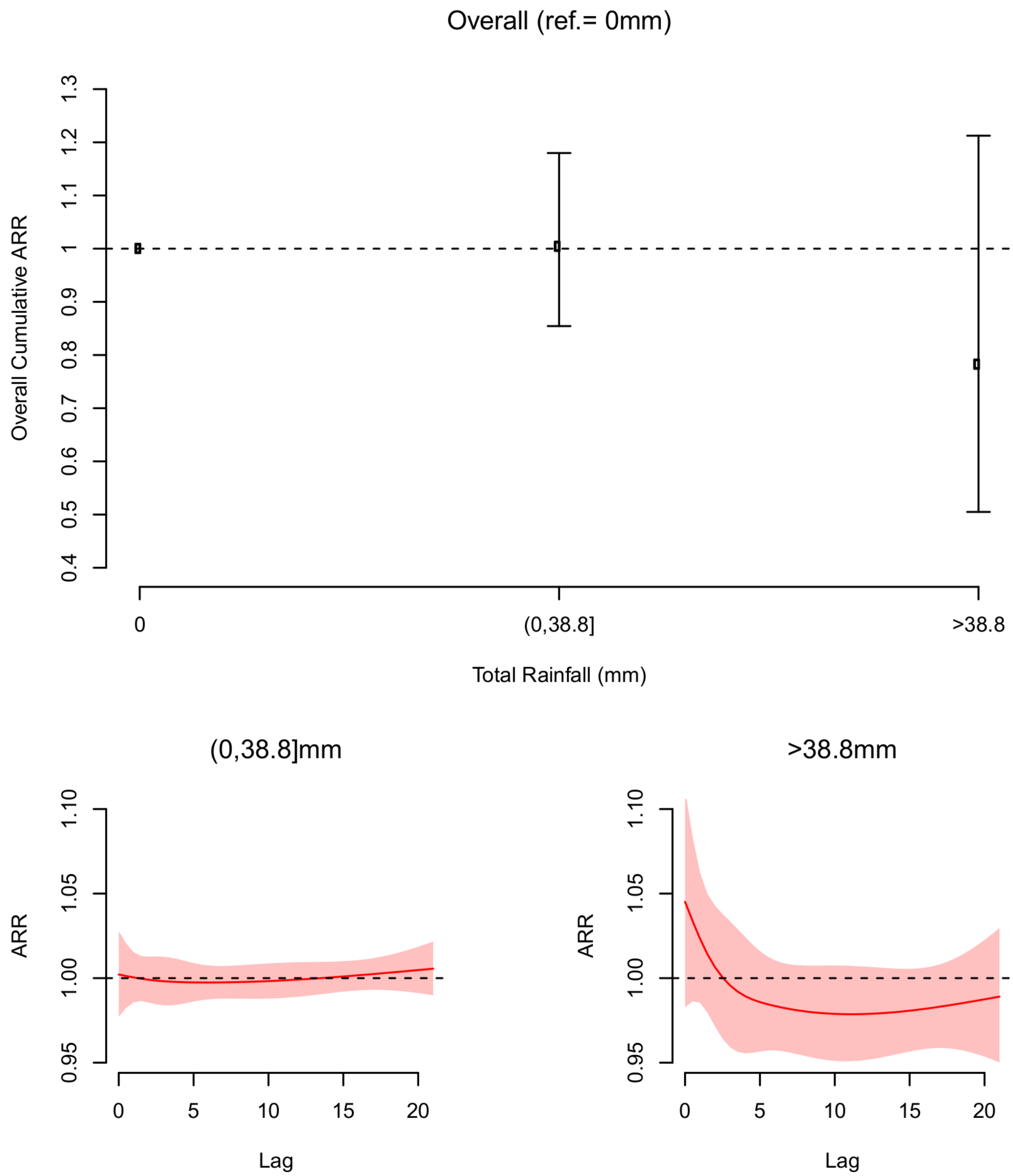

Figure 3 Adjusted cumulative relative risk along lags and adjusted relative risk by lag at selected percentiles against total rainfall. The reference value for a comparison was set to zero.

DISCUSSION

To our knowledge, few studies have investigated the short-term effects of meteorological variables and outdoor air pollution on acute bronchiolitis admissions in subtropical settings. In this study, a total of 29 688 emergency paediatric acute bronchiolitis admissions from all Hong Kong public hospitals over a 10-year period were analysed and studied whether they were associated with meteorological variables and outdoor air pollutants. Our results showed that increased acute bronchiolitis-related hospitalisation was associated with high temperature (ie, ambient temperature and apparent temperature), and was marginally associated with absolute humidity. Although the result is generally in line with the study from Mäkinen *et al*[28], which showed an increasing trend in the risk of LTRIs when temperature and absolute humidity increased, we acknowledge that an effect of high temperature on bronchiolitis has not been well established in the literature. An investigation conducted in Malta suggested that majority of bronchiolitis-related hospital admissions occurred in winter in subtropical region,[29] while another study conducted in China indicated that ambient temperature was negatively correlated with bronchiolitis-related hospitalisations among children.[30] Yet, by now, there has not been much consensus within the field on 'risky' temperature range for acute bronchiolitis. This was similar with another study on pneumonia in children aged <5 years old where the temperature effect was inconsistent.[31] Apart from that, a large proportion of admissions for LRTI (many of which were attributed to RSV) was shown to be independently associated with absolute humidity in children in northern Spain.[32] Nevertheless, only limited literatures have documented the association between absolute humidity and acute bronchiolitis-related or RSV-related admissions, especially when compared with other respiratory infections such as influenza.[21 22]

Among the air pollutants, high level of NO_2 was associated with increased risk of acute bronchiolitis admission and the overall effect became statistically significant over the range 66.2–119.6 μg/m^3 when compared with value at the 5th percentile. NO_2 is a common outdoor air pollutant primarily produced

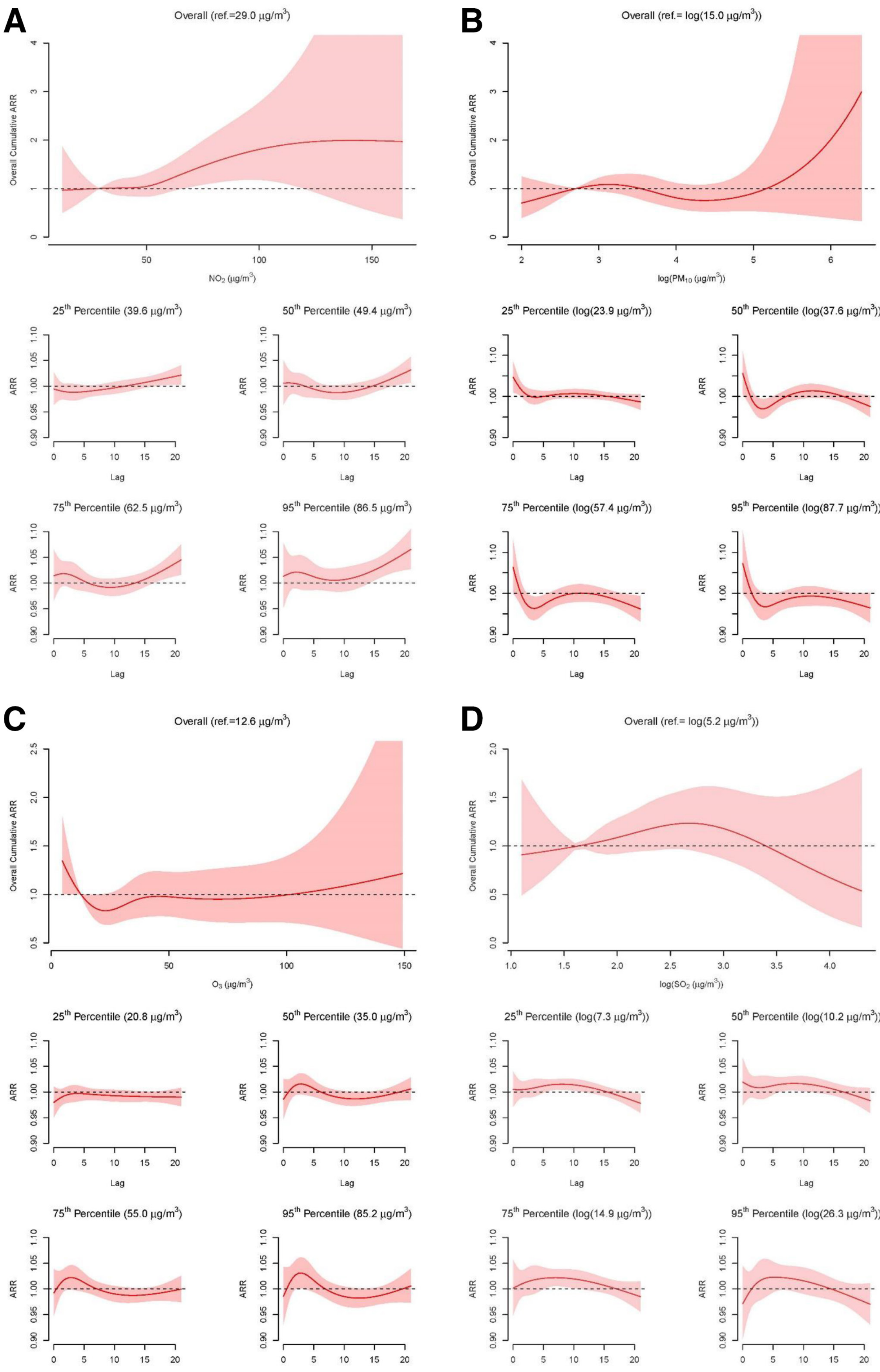

Figure 4 Overall cumulative adjusted relative risk along lags and adjusted relative risk by lag at selected percentiles against different pollutants, including (A) NO_2, (B) PM_{10}, (C) O_3, and (D) SO_2. The reference values for comparison were their corresponding 5th percentile.

by motor vehicles and power plants as a byproduct of high-temperature combustion. At ambient pressure and temperature, NO_2 exists in its gaseous state and is relatively insoluble in water. These properties allow deeper penetration of NO_2 into the respiratory tree (ie, the lower respiratory tracts) where it would react with water from mucosal lining of the bronchioles and form corrosive chemicals including nitric and nitrous acids.[33] The nitrous vapour could cause microlesions in the respiratory tract and increase susceptibility to infections, including those caused by RSV.[33] According to a recent large birth cohort study conducted in Indonesia among children aged 0–3 years, an IQR increase in NO_2 exposure would increase the risk for acute respiratory tract infection by an estimated 18%.[34] With reference to the WHO guideline for air quality, the annual mean level of NO_2 should not exceed 40 $\mu g/m^3$.[16] During our study period, the median (IQR) daily mean NO_2 level was 49.4 $\mu g/m^3$ (39.6 to 62.5 $\mu g/m^3$), and in 1770 days (48.5%) it exceeded the WHO's annual safe level.[17] Considering the aforementioned, it is thus very important for Hong Kong to adopt sustainable clean air policies as soon as possible to protect young children's health. Regarding the sustained effect of NO_2 observed in our study, we tend to interpret the findings from toxicological perspectives. Seaton and Dennekamp[35] proposed the epidemiological association between illness and NO_2 might be confounded by particles number. Given the toxic effects of ultrafine particles has been evident at low concentrations in animals, we speculate the delayed effect of NO_2 might actually be the cumulative effect of successive exposure to ultrafine particles.[35] Follow-up studies should be conducted to test and verify this speculation.

A number of studies have been showing that exposure to PM would increase the risk of respiratory infections and other illnesses.[13 36 37] In an investigation conducted in the USA, Karr *et al*[13] found both chronic and subchronic exposures to $PM_{2.5}$ were associated with elevated risk of bronchiolitis hospitalisation in infants (ie, around a 9% increase in risk for every 10 $\mu g/m^3$ increase in $PM_{2.5}$). PM_{10} was found to be related to bronchiolitis consultation and hospitalisation in both Malaysia and France.[36 37] We found a significant positive effect of PM_{10} on acute bronchiolitis admissions only within a short time window, suggesting that most of the effects of PM_{10} were acute. This might explain why we did not find cumulative effects of PM_{10} over 21 days. One possible reason might be the relatively low PM_{10} concentration in Hong Kong (ie, 43.2 $\mu g/m^3$) as compared with the WHO guideline level of 50 $\mu g/m^3$ for 24 hours mean. At low concentration, the adverse effect of PM_{10} on pulmonary health might not be clinically severe enough to cause hospitalisation, which might also explain why we could not find a cumulative effect of PM_{10} on bronchiolitis hospitalisations. Given that $PM_{2.5}$ has the ability to go even deeper into the lungs than PM_{10} does, and furthermore to enter the blood system, the damaging effect of $PM_{2.5}$ on respiratory health might be stronger than that of PM_{10} at low concentrations. It is thus speculated that replacing PM_{10} with $PM_{2.5}$ might be a better way to explore the overall cumulative risk of exposure to particular matters on acute bronchiolitis hospitalisation. Further research is needed to verify this hypothesis.

Similarly, no positive association was observed between O_3 and acute bronchiolitis admission. In a recent study, a 20-ppb increase in O_3 was associated with a significant increase in emergency department visits for respiratory conditions (by 1.7%–5.1%).[38] Children exposed to high ozone levels had significantly decreased lung function, which may have reduced their defence against viral infections (eg, RSV) and increased their susceptibility to bronchiolitis.[39] Nevertheless, it was argued that O_3 could reduce the risk of respiratory infection that might be attributed to the virucidal activity of O_3 and its relationship with host defence.[40]

The present study has several potential limitations. First, acute bronchiolitis is a clinical diagnosis, and therefore subject to variation among public hospitals due to differences in the availability of virus testing, differences in the diagnostic criteria used by doctors to diagnose bronchiolitis, and differences in coding practices. It is thus possible that acute bronchiolitis might be coded in the medical record system as other respiratory conditions. Meanwhile, criteria adopted in determining the need for hospitalisation changes over time. That being so, we might have underestimated the frequency of acute bronchiolitis hospitalisation in our study. Nevertheless, since over 90% of admissions in our dataset were principally diagnosed with acute bronchiolitis, our results shall remain robust (table 1). Second, this study used surveillance data in public hospitals which does not include data from private hospitals. However, the public healthcare services accounted for over 90% inpatient services in Hong Kong. Third, exposure measurement error is a common concern in environmental epidemiology, especially when studying the short-term impacts of environmental variables, given that meteorological condition and air pollutant levels change across time and space. For example, a child might be exposed to more air pollutants if she/he has smoking parents and lives in a household with 24 hours air conditioning that located close to busy roads. The error in exposure measurement might lead to inaccurate estimation of relative risks which, unfortunately, can hardly be avoided. Fourth, the increased incidence rate observed in this study might be affected by residual confounding. Unmeasured factors, such as parental smoking status, household crowding, indoor metrological condition (eg, temperature, relative humidity and air movement) and indoor air pollution (eg, NO_2, PM_{10}, $PM_{2.5}$, O_3, formaldehyde, volatile organic compounds, radon and airborne bacteria level) could be potential confounders and/or effect modifiers that might distort the results of the study. Fifth, given that different pathogens prefer different environment for survival and transmission,[21] the findings of our study may not be consistent with results from pathogen-specific (eg, RSV, influenza, etc) analyses of acute bronchiolitis. We acknowledge the lack of information about pathogen causing the admissions is one of the main limitations in this study. Also, as RSV infection is a major determinant for acute bronchiolitis hospitalisation in children, we took the incubation period into account in addition to the symptomatic period and assumed a maximum lag of 21 days for the delayed effects in our study. Our results may thus be less compatible with other similar investigations that generally studied the short-term effects of pollutants using a shorter maximum lag (eg, 3–7 days). Last but not least, interaction effects between the meteorological factors and pollutants were not considered in this study. Our preliminary analysis has shown that although the interaction effects were not strong in general, when meteorological factors were at medium level and pollutants were at medium or high level, their joint effects on the outcome were usually statistically significant (detailed results not given), hence worth further investigation in future studies.

