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Manuscript title: Temperature as a Risk Factor for Hospitalizations among Young Children in the Mekong Delta Area, Vietnam

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Abstract

Background: The Mekong Delta is the most vulnerable region to climate change in South-East Asia however the association between climate and children's health has rarely been studied in this region.

Objective: We examined the short-term association between daily temperature and hospital admissions for all causes, gastrointestinal, and respiratory infection among young children in the Mekong Delta area in Vietnam.

Methods: Daily paediatric hospital admissions and meteorological data were obtained from January 2008 to December 2012. A time-series approach was used with a combination of a Poisson regression and constrained distributed lag models to analyse the data. The long-term and seasonal trends, as well as other time-varying covariates, were adjusted using spline functions. The temperature-admissions relationship was evaluated by age-specific (0-2 and 3-5 year-olds) and cause of admission groupings.

Results: A 1°C increase in the 2-day moving average temperature was significantly associated with 3.4% (95%CI: 1.2-5.5), 4.6% (95%CI: 2.2-7.3), 2.6% (95%CI: 0.6-4.6), 4.4% (95%CI: 0.6-8.2), 3.8%(95%CI: 0.4-7.2) increase in hospital admissions with 0-2 year-old children, 3-5 year-old children, all causes, gastrointestinal infection, and respiratory infection, respectively. The cumulative effects of from 1-day to 6-day moving average temperature on hospital admissions were greater for 3-5 year-old children and gastrointestinal infection than 0-2 year-old children and other causes.

Conclusions: Temperature was found to be significantly associated with hospital admissions in young children with the highest association between temperature and gastrointestinal infection. The government agencies of Mekong Delta should implement measures to protect children from the changing temperature conditions related to climate change.

What this paper adds

- Previous studies indicate that temperature could be a risk factor for children hospitalizations.
- Mekong Delta area is one of the most vulnerable to climate change in South-East Asia, but there is a lack of evidence in the relationship between climate and child health.
- Our study shows a positive association between temperature and risk of hospitalizations with children under 5-year in the tropical Mekong Delta, Vietnam
- Age- and cause-specific factors are significant modifiers of the relationship between temperature and hospitalizations among young children.
- The public health programs should consider the temperature as a risk factor for preventing infection diseases among young children in urban areas.

1.0 INTRODUCTION

The effect of extreme weather events on health has emerged as a major public health threat. Every year, a significant number of hospitalizations occur in association with exposure to ambient high temperatures [1-3]. Previous studies have indicate that the predominant causes of hospital admissions associated with elevated temperature are: cardiovascular diseases [4-7], respiratory diseases [3, 8-10], and infectious diarrhoea [11-14].

Children are considered as the most vulnerable group resulting from the adverse effects of environmental hazards, including elevated temperature for several reasons. First, children

bear a greater temperature transfer between their environment and their body since they have a greater body surface area-to-mass ratio compared with adults [15]. Second, children are sensitive to temperature due to a higher metabolic rate [16]. Third, children create somewhat less cardiac output values than adults [17], and fourth, children spend more time outdoor and do more vigorous activities, leading to more exposure to outdoor extreme temperature [18]. Furthermore, children are much more dependent in terms of protection to unsafe environments. Nevertheless, effects of temperature on children have not been studied adequately [19]. A recent review by Xu et al (2012) indicated that additional studies need to be conducted to increase knowledge relating the modification roles of gender, age, and socio-economic status in the relationship between climate factors, including temperature and children health [20]. Moreover, most epidemiological studies of elevated temperature on children health have been done in Western countries and in temperate areas [21-25], but little work has been conducted in developing countries and in tropical areas.

