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Weather variability and paediatric infectious gastroenteritis

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SUMMARY

Investigations of the relationship between weather variability and infectious gastroenteritis (IG) are becoming increasingly important in light of international interest in the potential health effects of climate change. However, few studies have examined the impact on children, despite the fact that children are considered particularly vulnerable to climate change. We acquired data about cases of IG in children aged <15 years and about weather variability in Fukuoka, Japan from 2000 to 2008 and used time-series analyses to assess how weather variability affected IG cases, adjusting for confounding factors. The temperature–IG relationship had an inverted V shape, with fewer cases at temperatures lower and higher than ∼13 °C. Every 1 °C increase in temperature below the threshold (13 °C) was associated with a 23·2% [95% confidence interval (CI) 16·6–30·2] increase, while every 1 °C increase in temperature above the threshold (13 °C) was associated with an 11·8% (95% CI 6·6–17·3) decrease in incidence. The increase in cases per 1% drop in relative humidity was 3·9% (95% CI 2·8–5·0). The percentage increase of IG cases was greatest in the 0–4 years age group and tended to decrease with increasing age. We found a progressive reduction in weather-related IG cases in children aged >4 years. Our results suggest that public health interventions aimed at controlling weather-related IG may be most effective when focused on young children.

Key words: Children, humidity, infectious gastroenteritis (IG), temperature, weather.

INTRODUCTION

Infectious gastroenteritis (IG) is one of the most common diseases worldwide, and one of its primary symptoms, diarrhoea, causes around 1 billion disease episodes and 3 million deaths annually in children aged <5 years [1, 2]. In industrialized countries, the associated mortality is low, but morbidity remains high. Most episodes of IG are brief and do not require medical attention, but the social burden is substantial because of the high incidence. Additionally, in recent years, with growing concerns about global climate change, many studies have focused on associations between weather variability and fluctuations in the incidence of IG. Enteric diseases in temperate latitudes have been noted to have a seasonal pattern, with the highest incidence of illness during the summer

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months [3]. The incidence of IG also exhibits bimodal annual distribution in Japan [4]. The seasonality of the disease suggests that weather factors might play an important role in the incidence and indicates the possibility of multiple functional pathways.

The relationship between climate factors and IG has been studied for one pathogen or for several pathogens separately. Results from European, North American, and Australian studies have indicated that weather variables may influence the growth and dissemination of aetiological agents of IG, including *Campylobacter* [5–11], *Salmonella* [6, 12–14], *Escherichia coli* [6], and rotavirus infections [15–17]. However, few studies have focused on how this relationship affects children, despite the fact that children are considered particularly vulnerable to climate change or extreme weather events. In addition, few data are available about climate effects on all-cause enteric diseases, although studies have investigated some subsets of total incidence. Therefore, we investigated a possible relationship between weather variability and paediatric IG using surveillance data from 2000 to 2008 in Fukuoka, Japan.

METHODS

Data sources

In Japan, systematic surveillance of IG as a notifiable disease began in 1981 under the Infectious Disease Control Law. This system, organized by the Ministry of Health and Welfare, involves about 3000 sentinel medical institutions and accounts for ∼8% of the total number of paediatric hospitals and clinics throughout the entire country [18]. The number of sentinels is based on population density so that regions with populations of <30 000, 30 000–75 000, and >75 000 are assigned 1, 2, and ⩾3 sentinel institutions, respectively [18]. This study was conducted within Fukuoka Prefecture in southwestern Tokyo, Japan, where 120 sentinel medical institutions report the number of patients with IG on a weekly basis. Clinical data were recorded and reported by sentinel volunteers to the Fukuoka Institute of Health and Environmental Sciences, the municipal public health institute of the Fukuoka prefectural government.