In conclusion, our findings showed that high temperature (ambient temperature and apparent temperature) and exposure to NO_2 and PM_{10} were associated with acute bronchiolitis-related hospitalisation among children at different lag times. The significant relationship with pollutants suggests the need to adopt sustainable clean air policies in Hong Kong, especially to target pollutants produced by motor vehicles, to protect young children's health. Since acute bronchiolitis continues to be a public health burden on the already-stressed healthcare system, policy-makers are urged to develop more cost-effective approaches to manage acute bronchiolitis in children. We believe that our findings could rationalise an evidence-based allocation of resources and formulation of environmental policies to minimise the burden of disease associated with acute bronchiolitis in young children.

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Contributors SYL and KCC conceived the study. SYL, KCC and SYFL performed the analysis. KLK and SYL contributed to the acquired data of the study. SYL, PKSC, KCC and KM contributed to the results interpretation. SYL, KCC, SYFL, PKSC and KM drafted the paper. All authors have read and approved the final paper.

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Data availability statement Data may be obtained from a third party and are not publicly available. The sharing of data is restricted by the Hong Kong Hospital Authority.

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REFERENCES

1 Kyu HH, Pinho C, *et al*, Global Burden of Disease Pediatrics Collaboration. Global and national burden of diseases and injuries among children and adolescents between 1990 and 2013: findings from the global burden of disease 2013 study. *JAMA Pediatr* 2016;170:267–87.
2 Shi T, McAllister DA, O'Brien KL, *et al*. Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in young children in 2015: a systematic review and modelling study. *Lancet* 2017;390:946–58.
3 American Academy of Pediatrics Subcommittee on Diagnosis and Management of Bronchiolitis. Diagnosis and management of bronchiolitis. *Pediatrics* 2006;118:1774–93.
4 Pfuntner A, Wier LM, Stocks C. Most frequent conditions in US hospitals, 2011. HCUP Statistical Brief #162. Available: https://hcup-us.ahrq.gov/reports/statbriefs/sb162.pdf [Accessed 23 Oct 2018].
5 Piedimonte G, Perez MK. Respiratory syncytial virus infection and bronchiolitis. *Pediatr Rev* 2014;35:519–30.
6 Obando-Pacheco P, Justicia-Grande AJ, Rivero-Calle I, *et al*. Respiratory syncytial virus seasonality: a global overview. *J Infect Dis* 2018;217:1356–64.
7 Broberg EK, Waris M, Johansen K, *et al*. Seasonality and geographical spread of respiratory syncytial virus epidemics in 15 European countries, 2010 to 2016. *Euro Surveill* 2018;23.
8 DKK N, Kwok KL. Acute bronchiolitis: a Hong Kong perspective. *HK Pract* 2002;24:16–19.
9 Sung RY, Chan RC, Tam JS, *et al*. Epidemiology and aetiology of acute bronchiolitis in Hong Kong infants. *Epidemiol Infect* 1992;108:147–54.
10 Haynes AK, Manangan AP, Iwane MK, *et al*. Respiratory syncytial virus circulation in seven countries with global disease detection regional centers. *J Infect Dis* 2013;208 Suppl 3:S246–54.
11 Yusuf S, Piedimonte G, Auais A, *et al*. The relationship of meteorological conditions to the epidemic activity of respiratory syncytial virus. *Epidemiol Infect* 2007;135:1077–90.
12 Wang VJ, Cavagnaro CS, Clark S, *et al*. Altitude and environmental climate effects on bronchiolitis severity among children presenting to the emergency department. *J Environ Health* 2012;75:8–15.
13 Karr C, Lumley T, Schreuder A, *et al*. Effects of subchronic and chronic exposure to ambient air pollutants on infant bronchiolitis. *Am J Epidemiol* 2007;165:553–60.
14 Rice MB, Rifas-Shiman SL, Oken E, *et al*. Exposure to traffic and early life respiratory infection: a cohort study. *Pediatr Pulmonol* 2015;50:252–9.
15 Census and Statistics Department,, HKSAR. Population By-census – summary results, 2016. Available: https://www.bycensus2016.gov.hk/data/16bc-summary-results.pdf [Accessed 29 Oct 2018].
16 World Health Organization. WHO air quality guidelines for particulate matter, ozone, nitrogen dioxide and sulfur dioxide: global update 2005: summary of risk assessment. Available: https://apps.who.int/iris/bitstream/handle/10665/69477/WHO_SDE_PHE_OEH_06.02_eng.pdf?sequence=1 [Accessed 29 Oct 2018].
17 Environmental Protection Department,, HKSAR. Air quality in Hong Kong 2017. Available: http://www.aqhi.gov.hk/api_history/english/report/files/AQR2017e_final.pdf [Accessed 29 Oct 2018].
18 Hsu C-H, Lin C-Y, Chi H, *et al*. Prolonged seasonality of respiratory syncytial virus infection among preterm infants in a subtropical climate. *PLoS One* 2014;9:e110166.
19 Wang H, Zheng Y, Deng J, *et al*. Prevalence of respiratory viruses among children hospitalized from respiratory infections in Shenzhen, China. *Virol J* 2016;13:39.
20 Census and Statistics Department, HKSAR. Thematic household survey report No. 63, 2018. Available: https://www.statistics.gov.hk/pub/B11302632017XXXXB0100.pdf [Accessed 29 Oct 2018].
21 Chong KC, Lee TC, Bialasiewicz S, *et al*. Association between Meteorological variations and activities of influenza A and B across different climate zones: a multi-region modelling analysis across the globe. *J Infect* 2020;80:84–98.
22 Chong KC, Liang J, Jia KM, *et al*. Latitudes mediate the association between influenza activity and Meteorological factors: a nationwide modelling analysis in 45 Japanese prefectures from 2000 to 2018. *Sci Total Environ* 2020;703:134727.
23 Tetens O. Über einige meteorologische Begriffe [In German]. *Z Geophys* 1930;6:297–309.
24 Steadman RG. A universal scale of apparent temperature. *J. Climate Appl. Meteor.* 1984;23:1674–87.
25 Gasparrini A, Armstrong B, Kenward MG. Distributed lag non-linear models. *Stat Med* 2010;29:2224–34.
26 Bush KF, O'Neill MS, Li S, *et al*. Associations between extreme precipitation and gastrointestinal-related hospital admissions in Chennai, India. *Environ Health Perspect* 2014;122:249–54.
27 Wong C-M, Vichit-Vadakan N, Kan H, *et al*. Public health and air pollution in Asia (PAPA): a multicity study of short-term effects of air pollution on mortality. *Environ Health Perspect* 2008;116:1195–202.
28 Mäkinen TM, Juvonen R, Jokelainen J, *et al*. Cold temperature and low humidity are associated with increased occurrence of respiratory tract infections. *Respir Med* 2009;103:456–62.
29 Casha FC, Farrugia Preca J, Pisani R. Higher number of hospital admissions for bronchiolitis with lower mean ambient temperature. *J Family Med Prim Care* 2016;5:7–12.
30 Chen Z-R, Ji W, Wang Y-Q, *et al*. Etiology of acute bronchiolitis and the relationship with Meteorological conditions in hospitalized infants in China. *J Formos Med Assoc* 2014;113:463–9.
31 Lam HCY, Chan EYY, Goggins WB. Short-Term association between Meteorological factors and childhood pneumonia hospitalization in Hong Kong: a time-series study. *Epidemiology* 2019;30 Suppl 1:S107–14.
32 Lapeña S, Robles MB, Castañón L, *et al*. Climatic factors and lower respiratory tract infection due to respiratory syncytial virus in hospitalised infants in northern Spain. *Eur J Epidemiol* 2005;20:271–6.
33 Darke CS, Warrack AJ. Bronchiolitis from nitrous fumes. *Thorax* 1958;13:327–33.
34 Suryadhi MAH, Abudureyimu K, Kashima S, *et al*. Nitrogen dioxide and acute respiratory tract infections in children in Indonesia. *Arch Environ Occup Health* 2020;75:274–80.
35 Seaton A, Dennekamp M. Hypothesis: ill health associated with low concentrations of nitrogen dioxide--an effect of ultrafine particles? *Thorax* 2003;58:1012–5.
36 Ségala C, Poizeau D, Mesbah M, *et al*. Winter air pollution and infant bronchiolitis in Paris. *Environ Res* 2008;106:96–100.
37 Rahman SA, Ismail SS, Sahani M, *et al*. A case crossover analysis of primary air pollutants association on acute respiratory infection (ArI) among children in urban region of Klang Valley, Malaysia. *Ann Trop Med PH* 2017;10:44.
38 Strosnider HM, Chang HH, Darrow LA, *et al*. Age-Specific associations of ozone and fine particulate matter with respiratory emergency department visits in the United States. *Am J Respir Crit Care Med* 2019;199:882–90.
39 Kim BJ, Seo JH, Jung YH, *et al*. Air pollution interacts with past episodes of bronchiolitis in the development of asthma. *Allergy* 2013;68:517–23.
40 Ali ST, Wu P, Cauchemez S, *et al*. Ambient ozone and influenza transmissibility in Hong Kong. *Eur Respir J* 2018;51:1800369.

Appendix

Short-term Association among Meteorological Variation, Outdoor Air Pollution and Acute Bronchiolitis in Children in a Subtropical Setting

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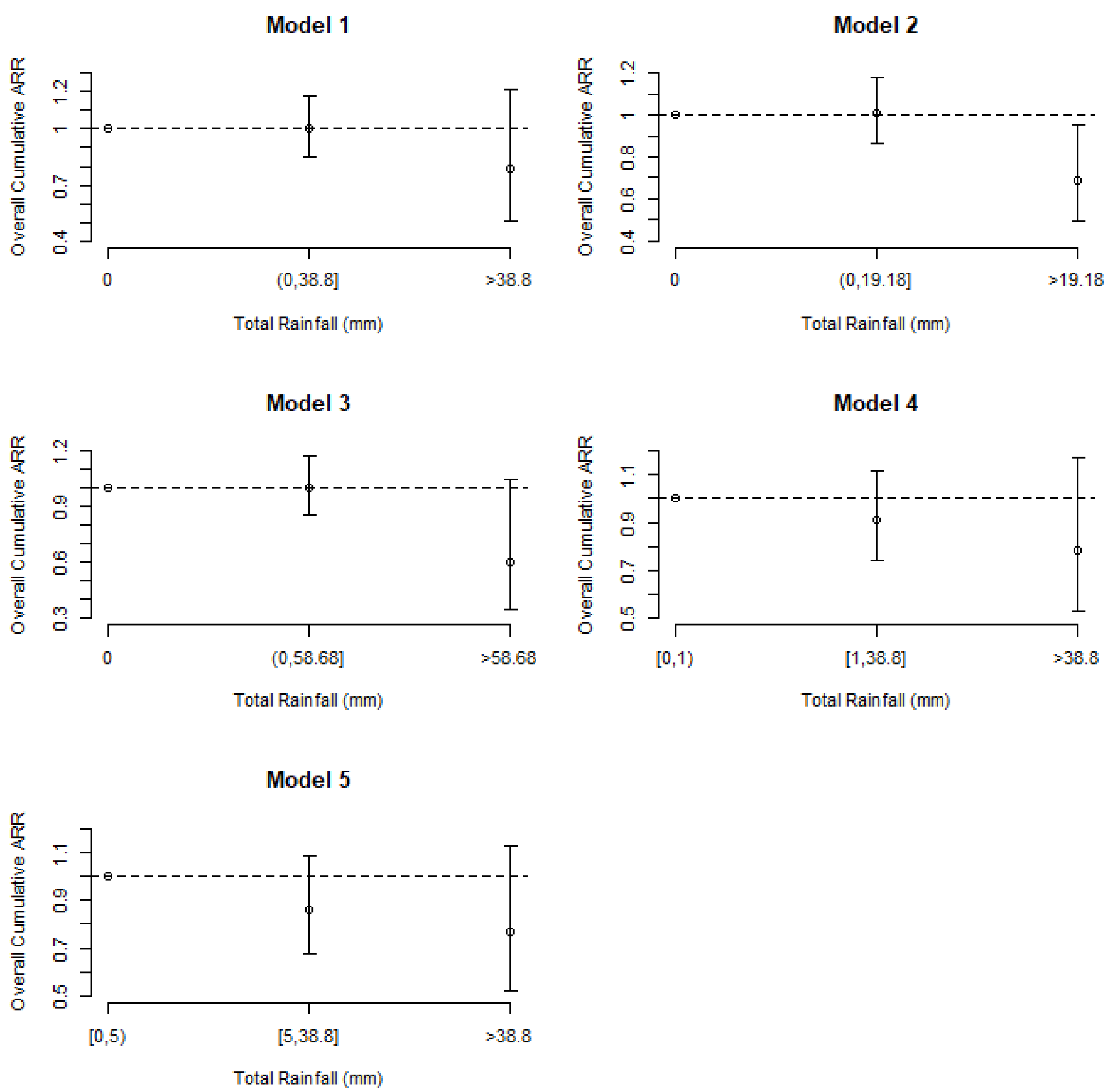
A. Pearson correlation coefficient between the meteorological factors and pollutants during the study period (2008 - 2017)

	Ambient Temperature	**Apparent Temperature**	**Relative Humidity**	**Vapour Pressure**	**Rainfall**	**NO_2**	**$\log(SO_2)$**	**O_3**	**$\log(PM_{10})$**
Ambient Temperature		0.973	0.227	0.942	0.121	-0.337	0.023	-0.093	-0.468
Apparent Temperature			0.281	0.939	0.105	-0.250	0.097	-0.199	-0.476
Relative Humidity				0.506	0.352	-0.329	-0.384	-0.439	-0.515
Vapour Pressure					0.239	-0.439	-0.095	-0.277	-0.619
Rainfall						-0.133	-0.150	-0.191	-0.309
NO_2							0.576	0.191	0.697
$\log(SO_2)$								-0.068	0.417
O_3									0.566
$\log(PM_{10})$									