The Mekong Delta region in Vietnam is one of the most vulnerable areas to climate change in South-East Asia [26]. Can Tho city is a tropical city in the lower Mekong Delta Basin in Vietnam where residential life is highly dependent on local meteorological factors and vulnerable to climate change. A previous investigation [27] reported that the mean temperature in Can Tho increased roughly 0.5°C from 1978 to 2008, and the temperature is projected to increase from 0.4 to2.6°C by the year 2020 and 2100 [28]. The number of days which have an average temperature higher than 35°C is also increasing. An abnormal hydrological regime (severe dry season and deeper inundation), saltwater intrusion, and more frequent extreme weather events (hurricanes, etc.) have already been observed. Moreover, some physical and social problems such as ground surface deformation, environmental pollution, rapid urbanization, unsustainable development, low socioeconomic status, limited

resources to respond to climate change and difficulties in coordination between local agencies all lead to a low adaptation capacity in residents [29].

Based on their hospital records, the Can Tho Paediatric Hospital (CTPH) has reported that the rate of hospital admissions for all causes, gastrointestinal (GI), and respiratory infection (RI) among young children has increased from 2008 to 2011, and GI and RI were the most frequent disease groups observed in the research location. However, no study of the effect of temperatures on health outcomes among children in the Mekong Delta area in Vietnam has been conducted. This study examines the relationship between temperature and hospital admissions in young children in Can Tho city: a city that is representative of the Mekong Delta area of Vietnam.

2.0 METHODS

2.1 Data collection

We collected daily paediatric hospital admissions (PHA) data from 1st January 2008 to 30th December 2011 from the Can Tho City Paediatric Hospital (CTCPH) which is the sole public hospital for children in Can Tho city. Thus, this hospital represents the majority of paediatric patients in the research location. The data collected included date of birth, date of admission, diagnosis, International Classification of Disease (ICD10), and date of hospital discharge. We cleaned the data to exclude patients who were not Can Tho residents and to collapse the data into categories by date of admission, age groups representing to home-care children (0-2 year-olds) and kindergarten-care children (3-5 year-olds), and disease groups comprising: all causes (excluding external causes of morbidity and mortality, ICD10: V01-Y98), gastrointestinal infection (ICD10: A00-09.1, and B65-B83) and respiratory infection (ICD10: J00-22).

Daily meteorological data for the same time period were obtained from the Southern Regional Hydro-Meteorological Centre. The parameters included daily mean temperature (°C), daily mean relative humidity (%), and rainfall.

2.2 Data analysis

A time-series approach [30, 31] was used to examine the relationship between temperature and PHA.

Since the research location has only a hot climate and we assumed that the daily PHA would have a Poisson distribution, for which independence of events is a necessity, we used generalised linear (Poisson) regression models allowing for over-dispersion to examine the temperature-PHA relationship. We applied the flexible spline function of the main time variables to adjust for long-term and seasonal trends, using 7 degrees of freedom per year. In order to adjust for potential nonlinear effects of humidity, we incorporated the natural smooth functions of relative humidity (3 degrees of freedom). We also included other time-varying covariates such as day of the week and rainfall as independent variables in the regression models. The daily mean temperature was then introduced into the model to evaluate its association with PHA by age- and cause-specific groups. For age groups, admissions were classified into two groups, broadly representing home-care (0-2 year-olds) and kindergarten-care (3-5 year-olds). Due to the limited number of counts for individual disease conditions, we conducted the analyses with three groups of causes, including: all causes, gastrointestinal infection (GI), and respiratory infection (RI). The model used is as follows:

$$Y_t \sim Poisson\ (\mu_t)$$

$$Log\ (\mu_t) = \alpha + \beta_1 T_{t,l} + ns(RH_t, 3) + \beta_2 RA + s\left(Time_{t,}7\right) + \omega DOW_t$$

where t is the day of the observation, Y_t is rthe observed daily PHA on day t, α is the intercept, $T_{t,l}$ is temperature at lag time t obtained from the distributed lag models, $ns(RH_t, 3)$ is a natural cubic spline with *3 df* for relative humidity, $s(Time_t, 7)$ is a flexible spline

function with *7 df* for seasonality and long-term trend, and DOW_t is the categorical day of the week with a reference day of Sunday.