A case of IG is defined by symptoms of a sudden stomach ache, vomiting, and diarrhoea. We analysed the data of 423 142 IG cases in children aged <15 years from 2000 to 2008 in Fukuoka Prefecture. These data were obtained from the National Epidemiological Surveillance of Infectious Diseases system, which monitors infectious disease events among the ∼5 million residents of Fukuoka Prefecture. We also obtained data on daily average temperature and relative humidity in Fukuoka Prefecture from the Japan Meteorological Agency. Weekly means for average temperatures and relative humidity were calculated from the daily records. The ethics committee of the Fukuoka Prefecture Environmental Health Research Advancement Committee approved this study on 27 December 2006 (reference number: 18-3515).

Statistical analysis

We examined the relationship between the number of weekly IG cases and temperature and humidity using negative binomial regression to account for over-dispersion in the data. To account for the seasonality of IG cases that are not directly due to the weather, the model included Fourier terms up to the sixth harmonic. Fourier terms can be used to re-create any periodic signal (such as a consistent seasonal pattern) using a linear combination of sine and cosine waves of varying wavelength. The number of harmonics defines the lowest wavelength reproduced (i.e. the level of seasonal adjustment), with six harmonics corresponding to a wavelength of 9 weeks (one-sixth of a year). Indicator variables for the years of the study were incorporated into the model to allow for long-term trends and inter-annual variations. Rainfall was also initially considered, but as there was no evidence that it was associated with the number of IG cases ($P > 0{\cdot}1$), it was not included in the final analysis. To allow for autocorrelations, an autoregressive term at order 1 was incorporated into the models [19]. Plots of model residuals, predicted and observed time-series plots, and partial autocorrelation function of the residuals (Supplementary Fig. S1, available online) suggested that this was an adequate adjustment for seasonal trends.

Temperature models

Based on our exploratory analyses, we considered lags (delays in effect) of up to 6 weeks when analysing the influence of temperature on the number of IG cases. In the initial analyses designed to identify the broad shape of any association, we fitted a natural cubic spline (3 D.F.) [20] to the average over lags of 0–6 weeks. We also included humidity as a natural cubic spline (3 D.F.) in the model to control confounding, with lags of 0–6 weeks. Because the smoothed relationships with temperature at lags of 0–6 weeks suggested an inverted 'V' shape, we then fitted the data to linear threshold models, assuming a log-linear increase in risk below the threshold and a log-linear decrease in risk above the threshold, respectively. The choice of threshold was based on maximum-likelihood estimation for temperature over a grid of all possible integer values within a range indicated on the temperature-morbidity graphs. Likelihood profile confidence intervals (CIs) for each threshold were calculated as the thresholds for which deviance of the model was 3·84 more than the minimum [21]; the model with the smallest deviance is preferred. Using the simple threshold models, we then examined lag effects in more detail by fitting linear unconstrained distributed lag models comprising temperature terms at each lag period that could be as long as 6 weeks.

Humidity models

To evaluate the impact of relative humidity, we fitted a natural cubic spline (3 D.F.) to the average humidity over lags of 0–6 weeks and incorporated this into a model with the same confounders as were included in the temperature model. The lag period was set at 0–6 weeks, as with the temperature models. Because the plots of the smoothed relationships with humidity suggested a broadly linear negative relationship, we then fitted a linear model to estimate the effect (slope) [21]. With the simple linear model, we examined lag effects in more detail by fitting linear unconstrained distributed lag models comprising humidity terms at each lag period, which could be as long as 6 weeks.

In summary, the temperature and humidity models took the following form:

$$\begin{aligned}\log[E(Y)] = \alpha &+ \mathrm{NS}(\mathrm{temp}_{0-6}, 3\ \text{D.F.})\\ &+ \mathrm{NS}(\mathrm{hum}_{0-6}, 3\ \text{D.F.})\\ &+ \mathrm{time}(\mathrm{Fourier},\ 6\ \mathrm{harmonics/year})\\ &+ i.\mathrm{year},\end{aligned}$$

where $E(Y)$ is the expected weekly case count, 'temp' and 'hum' indicate average weekly temperature and relative humidity, respectively. NS indicates a natural cubic spline function, Fourier represents Fourier (trigonometric) terms, *i*.year represents indicator variables of year.