B. Sensitivity Analysis: Cumulative adjusted relative risks (ARRs) of rainfall using different sets of cutoffs

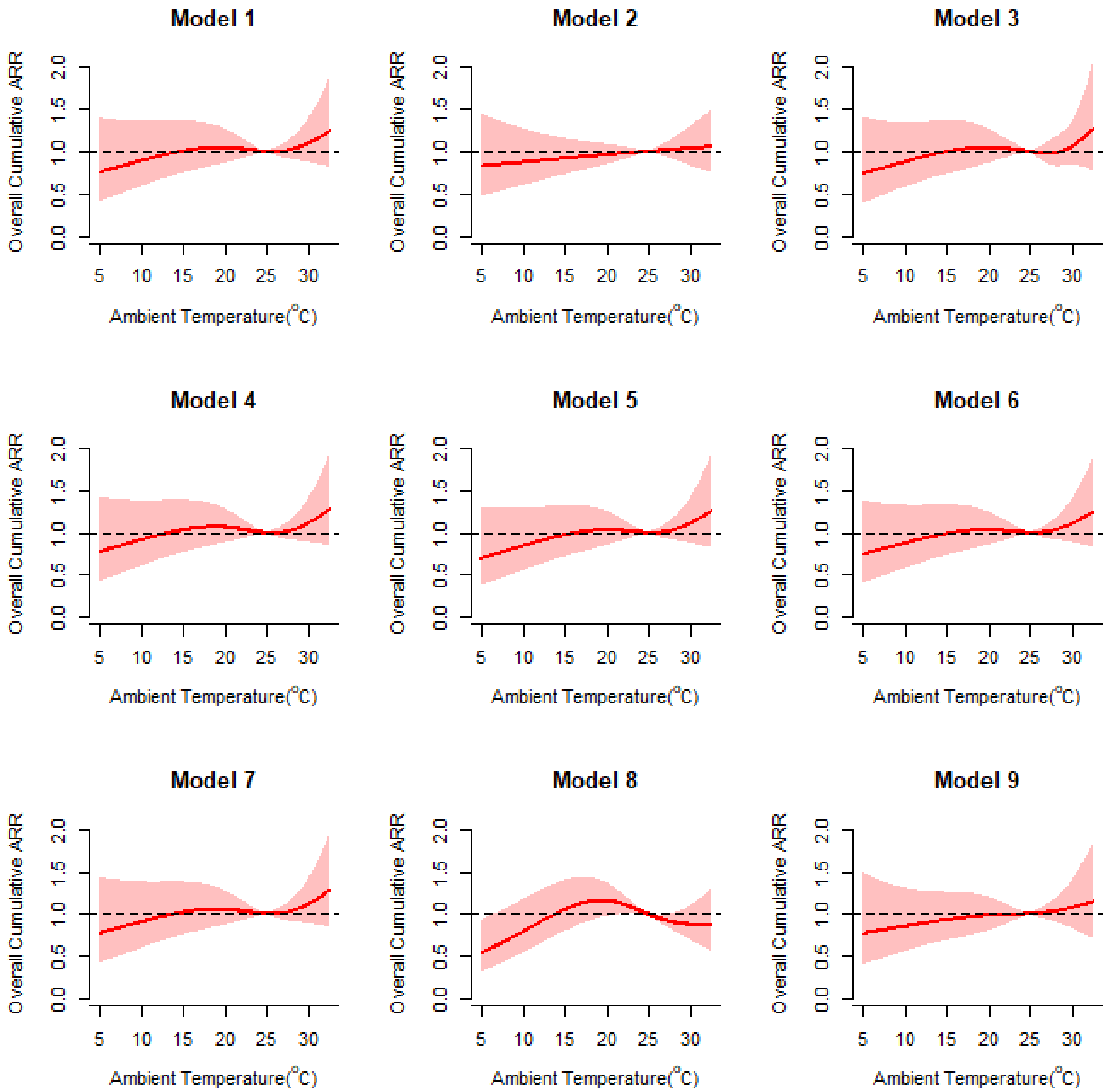
- **Model 1:** (i) Rainfall = 0; (ii) 0 < Rainfall ≤ 95th percentile; and (iii) Rainfall > 95th percentile
- **Model 2:** (i) Rainfall = 0; (ii) 0 < Rainfall ≤ 90th percentile; and (iii) Rainfall > 90th percentile
- **Model 3:** (i) Rainfall = 0; (ii) 0 < Rainfall ≤ 97.5th percentile; and (iii) Rainfall > 97.5th percentile
- **Model 4:** (i) 0 ≤ Rainfall ≤ 1; (ii) 1 < Rainfall ≤ 97.5th percentile; and (iii) Rainfall > 97.5th percentile
- **Model 5:** (i) 0 ≤ Rainfall ≤ 5; (ii) 5 < Rainfall ≤ 97.5th percentile; and (iii) Rainfall > 97.5th percentile



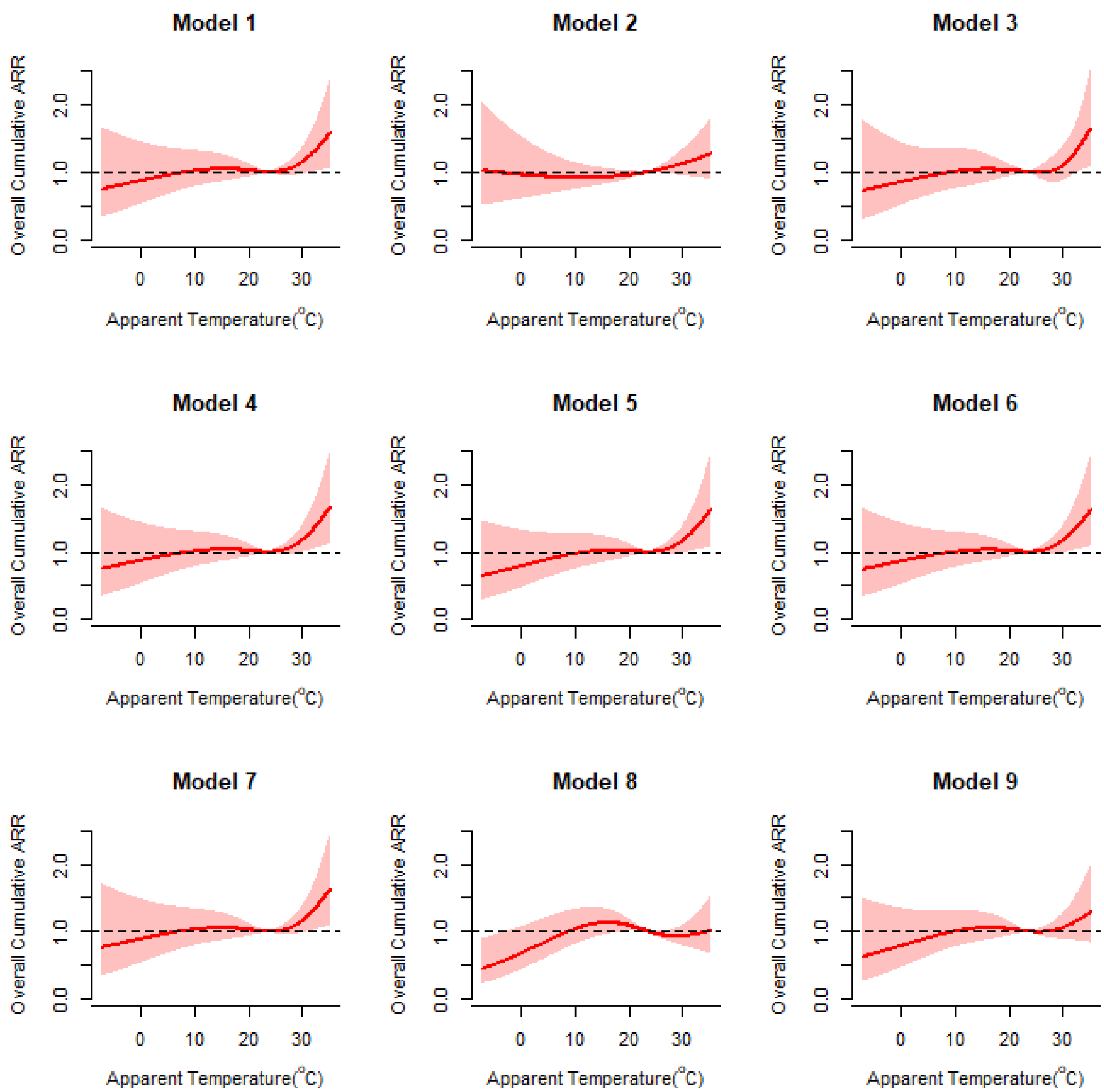
C. Sensitivity Analysis: Cumulative adjusted relative risks (ARRs) of meteorological parameters: (a) ambient temperature, (b) apparent temperature, (c) relative humidity, (d) vapour pressure, and (e) total rainfall at different parameter settings

- **Model 1:** df for the meteorological parameters = 3; df for the pollutants = 4; df for lag = 4, df for day of study per year = 7
- **Model 2:** df for the meteorological parameters = 2; df for the pollutants = 4; df for lag = 4, df for day of study per year = 7
- **Model 3:** df for the meteorological parameters = 5; df for the pollutants = 4; df for lag = 4, df for day of study per year = 7
- **Model 4:** df for the meteorological parameters = 3; df for the pollutants = 3; df for lag = 4, df for day of study per year = 7
- **Model 5:** df for the meteorological parameters = 3; df for the pollutants = 5; df for lag = 4, df for day of study per year = 7
- **Model 6:** df for the meteorological parameters = 3; df for the pollutants = 4; df for lag = 3, df for day of study per year = 7
- **Model 7:** df for the meteorological parameters = 3; df for the pollutants = 4; df for lag = 5, df for day of study per year = 7
- **Model 8:** df for the meteorological parameters = 3; df for the pollutants = 4; df for lag = 4, df for day of study per year = 6
- **Model 9:** df for the meteorological parameters = 3; df for the pollutants = 4; df for lag = 4, df for day of study per year = 8

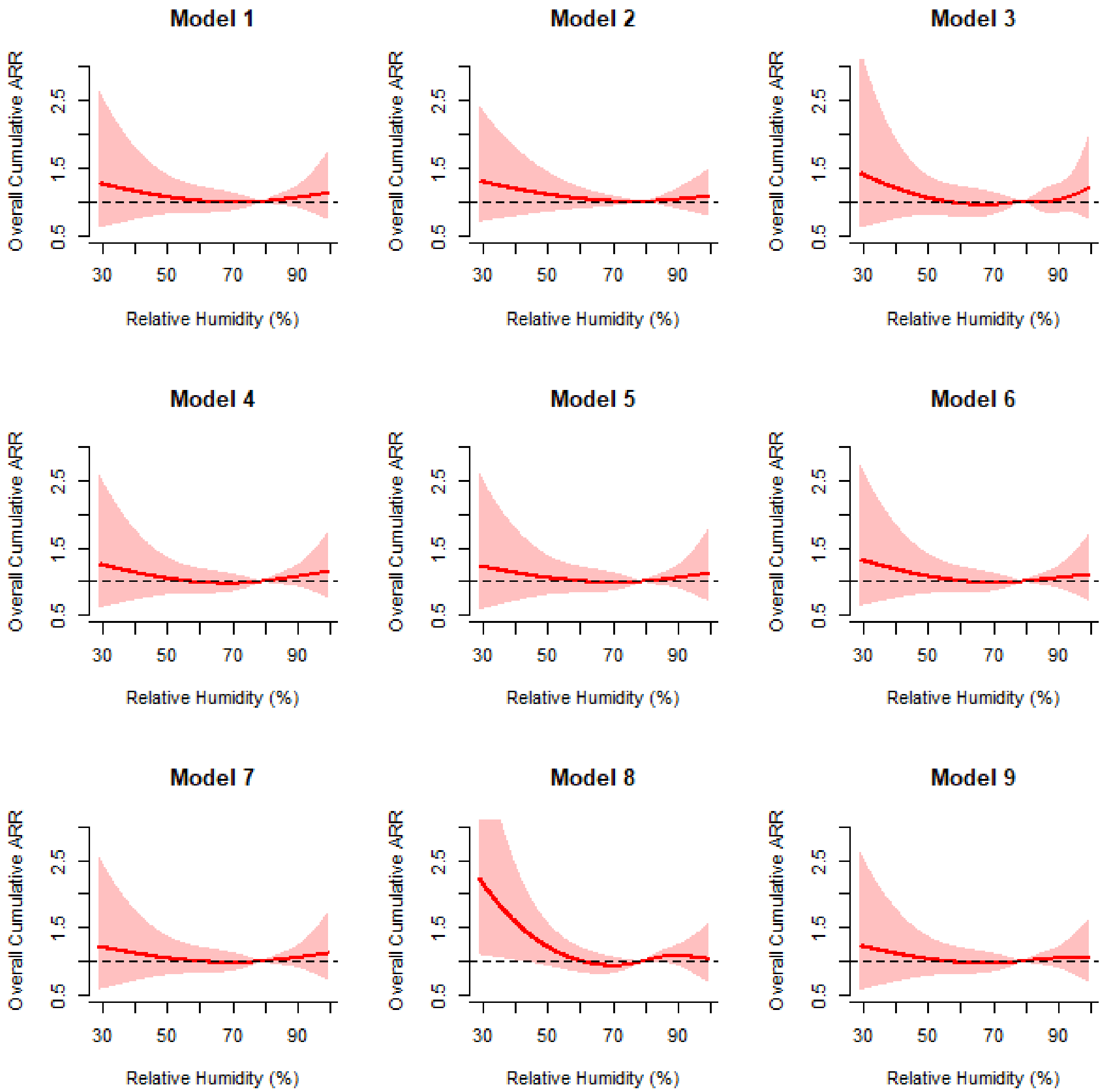
(a) Ambient Temperature (ref. = 24.8ºC)