In addition, the pattern of temperature-PHA relationship was examined using a polynomial regression, in which the relative risks of paediatric admission were computed using the average count of admission at the reference temperatures ranged 22-24^{o}C, as used in a previous study [32], and then the pattern of temperature-PHA risk was examined using a polynomial regression model (relative risk of hospital admission was the dependent variable, and temperature was the independent variable). Lag effects of temperature were also investigated, since the temperature is not only associated with hospitalizations on the current day but also can have an effect several days later [13, 33]. A distributed lags models (DLM) was applied to examine the lag effects of temperature for the period of 0-6 days. First, the univariate DLMs were built using the single lag day to estimate individual lag effects, in which the lag terms were modelled one at a time in the regression model. However, these different lag effects are not adjusted for each other, so as the second step, the multivariate constrained distributed lag models were developed to reduce collinearity effects due to high correlation between the lag terms by imposing some constraints on the same effect estimates of different lags which were justified by the broad patterns revealed in the univariate DLMs. Third, in addition to single-day lag models, the cumulative effects of temperature on PHA were also examined for 1-day, 2-day, 3-day, 4-day, 5-day, and 6-day using the moving average of temperatures on the current day and previous days (lag 0-1, lag 0-2, lag 0-3, lag 0-4, lag 0-5, and lag 0-6).

A sensitivity analysis was conducted to determine the optimal degrees of freedom to adjust for long-term and seasonal trend in the models, in which the tests were performed on the impact of degrees of freedom selection on the regression results. All data management and analyses were conducted using Stata 11.0 (Stata Corporation, College Station, TX, USA).

3.0 RESULTS

3.1 Admission and meteorology characteristics

The study was conducted in Can Tho city, a central area in the Mekong Delta in Vietnam. Can Tho has a population of 1,188,390 people with a population density of 842 people/km^2, and a total area of 1,411,49 km^2 [34]. Can Tho has more than 80% of communes with health clinics, however the city has an overload of patients in the provincial hospitals, especially the paediatric hospital [35]. From January 1, 2008 to December 31, 2011, a total of 1458 days of daily paediatric hospital admissions (PHA) records and weather variables were collected. The descriptive statistics for PHA were shown in Table 1. The total number of recorded PHA were 34,360, among which there were 7893, 8593, 8920, and 8957 cases recorded in 2008, 2009, 2010, and 2011, respectively. Over the 4 years studied, the number of daily PHAs ranged from 1 to 66 (mean, 23.6; sd, 7.8). 73% of admissions (25,060) were for the 0-2 years with 21.4% (7353) hospitalized for gastro-intestinal infection (GI) and 28% (9646) were hospitalized due to respiratory infection (RI).

Can Tho city is located in the tropics and has a monsoonal climate with 2 main seasons: rainy, from May to November, and dry, from December to April. During the study period, the daily mean temperature ranged from 21.5°C to 31.5°C (mean, 27.2°C; sd, 1.4), and the relative humidity ranged from 65% to 97% (mean, 82%; sd, 5.5). The number of rainfall days were 41% (599 days) of the total observed days, of which the daily cumulative rainfall ranged from 0 mm to 107 mm (mean, 3.8mm; sd, 9.6), reflecting the high rainfall during the wet season (May-November) compared with the dry season (December-April). Figure 1 shows the seasonal trends in daily mean temperature and number of daily PHAs during 2008-2011. The weather variables were moderately or weakly correlated each other (temperature-humidity, -r=-0.36; temperature-rainfall, -0.21; and humidity-rainfall, 0.47)

Table1. Daily and annual hospital admissions by age groups and causes

Day/Year	Age group		Cause		
	0-2 year-old	**3-5 year-old**	**All causes**	**Gastrointestinal**	**Respiratory**
Daily min	1	1	1	0	0
Daily mean	17	14	24	5	7
Daily max	57	57	66	17	24
2008	5850	2040	7890	1738	2159
2009	6263	2330	8593	1824	2412
2010	6386	2534	8920	2028	2754
2011	6561	2396	8957	1763	2321
Total	25060	9300	34360	7353	9646