To investigate whether the results were sensitive to the levels of control for seasonal patterns, the analyses were repeated using Fourier terms up to the 3rd and 12th harmonics per year. All statistical analyses were conducted using Stata version 11.0 (Stata Corporation, USA).

Table 1. *Characteristics of the weekly number of infectious gastroenteritis cases by age (0–4, 5–9, and 10–14 years age groups) and meteorological data in Fukuoka, Japan, 2000–2008*

Characteristics	Data
No. of weeks	468
No. of infectious gastroenteritis cases	
No. (%)	
0–4 years	270 016 (63·8)
5–9 years	120 591 (28·5)
10–14 years	32 535 (7·7)
Mean no. of cases per week	
Mean (5th to 95th percentile)	
0–4 years	577·0 (109–2487)
5–9 years	257·7 (44–1141)
10–14 years	69·5 (8–355)
Weekly mean temperatures (°C)	
Mean (5th to 95th percentile)	17·4 (6·0–29·0)
Weekly mean relative humidity (%)	
Mean (5th to 95th percentile)	65·2 (53·9–76·9)

RESULTS

We analysed a total of 423 142 (100 %) IG cases from 2000 to 2008, of which 270 016 (63·8 %) were from the 0–4 years age group, 120 591 (28·5 %) from the 5–9 years age group, and 32 535 (7·7 %) from the 10–14 years age group. Table 1 lists descriptive statistics for the number of patients and weather variables. Time-series IG had a bimodal peak in each year (Fig. 1). During the study period, major peaks occurred in winter and spring. This seasonal difference suggests that different causal mechanisms may occur, and seasonality may be varied among the primary pathogens such that norovirus and rotavirus infections tend to peak in winter and spring, respectively, in Japan [22].

Relationship with temperature

Figure 2 shows the relationships between the relative risk of IG cases and temperature. Morbidity is shown in the graph relative to the mean fitted morbidity over the observed temperature. In the crude relationship, the potential risk of IG for all age groups was highest