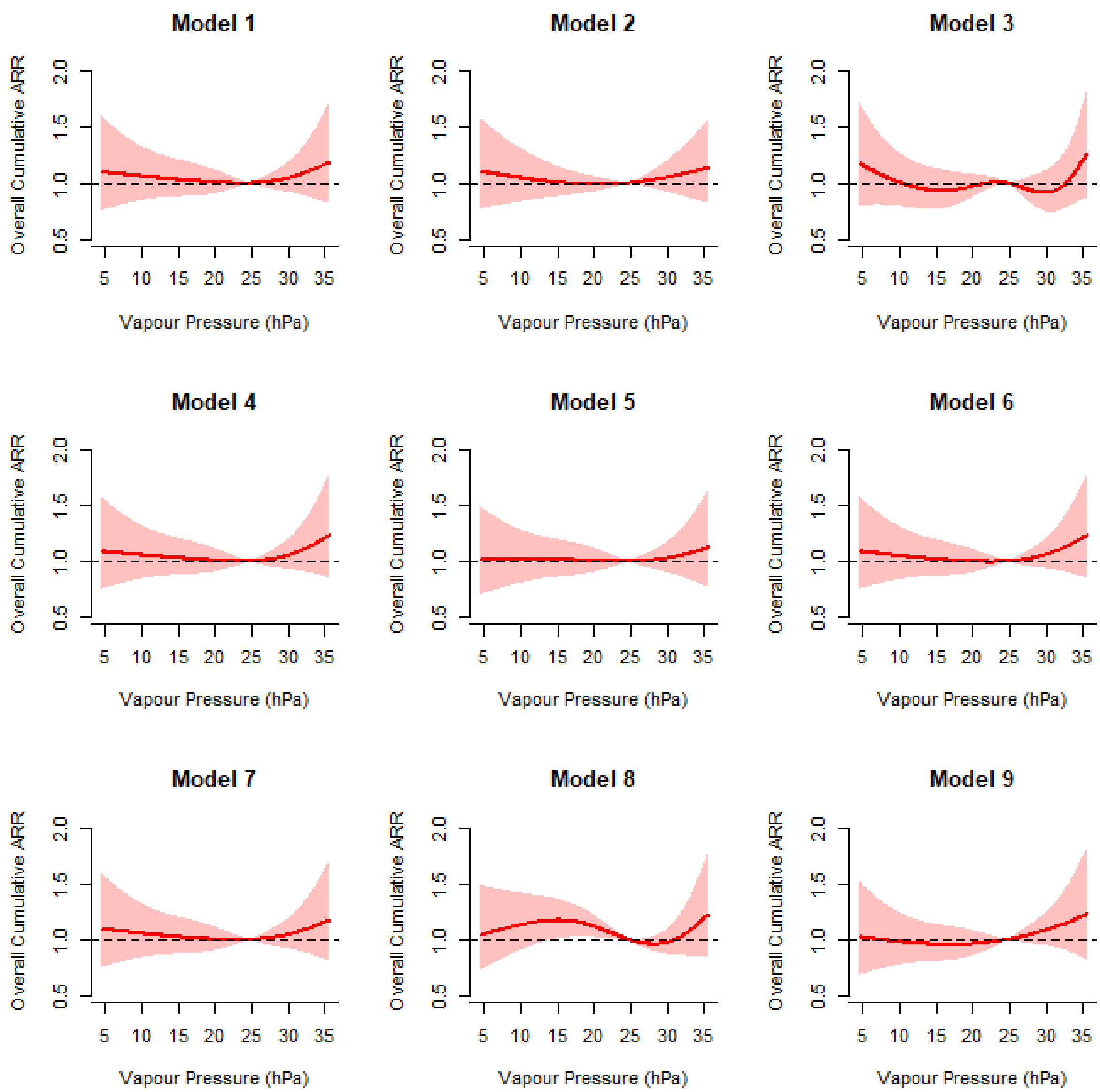
(b) Apparent Temperature (ref. = 23.6°C)



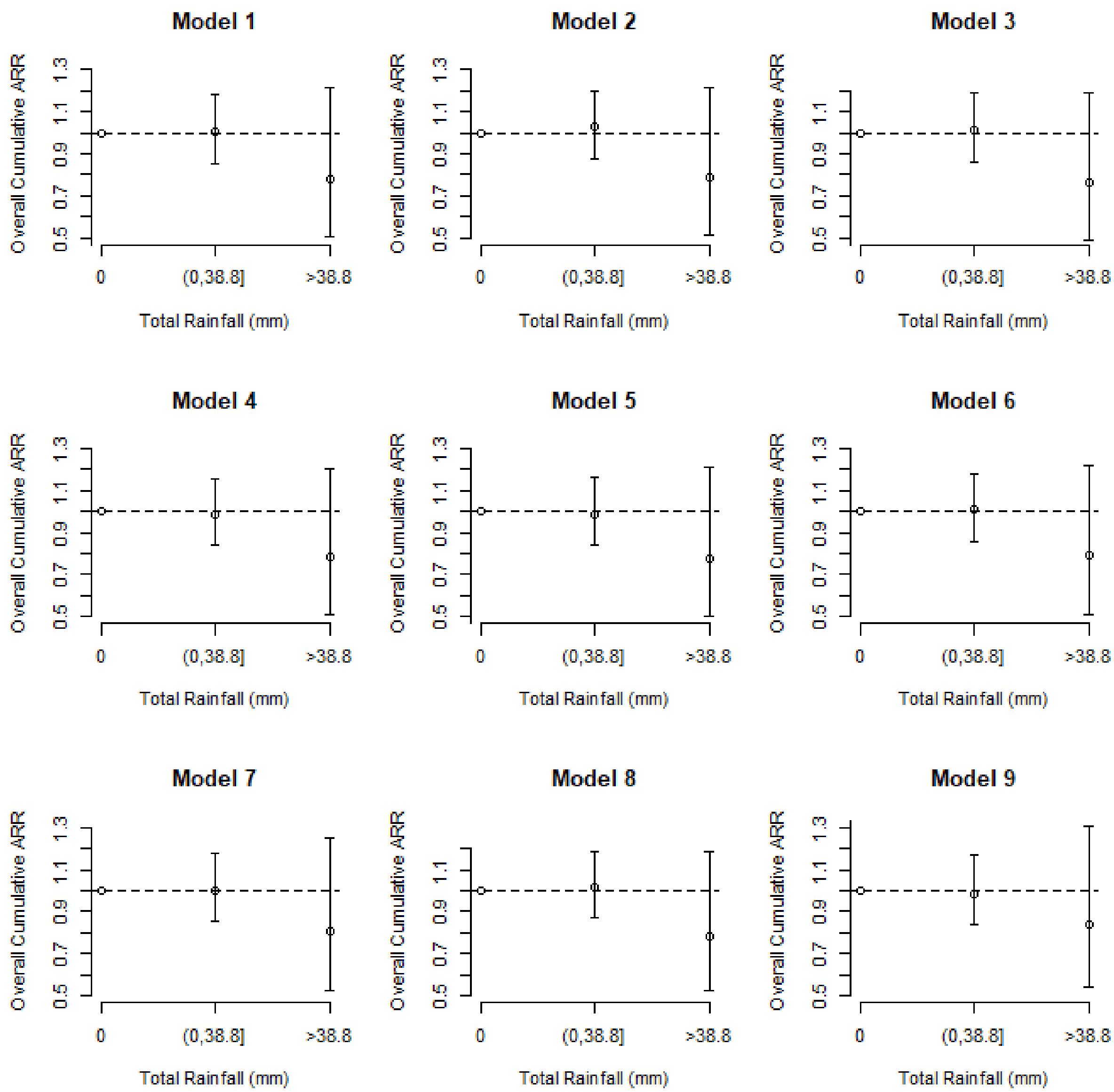
(c) Relative Humidity (ref. = 79.0%)



(d) Vapour Pressure (ref. = 24.7 hPa)



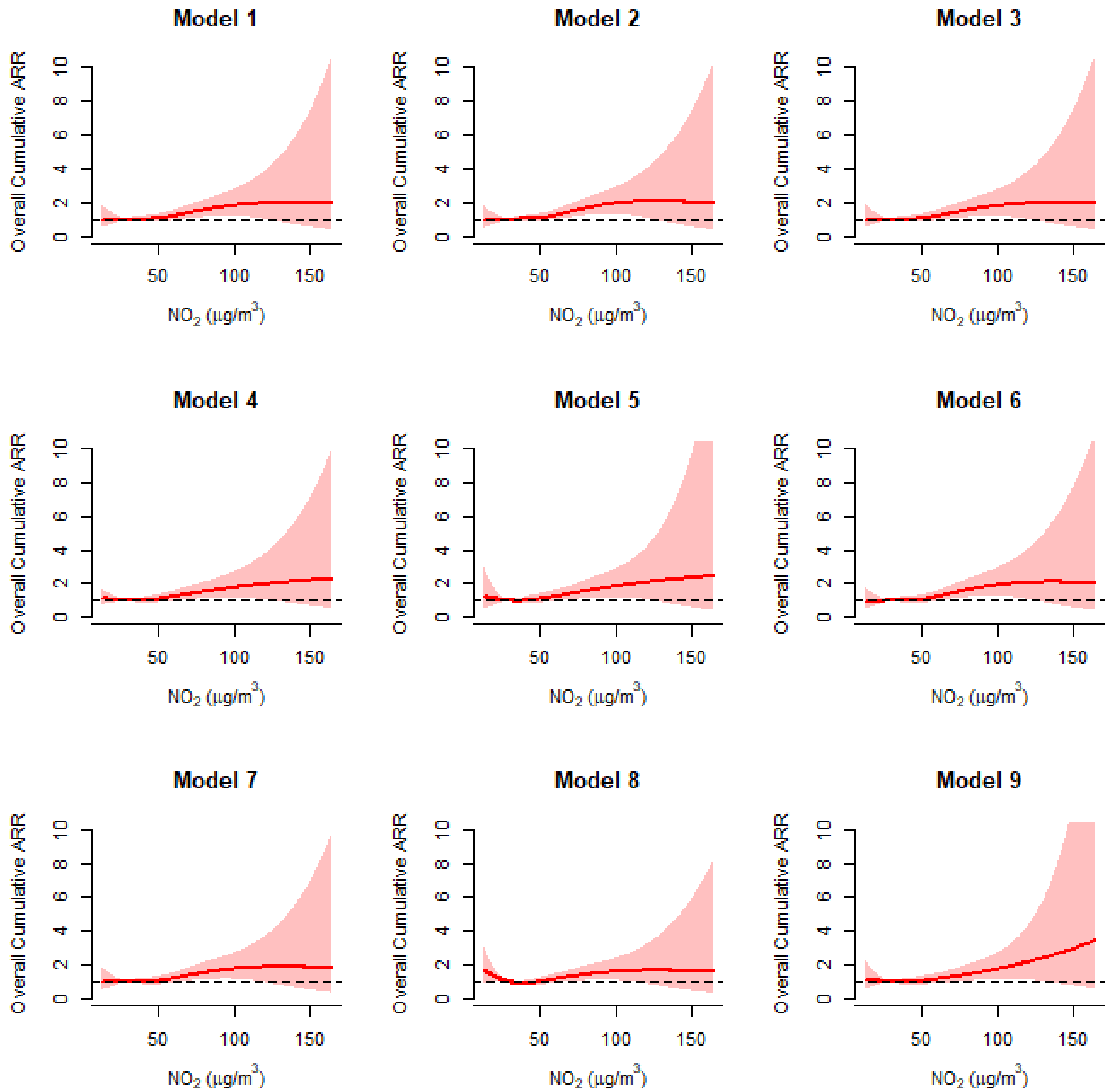
(e) Rainfall (ref. = 0)



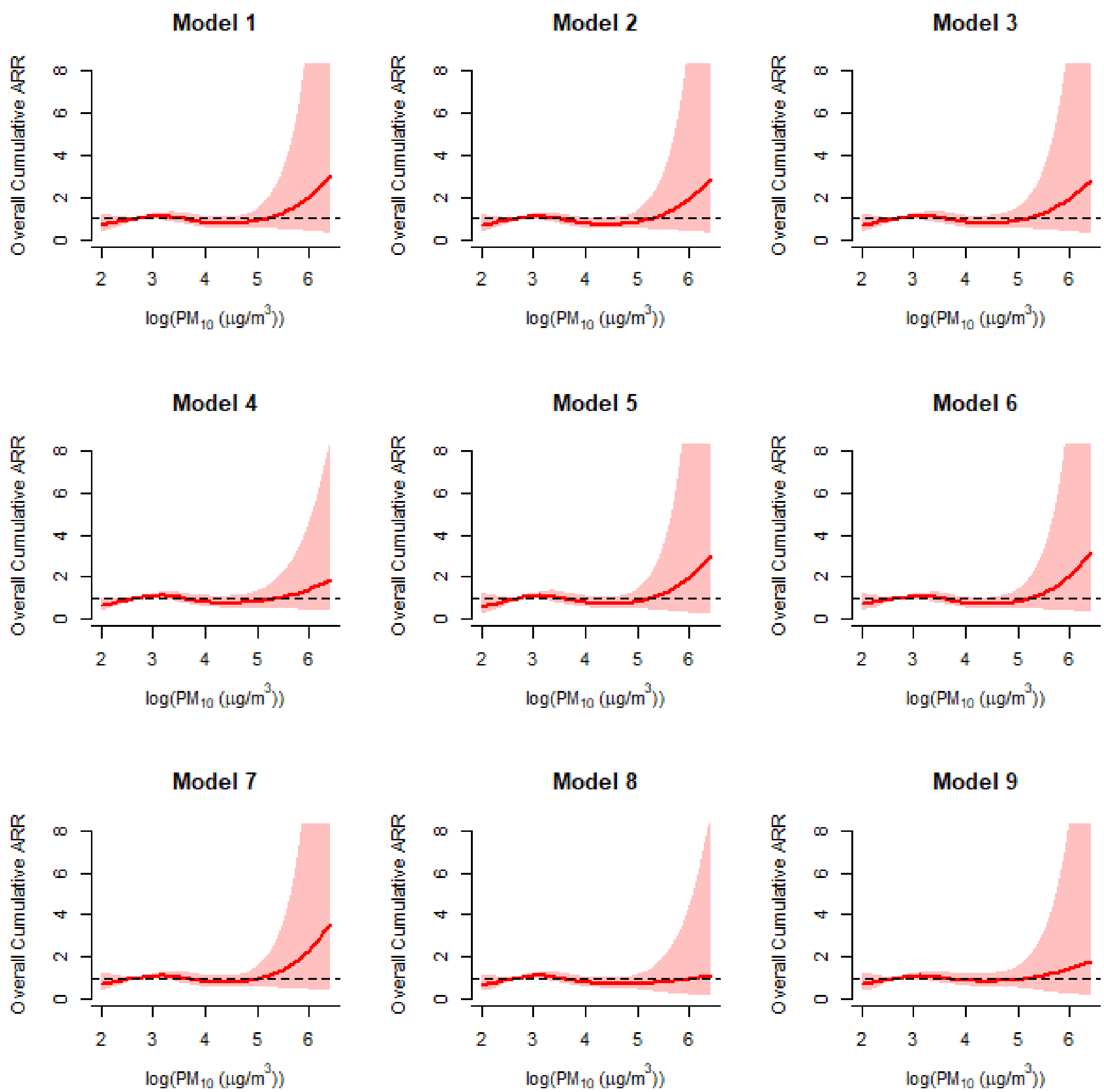
D. Sensitivity Analysis: Cumulative adjusted relative risks (ARRs) of pollutants: (a) NO_2, (b) PM_{10}, (c) O_3, and (d) SO_2 at different parameter settings