3.2 Association between temperature and paediatric hospital admissions (PHAs)

The association between temperature lags and PHAs by age, cause of admissions, is presented in Table 2. The results show that an increase in mean temperature is positively associated with an elevated risk of PHAs on the current day and the previous day among 0-2 year-old children and a lag of one day and the previous two days for 3-5 year-old children. In terms of cause of admission, a positive statistically significant association was found between the current day and the previous day average temperature and all causes as well as gastrointestinal infection; whereas a delayed effect of temperature was found (previous 1 and 2 days) with respiratory infection. For all age- and cause-groups, the effect was larger for the current day (lag 0) compared with the previous days (Figure 2).

The results of multivariate distributed lag models, constraining the similar lag effects, indicated smaller effects of temperature on PHAs compared with the single lag models. A 1°C increase in the current day and the previous 1 day average temperature was associated with an increase of 1.7% (95%CI:0.6-2.8) and 1.6% (95%CI: 0.7-2.5) with 0-2 and 3-5 year-old PHAs, respectively. However, the delayed temperature effect was one day longer among elder children than young children. In terms of disease-groups, a 1°C increase in the current day and the previous 1 day average temperature was associated with an increase of 1.3% (95%CI: 0.2-2.3) and 2.2% (95%CI: 0.7-2.5) in the risk of PHAs for all causes and GI, while

the risk of PHAs for RI increased by 1.9% (95%CI: 0.3-3.4) corresponding to a 1°C increase in the previous 2 days (lag 1 & 2) but not the current day (lag 0) temperature. No statistically significant association between rainfall and PHAs was found in the multivariate regression models reported in Table 2.

Table 2. Age- and Cause-specific hospital admissions increase in percent per 1°C of daily temperature increase in mean, by lag period (days).

Lag	Age group				Disease group					
	0-2 year-olds		3-5 year-olds		All causes		Gastrointestinal infection		Respiratory infection	
	Increase %	95%CI	Increase %	95%CI	Increase %	95%CI	Increase %	95%CI	Increase %	95%CI
Constrained Multivariate distributed lag model[a]										
Lag 0	1.7*	0.6-2.8	1.6*	0.7-2.5	1.3*	0.2-2.3	2.2*	0.2-4.2	-0.3	-1.2-0.5
Lag 1	1.7*	0.6-2.8	1.6*	0.7-2.5	1.3*	0.2-2.3	2.2*	0.2-4.2	1.9*	0.3-3.4
Lag 2	-0.1	-0.5-0.4	1.6*	0.7-2.5	0	-0.3-0.5	0.4	-0.5-1.2	1.9*	0.3-3.4
Lag 3	-0.1	-0.5-0.4	-0.1	-0.7-0.5	0	-0.3-0.5	0.4	-0.5-1.2	-0.3	-1.2-0.5
Lag 4	-0.1	-0.5-0.4	-0.1	-0.7-0.5	0	-0.3-0.5	0.4	-0.5-1.2	-0.3	-1.2-0.5
Lag 5	-0.1	-0.5-0.4	-0.1	-0.7-0.5	0	-0.3-0.5	0.4	-0.5-1.2	-0.3	-1.2-0.5
Lag 6	-0.1	-0.5-0.4	-0.1	-0.7-0.5	0	-0.3-0.5	0.4	-0.5-1.2	-0.3	-1.2-0.5
Cumulative lag models[b]										
Lag 0-1	3.4*	1.2-5.5	4.9*	2.5-7.3	2.8*	0.8-4.7	4.9*	1.1-8.6	3.2	-0.1-6.5
Lag 0-2	2.9*	0.2-4.8	4.6*	2.2-7.3	2.6*	0.6-4.6	4.4*	0.6-8.2	3.8*	0.4-7.2
Lag 0-3	2.5*	0.2-4.7	4.1*	1.5-6.8	2.4*	0.3-4.5	4.5*	0.5-8.5	3.2	-0.4-6.7
Lag 0-4	2.3	-0.07-4.7	3.6*	0.9-6.5	2.4*	0.3-4.7	4.7*	0.5-8.9	3.3	-0.4-6.9
Lag 0-5	2.5	-0.01-4.9	4.0*	1.1-7.0	2.6*	0.4-4.9	5.5*	1.1-9.9	2.8	-1-6.7
Lag 0-6	1.9	-0.6-4.6	3.7*	0.7-6.8	2.2	-0.1-4.6	5.5*	0.9-10.1	2.3	-1.7-6.4