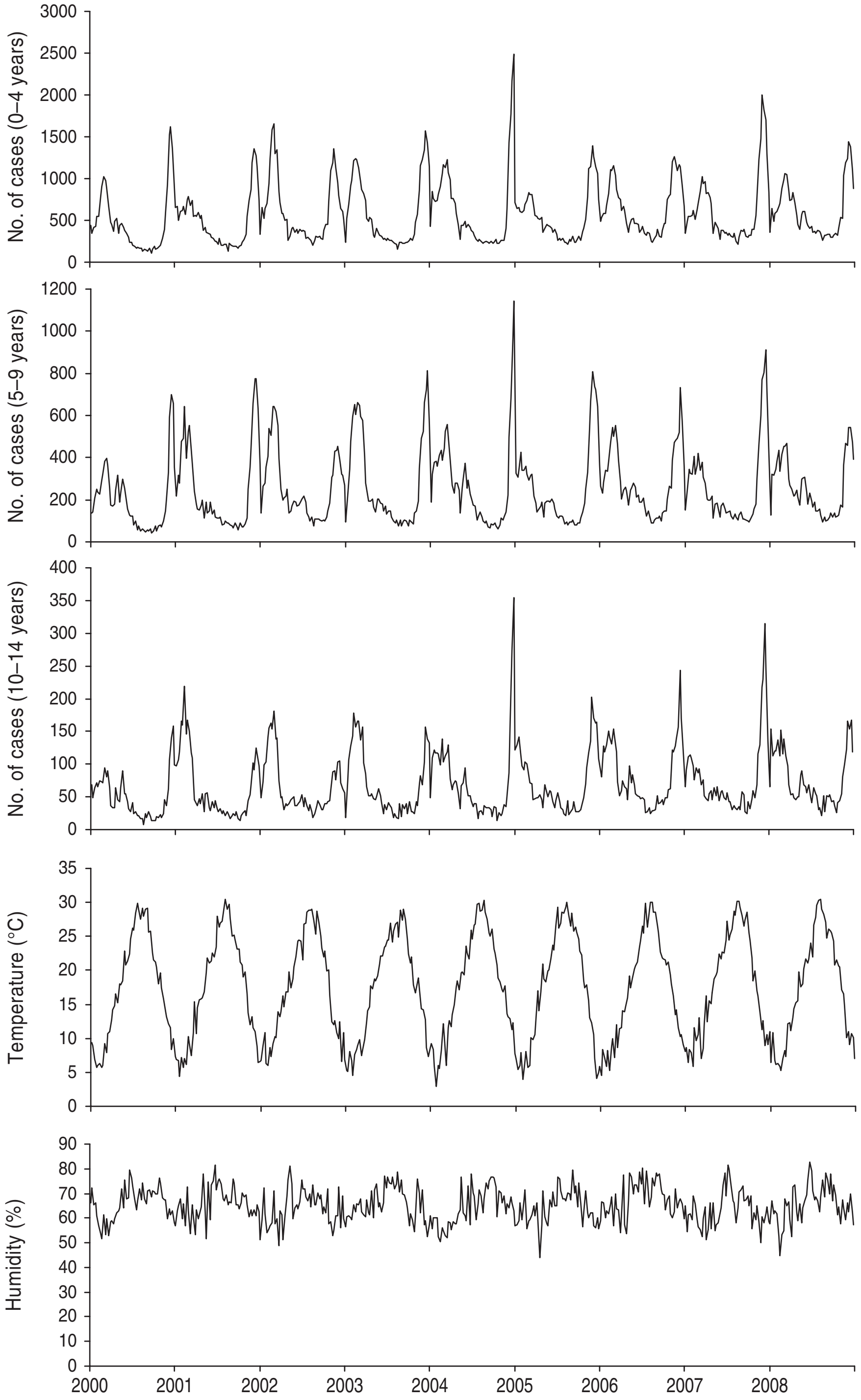

Fig. 1. Seasonal variations in the weekly number of infectious gastroenteritis cases by age (0–4, 5–9, 10–14 years age groups), temperature, and relative humidity in Fukuoka, Japan, 2000–2008.

at moderate temperatures and decreased at the extremes of temperature (Supplementary Fig. S2, online). After adjusting for seasonal, between-year, and humidity variations, the relationship between the relative risk of IG cases and temperature during a lag of 0–6 weeks was positive below and negative above the threshold (Fig. 2). The estimated threshold was 13 °C (95% CI 12–14).

For each 1 °C increase below the threshold (13 °C), the number of IG cases increased by 25·5% (95% CI 18·6–32·8) in the 0–4 years age group, by 18·5% (95% CI 12·2–25·3) in the 5–9 years age group, and