- **Model 1:** df for the meteorological parameters = 3; df for the pollutants = 4; df for lag = 4, df for day of study per year = 7
- **Model 2:** df for the meteorological parameters = 3; df for the pollutants = 4; df for lag = 4, df for day of study per year = 7
- **Model 3:** df for the meteorological parameters = 5; df for the pollutants = 4; df for lag = 4, df for day of study per year = 7
- **Model 4:** df for the meteorological parameters = 3; df for the pollutants = 3; df for lag = 4, df for day of study per year = 7
- **Model 5:** df for the meteorological parameters = 3; df for the pollutants = 5; df for lag = 4, df for day of study per year = 7
- **Model 6:** df for the meteorological parameters = 3; df for the pollutants = 4; df for lag = 3, df for day of study per year = 7
- **Model 7:** df for the meteorological parameters = 3; df for the pollutants = 4; df for lag = 5, df for day of study per year = 7
- **Model 8:** df for the meteorological parameters = 3; df for the pollutants = 4; df for lag = 4, df for day of study per year = 6
- **Model 9:** df for the meteorological parameters = 3; df for the pollutants = 4; df for lag = 4, df for day of study per year = 8

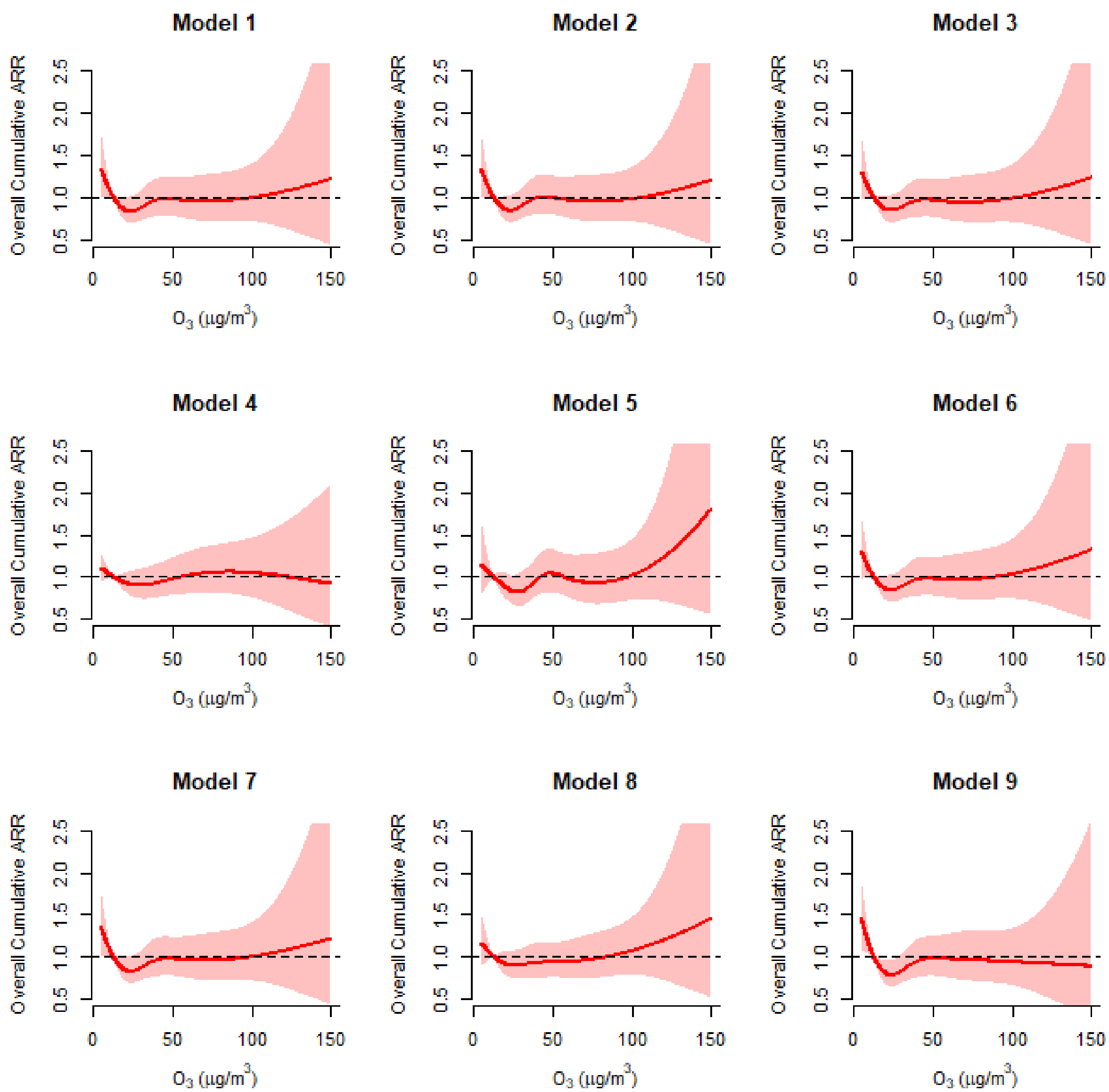
(a) NO_2 (ref. = 29.0 μg/m^3)



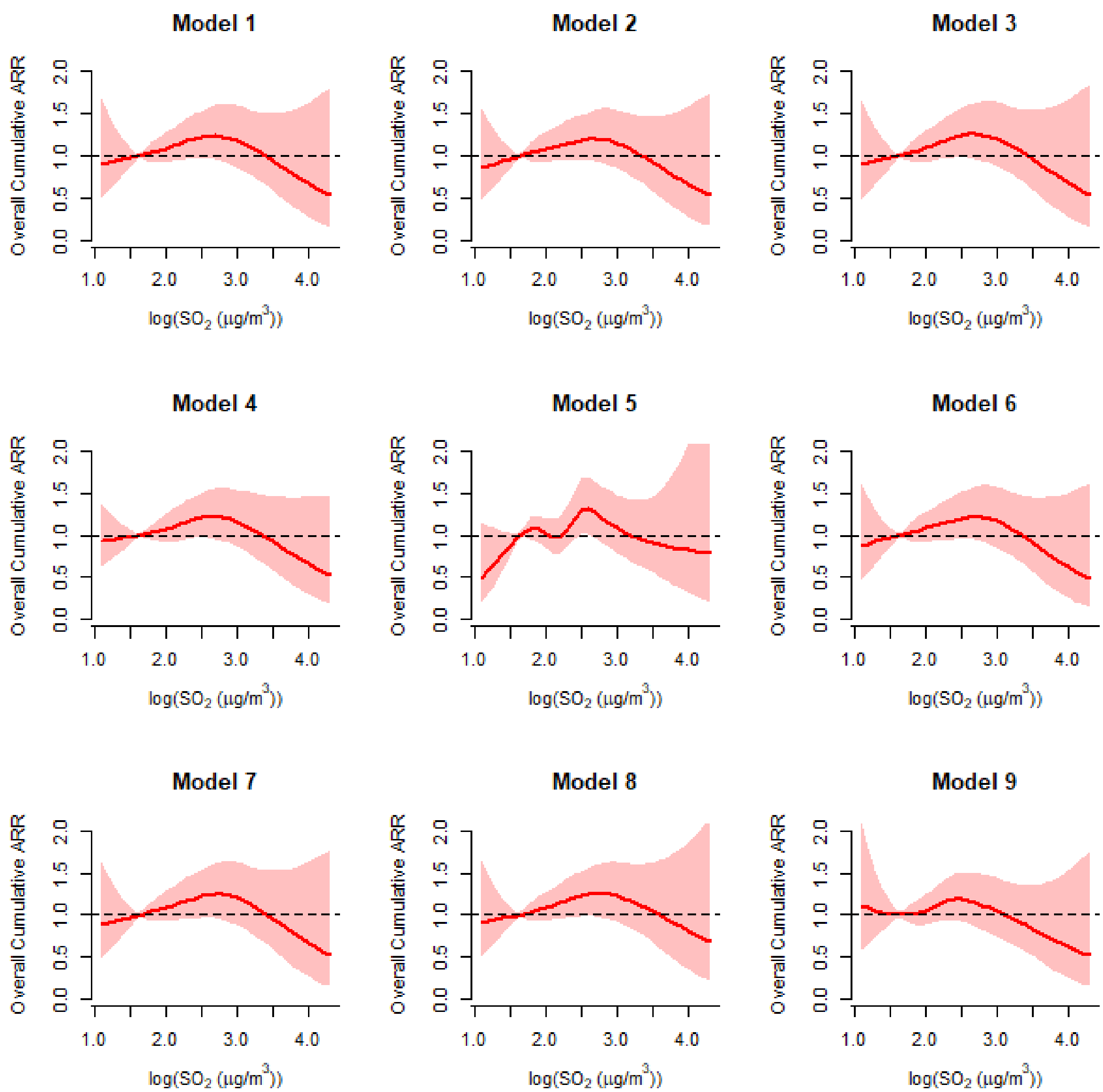
(b) log(PM_{10}) (ref. = log(15.0 μg/m^3))



(c) O_3 (ref. = 12.6 µg/m^3)



(d) log(SO_2) (ref. = log(5.2 μg/m^3))



E. R outputs of the modelling analysis

1. Primary model: $\log[E(Y_t)] = \alpha + cb(\text{temperature}_t) + cb(\text{relative humdity}_t) + cb(\text{factor}(\text{rainfall}_t)) + cb(NO_{2_t}) + cb(\log(SO_{2_t})) + cb(O_{3_t}) + cb(\log(PM_{10_t})) + cb(\text{factor}(\text{Holiday}_t)) + ns(DOS_t, df = 7 \text{ per year}) + \text{factor}(DOW_t) + s(\sqrt{\text{influenza}_t}, k = 7)$

```
Family: quasipoisson
Link function: log
Formula:
ad ~ temp.cb + humid.cb + rainfall.cb + o3.cb + so2.cb + no2.cb +
    pm10.cb + holiday.cb + factor(dow) + ns(dos, df = 10 * trend_df) +
    s(sqrt(influ), k = 7)

Parametric coefficients:
                              Estimate Std. Error t value Pr(>|t|)
(Intercept)                  1.4512548  0.7160001   2.027 0.042750 *
temp.cbv1.l1                 0.0439784  0.0418318   1.051 0.293187
temp.cbv1.l2                -0.0878345  0.0390152  -2.251 0.024430 *
temp.cbv1.l3                 0.0446216  0.0618343   0.722 0.470570
temp.cbv1.l4                -0.0034920  0.0423107  -0.083 0.934228
temp.cbv2.l1                 0.1231761  0.1142025   1.079 0.280852
temp.cbv2.l2                -0.1643616  0.1065041  -1.543 0.122864
temp.cbv2.l3                 0.1794677  0.1601544   1.121 0.262540
temp.cbv2.l4                -0.0698977  0.1133739  -0.617 0.537590
temp.cbv3.l1                 0.0137331  0.0511297   0.269 0.788258
temp.cbv3.l2                -0.1119861  0.0500760  -2.236 0.025394 *
temp.cbv3.l3                 0.0684730  0.0706839   0.969 0.332752
temp.cbv3.l4                 0.0674186  0.0498300   1.353 0.176153
humid.cbv1.l1               -0.0266661  0.0328741  -0.811 0.417331
humid.cbv1.l2                0.0259349  0.0323173   0.803 0.422314
humid.cbv1.l3                0.0136069  0.0448957   0.303 0.761849
humid.cbv1.l4               -0.0470236  0.0330892  -1.421 0.155373
humid.cbv2.l1               -0.0812557  0.1074348  -0.756 0.449505
humid.cbv2.l2                0.1865052  0.1062710   1.755 0.079349 .
humid.cbv2.l3               -0.0743799  0.1565142  -0.475 0.634655
humid.cbv2.l4               -0.1123834  0.1107212  -1.015 0.310171
humid.cbv3.l1               -0.0198497  0.0412145  -0.482 0.630106
humid.cbv3.l2                0.0941500  0.0406179   2.318 0.020511 *
humid.cbv3.l3               -0.0571965  0.0556244  -1.028 0.303899
humid.cbv3.l4                0.0217260  0.0391004   0.556 0.578488
rainfall.cbv1.l1            -0.0022131  0.0110607  -0.200 0.841422
rainfall.cbv1.l2            -0.0047411  0.0115397  -0.411 0.681211
rainfall.cbv1.l3             0.0032760  0.0145790   0.225 0.822220
rainfall.cbv1.l4             0.0045150  0.0105962   0.426 0.670061
rainfall.cbv2.l1            -0.0104598  0.0280257  -0.373 0.709005
rainfall.cbv2.l2            -0.0495716  0.0304926  -1.626 0.104106
rainfall.cbv2.l3             0.0254501  0.0361916   0.703 0.481977
rainfall.cbv2.l4            -0.0359519  0.0268185  -1.341 0.180151
o3.cbv1.l1                   0.0345359  0.0298613   1.157 0.247540
o3.cbv1.l2                  -0.0307839  0.0298265  -1.032 0.302099
o3.cbv1.l3                  -0.0591781  0.0410856  -1.440 0.149856
o3.cbv1.l4                   0.0178601  0.0293947   0.608 0.543494
o3.cbv2.l1                   0.0179539  0.0389989   0.460 0.645280
o3.cbv2.l2                   0.0066618  0.0398056   0.167 0.867098
o3.cbv2.l3                  -0.0294685  0.0524620  -0.562 0.574350
o3.cbv2.l4                  -0.0338190  0.0377101  -0.897 0.369880
o3.cbv3.l1                   0.0729922  0.0746161   0.978 0.328026
o3.cbv3.l2                  -0.0630899  0.0762029  -0.828 0.407773
o3.cbv3.l3                  -0.1670266  0.0999883  -1.670 0.094919 .
o3.cbv3.l4                   0.0555581  0.0730619   0.760 0.447053
o3.cbv4.l1                   0.1574924  0.0703358   2.239 0.025210 *
o3.cbv4.l2                  -0.1800452  0.0740213  -2.432 0.015052 *
o3.cbv4.l3                  -0.0433764  0.0938465  -0.462 0.643963
o3.cbv4.l4                   0.1376333  0.0706558   1.948 0.051503 .
so2.cbv1.l1                  0.0134665  0.0521547   0.258 0.796266
so2.cbv1.l2                  0.0984224  0.0509775   1.931 0.053602 .
```