[a]All lag terms of temperature modelled together (with constraint), adjusted for humidity, rainfall, day of the week, seasonality and long-term trend.
[b]Moving average of temperature for 2, 3, 4, 5, 6 days. The models were adjusted for humidity, rainfall, day of the week, seasonality and long-term trend.
*Statistically significant ($p<0.05$).

In addition to the effect of single lag days, the effect of the 1-day, 2-day, 3-day, 4-day, 5-day, and 6-day moving average of mean temperature (lag 0-1, lag 0-2, lag 0-3, lag 0-4, lag 0-5, and lag 0-6) were also estimated. A 1°C increase in the 1-day and 2-day moving average was associated with a 3.4% (95%CI: 1.2-5.5) and 2.9% (95%CI: 0.2-4.8) increase in PHAs among 0-2 year-old children; whereas, the increased risk of PHAs among 3-5 year-old children (4.9%, 95%CI: 2.5-7.3; 4.6%, 95%CI: 2.2-7.3; 4.1%, 95%CI: 1.5-6.8; 3.6%, 95%CI: 0.9-6.5; 4.0%, 95%CI: 1.1-7.0; 3.7%, 95%CI: 0.7-6.8) were significantly associated with a 1°C increase of mean temperature for all moving averages (from 1-day to 6-day, respectively) of mean temperature. Similarly, the elevated mean temperature in moving average from 1-day to 5-day were also significantly associated with the risk of all-cause and GI PHAs (Table 2), however the cumulative effect was statistically significantly associated with the 2-day moving average (lag 0-2) only (Table 2).

Figure 3 shows the exposure-response curve of relative risk in daily PHA, corresponding to 1°C increase from 24°C, over the 1-day moving average (lag 0-1, the biggest significant cumulative effect of mean temperature on PHAs by age-groups). The curve indicates a linear relationship with an apparent threshold at the temperature range of 22-24°C. The t-tests comparing coefficients between regression models indicated that the magnitude of cumulative effects was significantly larger among 3-5 year-old children than that among 0-2 year-old children, and the gastrointestinal infection effect was significantly larger than that for respiratory infection (p-values<0.05). It is noteworthy that the peak of the effect among younger children (0-2 years) corresponded to the mean temperature range of 28-30°C while among elder children (3-5 year-olds) it corresponded to a longer mean temperature range (28-32°C).

Sensitivity analysis revealed that the effects of mean temperature on PHAs were not substantially influenced by a change in degrees of freedom per year (6, 5, 4, and 3) for the time trend, indicating that our findings were relatively robust in this regard.

4.0 DISCUSSION

This current study has revealed that increasing temperatures above 24°C were associated with an increased risk of hospital admissions with children under 5-year in Can Tho city. This is the first study in the Mekong Delta area and one of only a few studies that have examined the association between elevated temperatures and hospitalizations with young children in tropical areas. Moreover, this study has evaluated the modification effects of age- and cause-specific groups in the relationship between temperature and paediatric hospital admissions, and found that these factors are significant modifiers of the relationship which has rarely been investigated before. Our findings suggest that public health programs should also consider the temperature as a factor for preventing infection diseases among young children in urban areas.