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so2.cbv1.l3                  0.0114321  0.0712974   0.160 0.872620
so2.cbv1.l4                 -0.0912327  0.0503946  -1.810 0.070326 .
so2.cbv2.l1                  0.0464193  0.0474932   0.977 0.328445
so2.cbv2.l2                  0.0811822  0.0475452   1.707 0.087824 .
so2.cbv2.l3                 -0.0280440  0.0639681  -0.438 0.661120
so2.cbv2.l4                 -0.0241849  0.0459626  -0.526 0.598792
so2.cbv3.l1                  0.0549618  0.1204914   0.456 0.648313
so2.cbv3.l2                  0.2331202  0.1208678   1.929 0.053847 .
so2.cbv3.l3                 -0.1215267  0.1657625  -0.733 0.463524
so2.cbv3.l4                 -0.1651787  0.1167885  -1.414 0.157352
so2.cbv4.l1                  0.0026564  0.0769013   0.035 0.972447
so2.cbv4.l2                  0.0560959  0.0811260   0.691 0.489319
so2.cbv4.l3                 -0.0973958  0.1074898  -0.906 0.364949
so2.cbv4.l4                 -0.0658722  0.0757302  -0.870 0.384455
no2.cbv1.l1                 -0.0616957  0.0527942  -1.169 0.242642
no2.cbv1.l2                  0.0017939  0.0542495   0.033 0.973623
no2.cbv1.l3                 -0.0009991  0.0715642  -0.014 0.988862
no2.cbv1.l4                  0.1019180  0.0538348   1.893 0.058420 .
no2.cbv2.l1                  0.0188803  0.0511363   0.369 0.711990
no2.cbv2.l2                 -0.0198304  0.0538109  -0.369 0.712508
no2.cbv2.l3                  0.0673643  0.0691143   0.975 0.329787
no2.cbv2.l4                  0.0877127  0.0512704   1.711 0.087210 .
no2.cbv3.l1                 -0.1785233  0.1212393  -1.472 0.140980
no2.cbv3.l2                  0.1512279  0.1246071   1.214 0.224969
no2.cbv3.l3                  0.0090424  0.1643940   0.055 0.956138
no2.cbv3.l4                  0.2665555  0.1212167   2.199 0.027944 *
no2.cbv4.l1                 -0.0688453  0.1023508  -0.673 0.501221
no2.cbv4.l2                  0.1026636  0.1061544   0.967 0.333554
no2.cbv4.l3                  0.0079176  0.1451105   0.055 0.956490
no2.cbv4.l4                  0.1460566  0.1029970   1.418 0.156262
pm10.cbv1.l1                -0.0236306  0.0549739  -0.430 0.667330
pm10.cbv1.l2                -0.0261759  0.0527177  -0.497 0.619553
pm10.cbv1.l3                 0.1661722  0.0743066   2.236 0.025395 *
pm10.cbv1.l4                -0.1381865  0.0528898  -2.613 0.009021 **
pm10.cbv2.l1                -0.0436518  0.0515316  -0.847 0.397004
pm10.cbv2.l2                -0.0538285  0.0513311  -1.049 0.294411
pm10.cbv2.l3                 0.0703806  0.0739057   0.952 0.341010
pm10.cbv2.l4                -0.1381750  0.0517831  -2.668 0.007658 **
pm10.cbv3.l1                 0.0970854  0.1293034   0.751 0.452804
pm10.cbv3.l2                -0.2039492  0.1259097  -1.620 0.105365
pm10.cbv3.l3                 0.3679024  0.1741204   2.113 0.034679 *
pm10.cbv3.l4                -0.2342362  0.1248315  -1.876 0.060682 .
pm10.cbv4.l1                 0.0010267  0.1237157   0.008 0.993379
pm10.cbv4.l2                -0.0726563  0.1305394  -0.557 0.577847
pm10.cbv4.l3                 0.2272455  0.1722491   1.319 0.187162
pm10.cbv4.l4                 0.0032430  0.1298638   0.025 0.980079
holiday.cbv1.l1              0.0195226  0.0139753   1.397 0.162523
holiday.cbv1.l2             -0.0377211  0.0125888  -2.996 0.002751 **
holiday.cbv1.l3             -0.0213359  0.0183454  -1.163 0.244904
holiday.cbv1.l4             -0.0291242  0.0132594  -2.196 0.028123 *
factor(dow)2                -0.0587772  0.0221779  -2.650 0.008080 **
factor(dow)3                -0.0737656  0.0235202  -3.136 0.001726 **
factor(dow)4                -0.0442848  0.0237874  -1.862 0.062731 .
factor(dow)5                -0.0751847  0.0237134  -3.171 0.001535 **
factor(dow)6                -0.0899525  0.0235340  -3.822 0.000135 ***
factor(dow)7                -0.0397347  0.0228790  -1.737 0.082524 .
ns(dos, df = 10 * trend_df)1   0.8616721  0.3091919   2.787 0.005351 **
ns(dos, df = 10 * trend_df)2  -0.0458647  0.4184533  -0.110 0.912729
ns(dos, df = 10 * trend_df)3   0.9980103  0.3923718   2.544 0.011017 *
ns(dos, df = 10 * trend_df)4   0.3362908  0.4123966   0.815 0.414868
ns(dos, df = 10 * trend_df)5   0.4138532  0.3848843   1.075 0.282331
ns(dos, df = 10 * trend_df)6  -0.2839202  0.4000807  -0.710 0.477965
ns(dos, df = 10 * trend_df)7  -0.0838325  0.3579476  -0.234 0.814841
ns(dos, df = 10 * trend_df)8   1.2097265  0.3573797   3.385 0.000720 ***
ns(dos, df = 10 * trend_df)9  -0.8398919  0.4148958  -2.024 0.043012 *
ns(dos, df = 10 * trend_df)10 -0.1715906  0.4126791  -0.416 0.677585
ns(dos, df = 10 * trend_df)11 -0.1609482  0.4416006  -0.364 0.715533
ns(dos, df = 10 * trend_df)12  0.6232963  0.3867686   1.612 0.107152
ns(dos, df = 10 * trend_df)13 -0.5633256  0.3747890  -1.503 0.132918
ns(dos, df = 10 * trend_df)14  1.3810768  0.3554162   3.886 0.000104 ***
ns(dos, df = 10 * trend_df)15  0.7007377  0.3546676   1.976 0.048262 *
```

```
ns(dos, df = 10 * trend_df)16  0.0950378  0.3999787   0.238 0.812200
ns(dos, df = 10 * trend_df)17 -0.7546348  0.4165587  -1.812 0.070136 .
ns(dos, df = 10 * trend_df)18  0.3153634  0.4294361   0.734 0.462775
ns(dos, df = 10 * trend_df)19  0.3169441  0.3761137   0.843 0.399465
ns(dos, df = 10 * trend_df)20  0.9033308  0.3660175   2.468 0.013635 *
ns(dos, df = 10 * trend_df)21 -0.1041196  0.3738877  -0.278 0.780662
ns(dos, df = 10 * trend_df)22  1.1412016  0.3575339   3.192 0.001426 **
ns(dos, df = 10 * trend_df)23  0.1288197  0.3916974   0.329 0.742270
ns(dos, df = 10 * trend_df)24  0.7538852  0.3893076   1.936 0.052891 .
ns(dos, df = 10 * trend_df)25  0.9750480  0.4100772   2.378 0.017474 *
ns(dos, df = 10 * trend_df)26  0.1975424  0.3802096   0.520 0.603402
ns(dos, df = 10 * trend_df)27 -0.4322074  0.3771566  -1.146 0.251890
ns(dos, df = 10 * trend_df)28  0.6356608  0.3621247   1.755 0.079286 .
ns(dos, df = 10 * trend_df)29  1.0673142  0.3595173   2.969 0.003011 **
ns(dos, df = 10 * trend_df)30  0.1287451  0.4219465   0.305 0.760292
ns(dos, df = 10 * trend_df)31  0.1093384  0.3945192   0.277 0.781687
ns(dos, df = 10 * trend_df)32  0.5879758  0.4081295   1.441 0.149771
ns(dos, df = 10 * trend_df)33  0.5000772  0.3804599   1.314 0.188798
ns(dos, df = 10 * trend_df)34  0.6856981  0.3469802   1.976 0.048213 *
ns(dos, df = 10 * trend_df)35  1.1784024  0.3723688   3.165 0.001566 **
ns(dos, df = 10 * trend_df)36  0.0960919  0.3497702   0.275 0.783541
ns(dos, df = 10 * trend_df)37  0.2188771  0.4076512   0.537 0.591356
ns(dos, df = 10 * trend_df)38  1.1243102  0.3909058   2.876 0.004050 **
ns(dos, df = 10 * trend_df)39  0.5472236  0.4055893   1.349 0.177359
ns(dos, df = 10 * trend_df)40  0.3836715  0.3869929   0.991 0.321551
ns(dos, df = 10 * trend_df)41 -0.0475495  0.3874454  -0.123 0.902332
ns(dos, df = 10 * trend_df)42 -0.5383873  0.3875989  -1.389 0.164913
ns(dos, df = 10 * trend_df)43  1.5538601  0.3523201   4.410 1.06e-05 ***
ns(dos, df = 10 * trend_df)44  0.4011037  0.4129479   0.971 0.331458
ns(dos, df = 10 * trend_df)45  0.1423757  0.4001527   0.356 0.722010
ns(dos, df = 10 * trend_df)46  0.1128887  0.4155741   0.272 0.785911
ns(dos, df = 10 * trend_df)47  0.4619514  0.3811831   1.212 0.225638
ns(dos, df = 10 * trend_df)48  0.1630531  0.3813022   0.428 0.668953
ns(dos, df = 10 * trend_df)49 -0.2127009  0.3906294  -0.545 0.586127
ns(dos, df = 10 * trend_df)50  0.6608814  0.3591247   1.840 0.065816 .
ns(dos, df = 10 * trend_df)51  0.2155257  0.4203650   0.513 0.608186
ns(dos, df = 10 * trend_df)52  0.1086832  0.4229558   0.257 0.797224
ns(dos, df = 10 * trend_df)53  0.6313049  0.3956350   1.596 0.110653
ns(dos, df = 10 * trend_df)54  0.3613383  0.4008369   0.901 0.367407
ns(dos, df = 10 * trend_df)55  0.5361872  0.3478824   1.541 0.123338
ns(dos, df = 10 * trend_df)56  0.9130877  0.3846419   2.374 0.017657 *
ns(dos, df = 10 * trend_df)57  0.6538293  0.3522626   1.856 0.063527 .
ns(dos, df = 10 * trend_df)58  0.8777681  0.4292818   2.045 0.040956 *
ns(dos, df = 10 * trend_df)59  0.2278709  0.4058652   0.561 0.574531
ns(dos, df = 10 * trend_df)60  0.1307263  0.4172703   0.313 0.754080
ns(dos, df = 10 * trend_df)61  0.6635502  0.3857125   1.720 0.085463 .
ns(dos, df = 10 * trend_df)62  0.6422523  0.3559697   1.804 0.071282 .
ns(dos, df = 10 * trend_df)63  0.4363803  0.3762755   1.160 0.246236
ns(dos, df = 10 * trend_df)64  1.1266372  0.3555550   3.169 0.001545 **
ns(dos, df = 10 * trend_df)65  0.0357018  0.4227793   0.084 0.932707
ns(dos, df = 10 * trend_df)66  0.5818062  0.4249520   1.369 0.171054
ns(dos, df = 10 * trend_df)67  1.0917789  0.4220827   2.587 0.009732 **
ns(dos, df = 10 * trend_df)68  0.5217567  0.3044827   1.714 0.086695 .
ns(dos, df = 10 * trend_df)69  0.5761929  0.7550888   0.763 0.445468
ns(dos, df = 10 * trend_df)70 -0.0060447  0.1776860  -0.034 0.972864
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

Approximate significance of smooth terms:
                 edf Ref.df     F  p-value
s(sqrt(influ)) 1.259  1.482 9.878 0.000315 ***
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

R-sq.(adj) =  0.474   Deviance explained = 47.9%
GCV = 1.0821  Scale est. = 0.98661   n = 3632
```

2. Secondary model 1: $\log[\mathrm{E}(\mathrm{Y_t})] = \alpha + \mathrm{cb}(\text{Apparent Temperature}_t) + \mathrm{cb}(\text{Relative Humdity}_t) + \mathrm{cb}(\mathrm{factor}(\text{Rainfall}_t)) + \mathrm{cb}(\mathrm{NO}_{2_t}) + \mathrm{cb}(\log(\mathrm{SO}_{2_t})) + \mathrm{cb}(\mathrm{O}_{3_t}) + \mathrm{cb}(\log(\mathrm{PM}_{10_t})) + \mathrm{cb}(\mathrm{factor}(\text{Holiday}_t)) + \mathrm{ns}(\mathrm{DOS_t}, \mathrm{df} = 7 \text{ per year}) + \mathrm{factor}(\mathrm{DOW_t}) + \mathrm{s}(\sqrt{\text{Influenza}_t}, \mathrm{k} = 7)$

```
Family: quasipoisson
Link function: log

Formula:
ad ~ AT.cb + humid.cb + rainfall.cb + o3.cb + so2.cb + no2.cb +
    pm10.cb + holiday.cb + factor(dow) + ns(dos, df = 10 * trend_df) +
    s(sqrt(influ), k = 7)