The positive association found between elevated temperature and paediatric admissions for gastro-infectious diseases is consistent with that of some previous studies. In London during hot weather conditions increased the risk of having a respiratory condition among children under 5-year as compared with other groups [36, 37]. Another study revealed that elevated temperature were significantly associated with an increase in daily admissions among Chinese children (0-14 years) [38]. In this study, each 1°C increase in temperature was associated with a 3.7% increase in risk of infectious admissions and a 19.5% increase in risk of respiratory admissions. Similarly, a study in Brazil indicated that both an increase and a decrease in temperature may result in an increase in hospitalization due to pneumonia for infants [39]. For gastrointestinal infection, daily admission for diarrhoea significantly increased among Peruvian children less than 10 years during the El Nino-Southern Oscillation, and it was found that a 8% increase in the risk of severe childhood diarrhoea was significantly associated with every 1°C increase in temperature [40]. A study in sub-Saharan Africa revealed that increased monthly maximum temperature caused significant increases in the prevalence

of diarrhoea among children under 3 [41]. Likewise, Lee et al (2012) found that there was a strong positive relationship between the incidence of rotavirus gastroenteritis among children under 5-year in Taiwan and monthly temperature variation [42].

Though the previous studies suggested that both low and high temperatures were associated with respiratory admissions [3, 43, 44], the mechanism underlying the present association between high temperature and respiratory infection is unclear. A possible explanation for this relationship is that the acute episodes of high temperature are associated with airways and systematic inflammation as well as cardiovascular comorbidity, and it may be triggered by exposures to heat [3]. In addition, the warm temperature may be involved with blood flow shifts to subcutaneous areas and away from the vital organs, which could increase stress on the lung [45]. Moreover, young children's susceptibility to respiratory diseases during higher temperatures may be attributed to their undeveloped respiratory system and poor adaptation abilities [18]. Further studies need to be conducted for better understanding the threshold of temperature influencing respiratory diseases among children [20].

In terms of the association between high temperature and gastrointestinal infection, some explanations seem feasible. First, temperature is known to influence the replication and survival of pathogens that cause GI-related diseases such as diarrhoea. Hence bacteria-related gastrointestinal diseases are more likely to be more common at high temperatures and hence bacteria causing food contamination is more prevalent in summer [46] and as a consequence, food poisoning happens more often in warm weather [47]. Second, vectors, such as plankton, which carry microbes proliferate faster in warm water [13] For example, rotavirus which causes diarrhoeal diseases proliferate in warm marine waters [48] . Third, temperature may influence dietary patterns and hygiene behaviour. For instance, the increased transmission of bacteria and other pathogens can be facilitated by higher demand for water on hot days [49].

This current study adds some new dimensions and information. First, this is the first study of the relationship between temperature and paediatric hospitalizations in the Mekong Delta region, one of the most vulnerable areas to climate change in Southeast-Asia. Second, most of the previous studies in

temperature-disease relationship have grouped children into two groups: 0-5 and 6-14 year-olds but none of them further examined children less than 5. Importantly previous findings may not reflect for the potential interaction between temperature and childcare types, comprising: home-care children (0-2 year-olds) and kindergarten-care children (3-5 year-olds) as commonly found in Vietnam. Our findings found a difference in the patterns of temperature-related admission between these age groups in terms of both magnitude and time. Figure 3 shows that the exposure-response curve among home-care children (0-2 years) peaked at a temperature of 28°C (the 75th percentile of temperature) and is lower at the temperature of 30°C; whereas, the temperature affect among kindergarten-care children peaks at 29°C and remains at this higher temperature. This difference can be attributed to two possible factors. First, the home-care children (0-2 year-olds) do not have as much out-door activity as the kindergarten-care children (3-5 year-olds), parents may not take the young children out when the outdoor temperature is increasing; whereas, the elder groups may have more outdoor activities at their kindergarten settings. Second, adaptation to high temperature at home for each individual child may be more effective than in kindergarten care which usually has a large number of children. More in-depth studies should be conducted on the modification effects of temperature on young children and their care and adaption patterns to the high temperature conditions.