Parametric coefficients:
                                Estimate Std. Error t value Pr(>|t|)
(Intercept)                    1.6660412  0.7586414   2.196 0.028155 *
AT.cbv1.l1                     0.0552618  0.0477023   1.158 0.246754
AT.cbv1.l2                    -0.1034158  0.0444522  -2.326 0.020054 *
AT.cbv1.l3                     0.0631939  0.0685733   0.922 0.356829
AT.cbv1.l4                    -0.0334739  0.0473336  -0.707 0.479496
AT.cbv2.l1                     0.2376932  0.1459218   1.629 0.103427
AT.cbv2.l2                    -0.2115769  0.1356748  -1.559 0.118987
AT.cbv2.l3                     0.1915229  0.2004322   0.956 0.339369
AT.cbv2.l4                    -0.1378967  0.1445228  -0.954 0.340076
AT.cbv3.l1                     0.0423648  0.0472982   0.896 0.370479
AT.cbv3.l2                    -0.0966215  0.0457569  -2.112 0.034793 *
AT.cbv3.l3                     0.1121366  0.0661026   1.696 0.089903 .
AT.cbv3.l4                    -0.0018263  0.0468047  -0.039 0.968877
humid.cbv1.l1                 -0.0218804  0.0356452  -0.614 0.539365
humid.cbv1.l2                  0.0224829  0.0347639   0.647 0.517850
humid.cbv1.l3                 -0.0009628  0.0477471  -0.020 0.983914
humid.cbv1.l4                 -0.0370310  0.0348635  -1.062 0.288234
humid.cbv2.l1                 -0.0646684  0.1164570  -0.555 0.578728
humid.cbv2.l2                  0.1329434  0.1113794   1.194 0.232716
humid.cbv2.l3                 -0.0641735  0.1653667  -0.388 0.697990
humid.cbv2.l4                 -0.0963373  0.1162263  -0.829 0.407234
humid.cbv3.l1                 -0.0068002  0.0432011  -0.157 0.874933
humid.cbv3.l2                  0.0665029  0.0423867   1.569 0.116753
humid.cbv3.l3                 -0.0534840  0.0575815  -0.929 0.353040
humid.cbv3.l4                  0.0285791  0.0404871   0.706 0.480312
rainfall.cbv1.l1              -0.0031316  0.0115235  -0.272 0.785827
rainfall.cbv1.l2              -0.0049700  0.0121226  -0.410 0.681846
rainfall.cbv1.l3               0.0040544  0.0150196   0.270 0.787220
rainfall.cbv1.l4               0.0053266  0.0109031   0.489 0.625197
rainfall.cbv2.l1              -0.0105060  0.0292174  -0.360 0.719184
rainfall.cbv2.l2              -0.0421359  0.0321307  -1.311 0.189816
rainfall.cbv2.l3               0.0412199  0.0378669   1.089 0.276433
rainfall.cbv2.l4              -0.0502319  0.0282973  -1.775 0.075965 .
o3.cbv1.l1                     0.0348665  0.0295563   1.180 0.238217
o3.cbv1.l2                    -0.0416967  0.0294356  -1.417 0.156711
o3.cbv1.l3                    -0.0463252  0.0409948  -1.130 0.258546
o3.cbv1.l4                     0.0248903  0.0290758   0.856 0.392031
o3.cbv2.l1                     0.0227358  0.0387075   0.587 0.556992
o3.cbv2.l2                     0.0025551  0.0397889   0.064 0.948801
o3.cbv2.l3                    -0.0224234  0.0527896  -0.425 0.671032
o3.cbv2.l4                    -0.0292102  0.0378654  -0.771 0.440512
o3.cbv3.l1                     0.0649870  0.0744233   0.873 0.382613
o3.cbv3.l2                    -0.0755945  0.0759536  -0.995 0.319676
o3.cbv3.l3                    -0.1363626  0.1003953  -1.358 0.174474
o3.cbv3.l4                     0.0494855  0.0731764   0.676 0.498929
o3.cbv4.l1                     0.1564937  0.0718709   2.177 0.029519 *
o3.cbv4.l2                    -0.1974352  0.0761727  -2.592 0.009585 **
o3.cbv4.l3                    -0.0179600  0.0957428  -0.188 0.851213
o3.cbv4.l4                     0.1257924  0.0725845   1.733 0.083180 .
so2.cbv1.l1                    0.0167104  0.0541531   0.309 0.757662
so2.cbv1.l2                    0.0831071  0.0531672   1.563 0.118118
so2.cbv1.l3                    0.0001811  0.0739389   0.002 0.998046
so2.cbv1.l4                   -0.0649959  0.0516835  -1.258 0.208634
so2.cbv2.l1                    0.0512144  0.0489616   1.046 0.295632
so2.cbv2.l2                    0.0676012  0.0492383   1.373 0.169864
so2.cbv2.l3                   -0.0380584  0.0660353  -0.576 0.564428
so2.cbv2.l4                   -0.0034456  0.0473060  -0.073 0.941941
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so2.cbv3.l1                        0.0512808  0.1243337   0.412 0.680040
so2.cbv3.l2                        0.1955869  0.1250029   1.565 0.117758
so2.cbv3.l3                       -0.1419627  0.1713154  -0.829 0.407355
so2.cbv3.l4                       -0.1093854  0.1195790  -0.915 0.360387
so2.cbv4.l1                       -0.0021016  0.0774203  -0.027 0.978345
so2.cbv4.l2                        0.0148940  0.0813678   0.183 0.854773
so2.cbv4.l3                       -0.1435432  0.1088079  -1.319 0.187182
so2.cbv4.l4                       -0.0180096  0.0761196  -0.237 0.812985
no2.cbv1.l1                       -0.0651355  0.0527155  -1.236 0.216693
no2.cbv1.l2                        0.0240398  0.0527676   0.456 0.648722
no2.cbv1.l3                       -0.0233851  0.0722192  -0.324 0.746104
no2.cbv1.l4                        0.0724792  0.0537295   1.349 0.177440
no2.cbv2.l1                        0.0133337  0.0507296   0.263 0.792692
no2.cbv2.l2                        0.0124311  0.0529264   0.235 0.814321
no2.cbv2.l3                        0.0291712  0.0688185   0.424 0.671676
no2.cbv2.l4                        0.0585159  0.0513353   1.140 0.254420
no2.cbv3.l1                       -0.1983282  0.1208347  -1.641 0.100826
no2.cbv3.l2                        0.2152031  0.1223656   1.759 0.078722 .
no2.cbv3.l3                       -0.0379806  0.1657823  -0.229 0.818806
no2.cbv3.l4                        0.2064575  0.1214117   1.700 0.089135 .
no2.cbv4.l1                       -0.0736111  0.1029959  -0.715 0.474845
no2.cbv4.l2                        0.1499224  0.1062928   1.410 0.158496
no2.cbv4.l3                        0.0300032  0.1462432   0.205 0.837460
no2.cbv4.l4                        0.1414452  0.1034423   1.367 0.171598
pm10.cbv1.l1                      -0.0413979  0.0564995  -0.733 0.463785
pm10.cbv1.l2                      -0.0148565  0.0534441  -0.278 0.781043
pm10.cbv1.l3                       0.1699841  0.0763136   2.227 0.025984 *
pm10.cbv1.l4                      -0.1356220  0.0539619  -2.513 0.012008 *
pm10.cbv2.l1                      -0.0655134  0.0532196  -1.231 0.218409
pm10.cbv2.l2                      -0.0535008  0.0528486  -1.012 0.311449
pm10.cbv2.l3                       0.0908371  0.0754894   1.203 0.228942
pm10.cbv2.l4                      -0.1419105  0.0531216  -2.671 0.007590 **
pm10.cbv3.l1                       0.0621278  0.1325245   0.469 0.639242
pm10.cbv3.l2                      -0.1970264  0.1281867  -1.537 0.124382
pm10.cbv3.l3                       0.3798868  0.1784794   2.128 0.033372 *
pm10.cbv3.l4                      -0.2472232  0.1270476  -1.946 0.051750 .
pm10.cbv4.l1                       0.0051321  0.1264202   0.041 0.967621
pm10.cbv4.l2                      -0.0879770  0.1327344  -0.663 0.507501
pm10.cbv4.l3                       0.2528895  0.1743678   1.450 0.147063
pm10.cbv4.l4                      -0.0317103  0.1314118  -0.241 0.809334
holiday.cbv1.l1                    0.0229240  0.0140656   1.630 0.103241
holiday.cbv1.l2                   -0.0384166  0.0127883  -3.004 0.002684 **
holiday.cbv1.l3                   -0.0271741  0.0184173  -1.475 0.140180
holiday.cbv1.l4                   -0.0262329  0.0133766  -1.961 0.049950 *
factor(dow)2                      -0.0649037  0.0225217  -2.882 0.003979 **
factor(dow)3                      -0.0786969  0.0238626  -3.298 0.000984 ***
factor(dow)4                      -0.0522564  0.0241511  -2.164 0.030556 *
factor(dow)5                      -0.0788882  0.0240608  -3.279 0.001054 **
factor(dow)6                      -0.0962840  0.0238861  -4.031 5.68e-05 ***
factor(dow)7                      -0.0411008  0.0231921  -1.772 0.076455 .
ns(dos, df = 10 * trend_df)1       0.9348702  0.3096874   3.019 0.002557 **
ns(dos, df = 10 * trend_df)2      -0.0803316  0.4164357  -0.193 0.847047
ns(dos, df = 10 * trend_df)3       1.0230267  0.3934626   2.600 0.009362 **
ns(dos, df = 10 * trend_df)4       0.2611783  0.4190711   0.623 0.533175
ns(dos, df = 10 * trend_df)5       0.4308111  0.3930425   1.096 0.273117
ns(dos, df = 10 * trend_df)6      -0.3433589  0.4087290  -0.840 0.400932
ns(dos, df = 10 * trend_df)7      -0.0118598  0.3584741  -0.033 0.973610
ns(dos, df = 10 * trend_df)8       1.1995473  0.3593351   3.338 0.000852 ***
ns(dos, df = 10 * trend_df)9      -0.9221487  0.4106954  -2.245 0.024812 *
ns(dos, df = 10 * trend_df)10 -0.1866354  0.4136076  -0.451 0.651848
ns(dos, df = 10 * trend_df)11 -0.2841876  0.4413071  -0.644 0.519641
ns(dos, df = 10 * trend_df)12  0.6536305  0.3931383   1.663 0.096487 .
ns(dos, df = 10 * trend_df)13 -0.5691370  0.3824402  -1.488 0.136800
ns(dos, df = 10 * trend_df)14  1.3880733  0.3552156   3.908 9.50e-05 ***
ns(dos, df = 10 * trend_df)15  0.7389734  0.3566781   2.072 0.038359 *
ns(dos, df = 10 * trend_df)16  0.0195143  0.3967728   0.049 0.960777
ns(dos, df = 10 * trend_df)17 -0.7927040  0.4170666  -1.901 0.057432 .
ns(dos, df = 10 * trend_df)18  0.2183160  0.4275896   0.511 0.609683
ns(dos, df = 10 * trend_df)19  0.3343548  0.3729369   0.897 0.370026
ns(dos, df = 10 * trend_df)20  0.9254000  0.3714831   2.491 0.012783 *
ns(dos, df = 10 * trend_df)21 -0.1336946  0.3742418  -0.357 0.720934
```

```
ns(dos, df = 10 * trend_df)22  1.1972173  0.3591861   3.333 0.000868 ***
ns(dos, df = 10 * trend_df)23  0.0118967  0.3885849   0.031 0.975578
ns(dos, df = 10 * trend_df)24  0.7251224  0.3867721   1.875 0.060907 .
ns(dos, df = 10 * trend_df)25  0.8458428  0.4134686   2.046 0.040862 *
ns(dos, df = 10 * trend_df)26  0.2569205  0.3719087   0.691 0.489729
ns(dos, df = 10 * trend_df)27 -0.4461225  0.3833977  -1.164 0.244669
ns(dos, df = 10 * trend_df)28  0.6629031  0.3611692   1.835 0.066530 .
ns(dos, df = 10 * trend_df)29  1.0391171  0.3682964   2.821 0.004810 **
ns(dos, df = 10 * trend_df)30  0.1485589  0.4257700   0.349 0.727173
ns(dos, df = 10 * trend_df)31  0.0513062  0.3928524   0.131 0.896100
ns(dos, df = 10 * trend_df)32  0.4906748  0.4061067   1.208 0.227040
ns(dos, df = 10 * trend_df)33  0.5155347  0.3745580   1.376 0.168796
ns(dos, df = 10 * trend_df)34  0.7009934  0.3520285   1.991 0.046530 *
ns(dos, df = 10 * trend_df)35  1.1763850  0.3748126   3.139 0.001712 **
ns(dos, df = 10 * trend_df)36  0.1230499  0.3514770   0.350 0.726291
ns(dos, df = 10 * trend_df)37  0.1355332  0.4026633   0.337 0.736446
ns(dos, df = 10 * trend_df)38  1.1019279  0.3907503   2.820 0.004830 **
ns(dos, df = 10 * trend_df)39  0.4670187  0.4022368   1.161 0.245703
ns(dos, df = 10 * trend_df)40  0.3887944  0.3783013   1.028 0.304148
ns(dos, df = 10 * trend_df)41 -0.0256821  0.3917498  -0.066 0.947734
ns(dos, df = 10 * trend_df)42 -0.5588517  0.3885952  -1.438 0.150490
ns(dos, df = 10 * trend_df)43  1.5858538  0.3556713   4.459 8.52e-06 ***
ns(dos, df = 10 * trend_df)44  0.3081121  0.4151729   0.742 0.458061
ns(dos, df = 10 * trend_df)45  0.0408652  0.4048381   0.101 0.919603
ns(dos, df = 10 * trend_df)46 -0.0130057  0.4174507  -0.031 0.975148
ns(dos, df = 10 * trend_df)47  0.4410692  0.3781409   1.166 0.243530
ns(dos, df = 10 * trend_df)48  0.1638694  0.3867899   0.424 0.671837
ns(dos, df = 10 * trend_df)49 -0.2254507  0.3913279  -0.576 0.564575
ns(dos, df = 10 * trend_df)50  0.6883038  0.3620310   1.901 0.057358 .
ns(dos, df = 10 * trend_df)51  0.1323519  0.4167186   0.318 0.750804
ns(dos, df = 10 * trend_df)52 -0.0167819  0.4269387  -0.039 0.968648
ns(dos, df = 10 * trend_df)53  0.5195820  0.3981041   1.305 0.191935
ns(dos, df = 10 * trend_df)54  0.3275957  0.3929122   0.834 0.404474
ns(dos, df = 10 * trend_df)55  0.5389357  0.3528137   1.528 0.126723
ns(dos, df = 10 * trend_df)56  0.8693710  0.3848434   2.259 0.023946 *
ns(dos, df = 10 * trend_df)57  0.7022714  0.3553213   1.976 0.048187 *
ns(dos, df = 10 * trend_df)58  0.7339430  0.4301806   1.706 0.088078 .
ns(dos, df = 10 * trend_df)59  0.1534584  0.4069458   0.377 0.706125
ns(dos, df = 10 * trend_df)60  0.0042170  0.4202259   0.010 0.991994
ns(dos, df = 10 * trend_df)61  0.6576398  0.3811990   1.725 0.084586 .
ns(dos, df = 10 * trend_df)62  0.6332635  0.3593769   1.762 0.078142 .
ns(dos, df = 10 * trend_df)63  0.3733542  0.3790214   0.985 0.324672
ns(dos, df = 10 * trend_df)64  1.1305471  0.3587700   3.151 0.001641 **
ns(dos, df = 10 * trend_df)65 -0.0773355  0.4220216  -0.183 0.854613
ns(dos, df = 10 * trend_df)66  0.5305942  0.4265496   1.244 0.213616
ns(dos, df = 10 * trend_df)67  0.8842477  0.4293260   2.060 0.039513 *
ns(dos, df = 10 * trend_df)68  0.5238019  0.2922416   1.792 0.073166 .
ns(dos, df = 10 * trend_df)69  0.5981283  0.7591184   0.788 0.430797
ns(dos, df = 10 * trend_df)70 -0.0693098  0.1784268  -0.388 0.697708
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Approximate significance of smooth terms:
                 edf Ref.df     F p-value
s(sqrt(influ)) 1.47  1.833 6.815 0.00122 **
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

R-sq.(adj) =   0.48   Deviance explained = 48.6%
GCV = 1.0847  Scale est. = 0.98601   n = 3507
```

3. Secondary model 2: $\log[E(Y_t)] = \alpha + cb(\text{Vapour Pressure}_t) + cb(\text{factor}(\text{Rainfall}_t)) + cb(NO_{2_t}) + cb(\log(SO_{2_t})) + cb(O_{3_t}) + cb(\log(PM_{10_t})) + cb(\text{factor}(\text{Holiday}_t)) + ns(DOS_t, df = 7 \text{ per year}) + \text{factor}(DOW_t) + s(\sqrt{\text{Influenza}_t}, k = 7)$

```
Family: quasipoisson
Link function: log

Formula:
ad ~ VP.cb + rainfall.cb + o3.cb + so2.cb + no2.cb + pm10.cb +
    holiday.cb + factor(dow) + ns(dos, df = 10 * trend_df) +
    s(sqrt(influ), k = 7)