Some limitations are evident in this study. First, even though the study attempted to examine the relationship between cause and specific disease groups (GI, and RES) and temperature, there was a lack of data on microbiological analysis. Thus the study was unable to identify or control for microbial factors. In addition, the GI-related admissions which were not infectious diseases were not excluded or separated for the purpose of data analyses. Second, some other conditions which potentially are associated with high temperature such as renal disease, fever, electrolyte imbalance, skin infection, malaria, and hand-foot-mouth diseases [20] were not investigated in this study due to a limited number of admissions. Third, potential confounding factors such as socioeconomic status, behaviour, and air pollution which could influence the association were not evaluated in this study.

In summary, high temperatures were found to be associated with increased hospital admissions among young children in Can Tho city in the Mekong Delta area of Vietnam. As the Mekong Delta is highly vulnerable to climate change, temperatures will continue to rise in this region thus our findings have important implications for the projected health impacts on children. Better understanding the underlying mechanisms for these associations will be important for governments within Mekong Delta to design and implement programs that target preventing children from suffering the impacts of increased temperatures.

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Conflict of interest: None declared

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FIGURES

Figure 1. Raw plots showing daily counts of hospital admissions (all causes) and average temperature over time

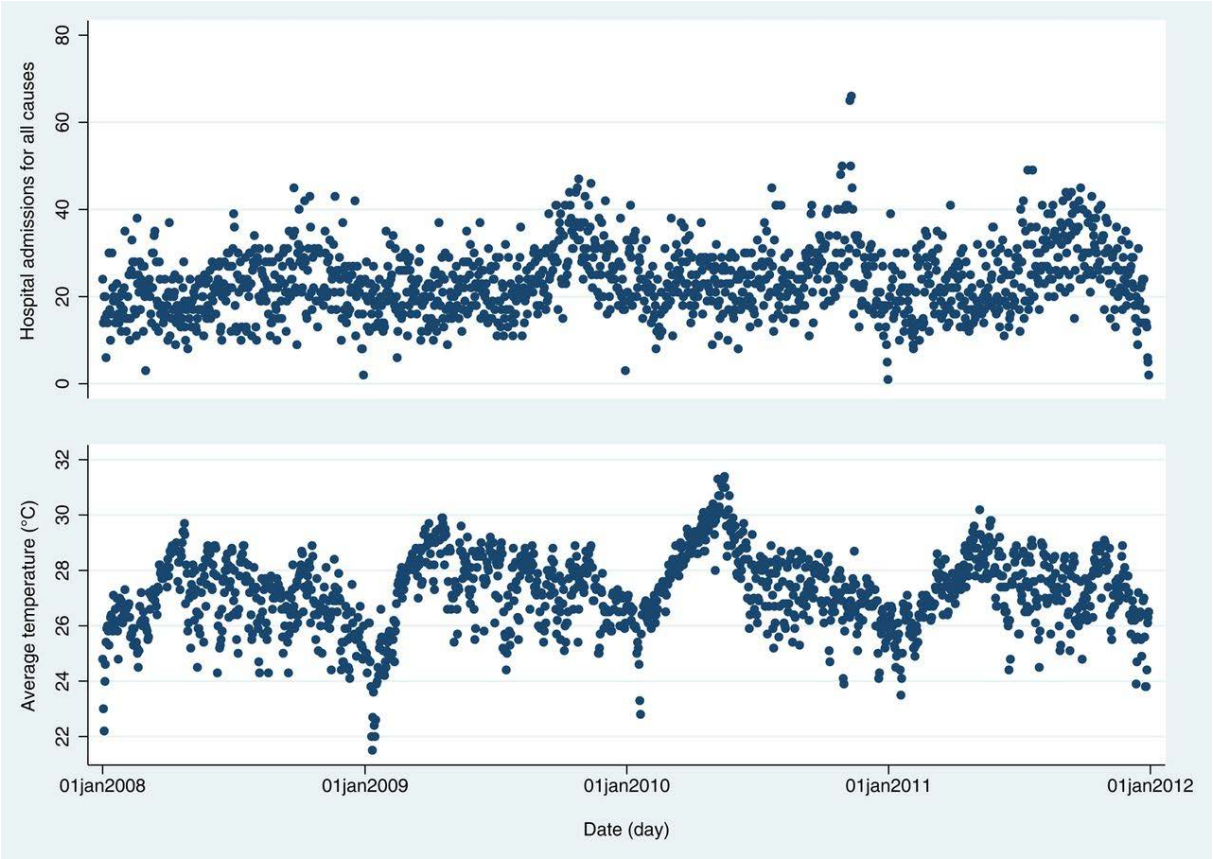

Figure 2. Relative risk for daily paediatric hospital admissions associated with a 1°C increase in mean temperature, by lag period and causes (univariate distributed lag models).

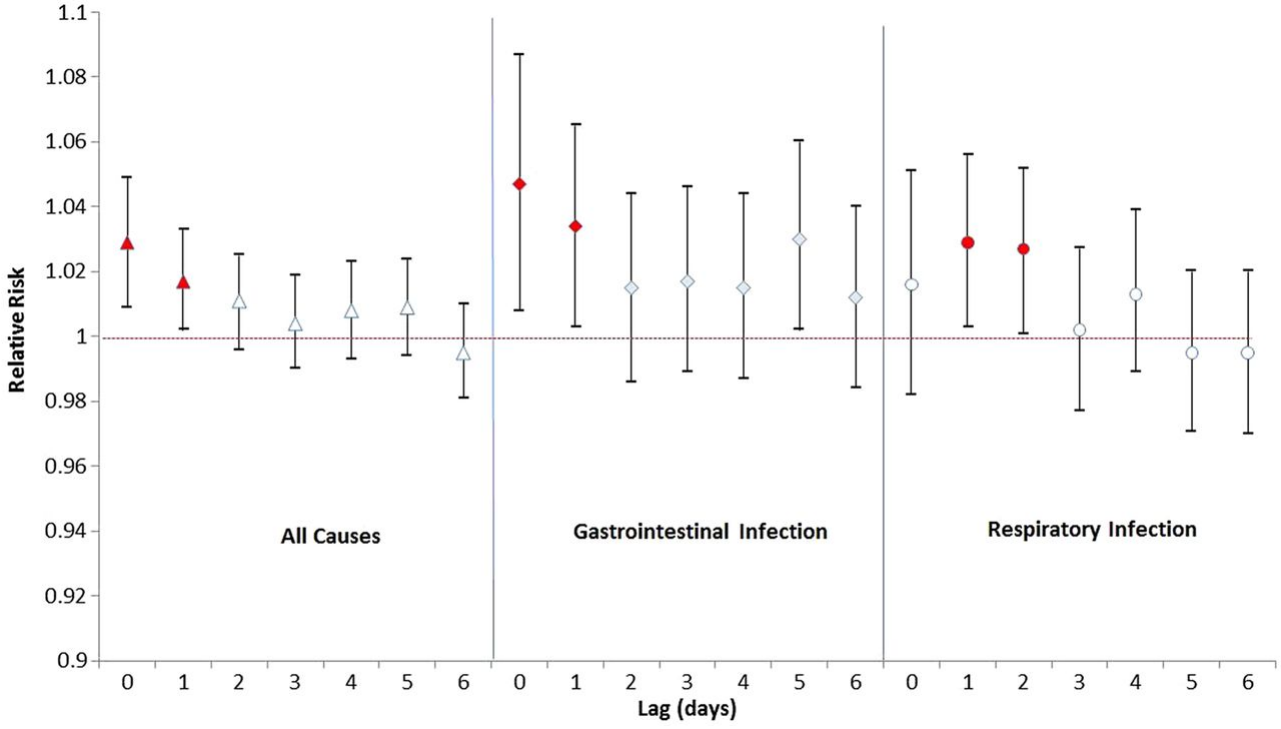

Figure 3. Relative risk (RRs) of daily paediatric hospital admissions among age groups associated with increase in daily mean temperature (compared with the baseline of 22-24°C) over lag 0-1 days. Dash lines are corresponding 95% confidence intervals