Parametric coefficients:
                              Estimate Std. Error t value Pr(>|t|)
(Intercept)                  1.3553095  0.5661917   2.394 0.016731 *
VP.cbv1.l1                  -0.0051677  0.0275582  -0.188 0.851264
VP.cbv1.l2                  -0.0370730  0.0268103  -1.383 0.166819
VP.cbv1.l3                   0.0166116  0.0390717   0.425 0.670749
VP.cbv1.l4                  -0.0001894  0.0271655  -0.007 0.994437
VP.cbv2.l1                   0.0736201  0.0682986   1.078 0.281147
VP.cbv2.l2                  -0.1653748  0.0687627  -2.405 0.016224 *
VP.cbv2.l3                   0.0694318  0.0948159   0.732 0.464047
VP.cbv2.l4                  -0.0303909  0.0677348  -0.449 0.653694
VP.cbv3.l1                   0.0501825  0.0367864   1.364 0.172606
VP.cbv3.l2                  -0.0702289  0.0341507  -2.056 0.039815 *
VP.cbv3.l3                  -0.0011149  0.0510029  -0.022 0.982561
VP.cbv3.l4                   0.0573688  0.0354223   1.620 0.105417
rainfall.cbv1.l1            -0.0089060  0.0095426  -0.933 0.350734
rainfall.cbv1.l2             0.0117857  0.0097057   1.214 0.224713
rainfall.cbv1.l3             0.0042138  0.0131819   0.320 0.749243
rainfall.cbv1.l4             0.0049149  0.0094476   0.520 0.602940
rainfall.cbv2.l1            -0.0185781  0.0234733  -0.791 0.428733
rainfall.cbv2.l2            -0.0031497  0.0254193  -0.124 0.901395
rainfall.cbv2.l3             0.0097602  0.0311368   0.313 0.753949
rainfall.cbv2.l4            -0.0329604  0.0236611  -1.393 0.163703
o3.cbv1.l1                   0.0350348  0.0279724   1.252 0.210480
o3.cbv1.l2                  -0.0471171  0.0278681  -1.691 0.090980 .
o3.cbv1.l3                  -0.0414443  0.0393413  -1.053 0.292206
o3.cbv1.l4                   0.0141358  0.0277313   0.510 0.610266
o3.cbv2.l1                   0.0324395  0.0363703   0.892 0.372497
o3.cbv2.l2                  -0.0195819  0.0370433  -0.529 0.597102
o3.cbv2.l3                  -0.0096331  0.0501870  -0.192 0.847797
o3.cbv2.l4                  -0.0289869  0.0358466  -0.809 0.418780
o3.cbv3.l1                   0.0665267  0.0717748   0.927 0.354053
o3.cbv3.l2                  -0.0888793  0.0732998  -1.213 0.225386
o3.cbv3.l3                  -0.1384151  0.0969419  -1.428 0.153435
o3.cbv3.l4                   0.0581507  0.0704800   0.825 0.409390
o3.cbv4.l1                   0.1555801  0.0703260   2.212 0.027013 *
o3.cbv4.l2                  -0.1850006  0.0742172  -2.493 0.012724 *
o3.cbv4.l3                  -0.0411989  0.0938417  -0.439 0.660670
o3.cbv4.l4                   0.1450825  0.0711142   2.040 0.041413 *
so2.cbv1.l1                  0.0192957  0.0464112   0.416 0.677615
so2.cbv1.l2                  0.0453044  0.0455387   0.995 0.319876
so2.cbv1.l3                  0.0652402  0.0636952   1.024 0.305786
so2.cbv1.l4                 -0.0983907  0.0451572  -2.179 0.029410 *
so2.cbv2.l1                  0.0575265  0.0423461   1.358 0.174398
so2.cbv2.l2                  0.0219654  0.0425749   0.516 0.605940
so2.cbv2.l3                  0.0162539  0.0574158   0.283 0.777124
so2.cbv2.l4                 -0.0230780  0.0414628  -0.557 0.577840
so2.cbv3.l1                  0.0597653  0.1104291   0.541 0.588398
so2.cbv3.l2                  0.1164419  0.1119523   1.040 0.298365
so2.cbv3.l3                 -0.0011307  0.1518771  -0.007 0.994060
so2.cbv3.l4                 -0.1620714  0.1076844  -1.505 0.132400
so2.cbv4.l1                 -0.0106711  0.0716659  -0.149 0.881640
so2.cbv4.l2                 -0.0269358  0.0756726  -0.356 0.721898
so2.cbv4.l3                 -0.0254380  0.1003181  -0.254 0.799840
so2.cbv4.l4                 -0.0690957  0.0707578  -0.977 0.328881
no2.cbv1.l1                 -0.0544867  0.0501652  -1.086 0.277490
no2.cbv1.l2                  0.0321086  0.0505383   0.635 0.525255
no2.cbv1.l3                 -0.0337680  0.0679432  -0.497 0.619218
no2.cbv1.l4                  0.1157413  0.0508129   2.278 0.022799 *
no2.cbv2.l1                  0.0281539  0.0492771   0.571 0.567807
```

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no2.cbv2.l2                   0.0265271  0.0510940   0.519 0.603667
no2.cbv2.l3                   0.0314189  0.0663276   0.474 0.635749
no2.cbv2.l4                   0.1039874  0.0496052   2.096 0.036128 *
no2.cbv3.l1                  -0.1666180  0.1183115  -1.408 0.159132
no2.cbv3.l2                   0.2087022  0.1203854   1.734 0.083075 .
no2.cbv3.l3                  -0.0291471  0.1604221  -0.182 0.855837
no2.cbv3.l4                   0.2799515  0.1178405   2.376 0.017571 *
no2.cbv4.l1                  -0.0545403  0.1007962  -0.541 0.588477
no2.cbv4.l2                   0.1379325  0.1043397   1.322 0.186270
no2.cbv4.l3                  -0.0173810  0.1432889  -0.121 0.903460
no2.cbv4.l4                   0.1642793  0.1012649   1.622 0.104836
pm10.cbv1.l1                 -0.0407622  0.0533743  -0.764 0.445095
pm10.cbv1.l2                 -0.0517256  0.0510717  -1.013 0.311224
pm10.cbv1.l3                  0.2054219  0.0720623   2.851 0.004389 **
pm10.cbv1.l4                 -0.1512313  0.0515482  -2.934 0.003371 **
pm10.cbv2.l1                 -0.0694038  0.0512745  -1.354 0.175961
pm10.cbv2.l2                 -0.0543270  0.0506952  -1.072 0.283956
pm10.cbv2.l3                  0.0810566  0.0727806   1.114 0.265480
pm10.cbv2.l4                 -0.1532471  0.0514432  -2.979 0.002912 **
pm10.cbv3.l1                  0.0800839  0.1273213   0.629 0.529397
pm10.cbv3.l2                 -0.2573946  0.1233464  -2.087 0.036983 *
pm10.cbv3.l3                  0.4379224  0.1715185   2.553 0.010716 *
pm10.cbv3.l4                 -0.2506877  0.1233479  -2.032 0.042193 *
pm10.cbv4.l1                  0.0507315  0.1222589   0.415 0.678203
pm10.cbv4.l2                 -0.1276988  0.1284987  -0.994 0.320402
pm10.cbv4.l3                  0.2442471  0.1718410   1.421 0.155304
pm10.cbv4.l4                 -0.0219763  0.1290729  -0.170 0.864814
holiday.cbv1.l1               0.0216149  0.0139777   1.546 0.122103
holiday.cbv1.l2              -0.0389137  0.0126002  -3.088 0.002029 **
holiday.cbv1.l3              -0.0243269  0.0182945  -1.330 0.183692
holiday.cbv1.l4              -0.0253565  0.0132018  -1.921 0.054853 .
factor(dow)2                 -0.0593118  0.0221940  -2.672 0.007566 **
factor(dow)3                 -0.0739103  0.0235176  -3.143 0.001688 **
factor(dow)4                 -0.0438628  0.0237731  -1.845 0.065114 .
factor(dow)5                 -0.0746431  0.0237100  -3.148 0.001657 **
factor(dow)6                 -0.0892264  0.0235227  -3.793 0.000151 ***
factor(dow)7                 -0.0417234  0.0228870  -1.823 0.068387 .
ns(dos, df = 10 * trend_df)1  1.0053188  0.3018644   3.330 0.000876 ***
ns(dos, df = 10 * trend_df)2 -0.0733716  0.4172199  -0.176 0.860415
ns(dos, df = 10 * trend_df)3  1.0199234  0.3882061   2.627 0.008645 **
ns(dos, df = 10 * trend_df)4  0.3463243  0.4060638   0.853 0.393784
ns(dos, df = 10 * trend_df)5  0.4701391  0.3666328   1.282 0.199818
ns(dos, df = 10 * trend_df)6 -0.2401648  0.3955762  -0.607 0.543807
ns(dos, df = 10 * trend_df)7 -0.0260474  0.3533197  -0.074 0.941236
ns(dos, df = 10 * trend_df)8  1.2971209  0.3541993   3.662 0.000254 ***
ns(dos, df = 10 * trend_df)9 -0.8712522  0.3967492  -2.196 0.028160 *
ns(dos, df = 10 * trend_df)10 -0.1775152  0.4185246  -0.424 0.671486
ns(dos, df = 10 * trend_df)11 -0.1639397  0.4219056  -0.389 0.697618
ns(dos, df = 10 * trend_df)12  0.6751854  0.3725418   1.812 0.070015 .
ns(dos, df = 10 * trend_df)13 -0.5013254  0.3614264  -1.387 0.165508
ns(dos, df = 10 * trend_df)14  1.3977460  0.3488010   4.007 6.27e-05 ***
ns(dos, df = 10 * trend_df)15  0.8347699  0.3524784   2.368 0.017925 *
ns(dos, df = 10 * trend_df)16  0.0515214  0.3942280   0.131 0.896029
ns(dos, df = 10 * trend_df)17 -0.7347354  0.4198475  -1.750 0.080206 .
ns(dos, df = 10 * trend_df)18  0.2638040  0.4153546   0.635 0.525386
ns(dos, df = 10 * trend_df)19  0.4053899  0.3674312   1.103 0.269970
ns(dos, df = 10 * trend_df)20  0.9291309  0.3633743   2.557 0.010602 *
ns(dos, df = 10 * trend_df)21 -0.1141378  0.3633280  -0.314 0.753430
ns(dos, df = 10 * trend_df)22  1.2252529  0.3535204   3.466 0.000535 ***
ns(dos, df = 10 * trend_df)23  0.0883765  0.3766806   0.235 0.814518
ns(dos, df = 10 * trend_df)24  0.7963751  0.3922070   2.030 0.042382 *
ns(dos, df = 10 * trend_df)25  0.9461921  0.3956940   2.391 0.016845 *
ns(dos, df = 10 * trend_df)26  0.2515012  0.3644274   0.690 0.490161
ns(dos, df = 10 * trend_df)27 -0.3910095  0.3693294  -1.059 0.289810
ns(dos, df = 10 * trend_df)28  0.6571490  0.3495717   1.880 0.060210 .
ns(dos, df = 10 * trend_df)29  1.2016442  0.3569473   3.366 0.000770 ***
ns(dos, df = 10 * trend_df)30  0.0220232  0.4114475   0.054 0.957316
ns(dos, df = 10 * trend_df)31  0.1566382  0.3897626   0.402 0.687796
ns(dos, df = 10 * trend_df)32  0.5486411  0.3934679   1.394 0.163294
ns(dos, df = 10 * trend_df)33  0.5550475  0.3643537   1.523 0.127756
ns(dos, df = 10 * trend_df)34  0.7738539  0.3409383   2.270 0.023282 *
```

```
ns(dos, df = 10 * trend_df)35  1.1660641  0.3613343   3.227 0.001262 **
ns(dos, df = 10 * trend_df)36  0.2220552  0.3445922   0.644 0.519359
ns(dos, df = 10 * trend_df)37  0.1518120  0.4031203   0.377 0.706500
ns(dos, df = 10 * trend_df)38  1.1555986  0.3847944   3.003 0.002691 **
ns(dos, df = 10 * trend_df)39  0.4897097  0.4063586   1.205 0.228240
ns(dos, df = 10 * trend_df)40  0.4762154  0.3646694   1.306 0.191679
ns(dos, df = 10 * trend_df)41 -0.0188192  0.3872195  -0.049 0.961240
ns(dos, df = 10 * trend_df)42 -0.5647915  0.3723370  -1.517 0.129387
ns(dos, df = 10 * trend_df)43  1.7093045  0.3491602   4.895 1.03e-06 ***
ns(dos, df = 10 * trend_df)44  0.3305572  0.3981937   0.830 0.406516
ns(dos, df = 10 * trend_df)45  0.1669668  0.4079098   0.409 0.682328
ns(dos, df = 10 * trend_df)46  0.0622764  0.4056984   0.154 0.878010
ns(dos, df = 10 * trend_df)47  0.5551462  0.3660050   1.517 0.129415
ns(dos, df = 10 * trend_df)48  0.1556012  0.3755963   0.414 0.678696
ns(dos, df = 10 * trend_df)49 -0.1621871  0.3828264  -0.424 0.671842
ns(dos, df = 10 * trend_df)50  0.7622711  0.3517725   2.167 0.030307 *
ns(dos, df = 10 * trend_df)51  0.1223278  0.4180436   0.293 0.769830
ns(dos, df = 10 * trend_df)52  0.1600776  0.4078557   0.392 0.694723
ns(dos, df = 10 * trend_df)53  0.5942923  0.3955386   1.502 0.133062
ns(dos, df = 10 * trend_df)54  0.3892705  0.3768845   1.033 0.301740
ns(dos, df = 10 * trend_df)55  0.6049207  0.3440421   1.758 0.078789 .
ns(dos, df = 10 * trend_df)56  0.8654396  0.3735774   2.317 0.020582 *
ns(dos, df = 10 * trend_df)57  0.8190290  0.3483579   2.351 0.018773 *
ns(dos, df = 10 * trend_df)58  0.7551938  0.4116690   1.834 0.066670 .
ns(dos, df = 10 * trend_df)59  0.2679309  0.4124670   0.650 0.516006
ns(dos, df = 10 * trend_df)60  0.0836855  0.4071016   0.206 0.837143
ns(dos, df = 10 * trend_df)61  0.6969491  0.3738524   1.864 0.062373 .
ns(dos, df = 10 * trend_df)62  0.7025813  0.3536095   1.987 0.047014 *
ns(dos, df = 10 * trend_df)63  0.4321847  0.3711280   1.165 0.244295
ns(dos, df = 10 * trend_df)64  1.2265577  0.3530616   3.474 0.000519 ***
ns(dos, df = 10 * trend_df)65 -0.0542336  0.4122271  -0.132 0.895338
ns(dos, df = 10 * trend_df)66  0.6087704  0.4147462   1.468 0.142245
ns(dos, df = 10 * trend_df)67  1.0404031  0.4240504   2.453 0.014197 *
ns(dos, df = 10 * trend_df)68  0.6124457  0.2615844   2.341 0.019273 *
ns(dos, df = 10 * trend_df)69  0.5883909  0.7494997   0.785 0.432481
ns(dos, df = 10 * trend_df)70  0.0603472  0.1696749   0.356 0.722114
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Approximate significance of smooth terms:
                edf Ref.df     F  p-value
s(sqrt(influ)) 1.03  1.059 14.78 9.19e-05 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

R-sq.(adj) =  0.472   Deviance explained = 47.6%
GCV =  1.081  Scale est. = 0.98971   n = 3632
```