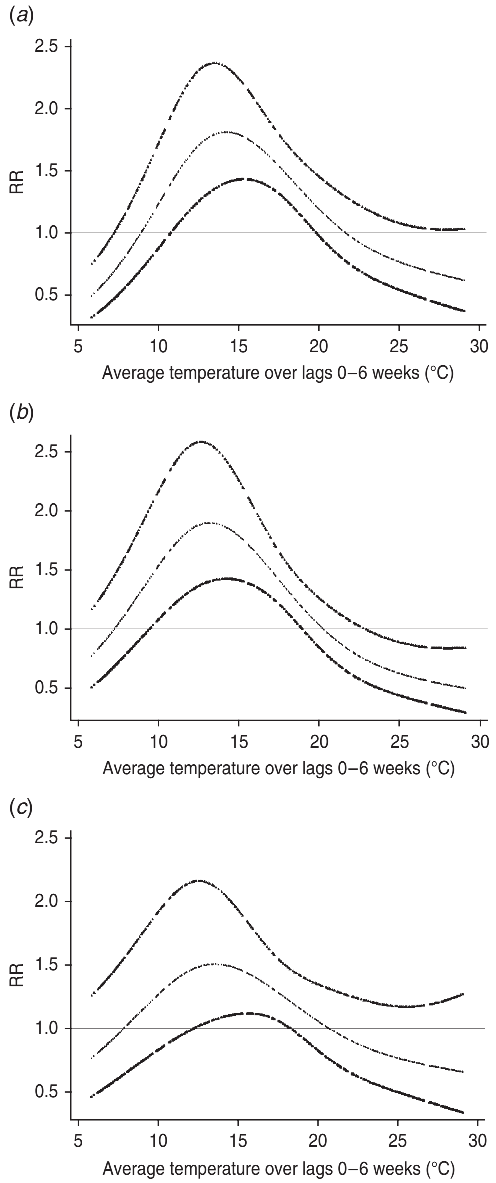

Fig. 2. Relationship between relative risk (RR) of infectious gastroenteritis (IG) (scaled to the mean weekly number of IG cases) and temperature over lags of 0–6 weeks (shown as a 3 D.F. natural cubic spline). Relationship adjusted for relative humidity, seasonal variations, and between-year variations by age: (*a*) 0–4 years age group, (*b*) 5–9 years age group, (*c*) 10–14 years age group. The centre line in the graph shows the estimated spline curve, and the upper and lower lines represent the 95% confidence limits.

by 16·1% (95% CI 8·9–23·9) in the 10–14 years age group. The percentage increase of IG cases was greatest in the 0–4 years age group and tended to decrease with increased age. In the distributed lag model, the temperature effect was significant for lags of 2, 3, 4, and 5 weeks in the 0–4 years age group, 3 and 4 weeks in the 5–9 years age group, and 3 weeks in the 10–14 years age group. Little effect was observed for the other lags (Fig. 3*a–c*).

For a 1 °C increase above the threshold (13 °C), the number of IG cases decreased by 10·8% (95% CI 5·5–16·2) in the 0–4 years age group, by 12·6% (95% CI 7·2–18·4) in the 5–9 years age group, and by 10·4% (95% CI 3·9–17·4) in the 10–14 years age group. In the distributed lag model, the effect of temperature above the threshold was negative at lags of 0–4 weeks, whereas a positive effect was observed at a lag of 6 weeks (Fig. 3*d–f*).

Relationship with humidity

Figure 4 shows the relationship between the relative risk of IG cases and humidity. Morbidity is shown in the graph relative to the mean fitted morbidity over the observed humidity. In the crude relationship, the potential risk of IG was highest around 60% relative humidity (Supplementary Fig. S3, online). After adjusting for seasonal, between-year, and temperature variations, we observed a significant increase in the number of cases of IG with a 1% decrease in relative humidity for lag periods between 0 and 6 weeks, as indicated by the negative linear slope with high humidity (Fig. 4).

For a 1% decrease, the number of IG cases increased by 4·2% (95% CI 3·1–5·3) in the 0–4 years age group, by 3·1% (95% CI 1·9–4·2) in the 5–9 years age group, and by 2·8% (95% CI 1·5–4·2) in the 10–14 years age group. The percentage increase of IG cases was greatest in the 0–4 years age group, and tended to decrease with increased age. In the distributed lag model, the effect of humidity was significant for lags of 0, 1, 2, 3, 4, and 5 weeks in the 0–4 years age group, 2, 3, 4 and 5 weeks in the 5–9 years age group, and 4 weeks in the 10–14 years age group (Fig. 5).

When we halved (three harmonics) or doubled (12 harmonics) the degree of seasonal control in sensitivity analyses, the estimated effects of temperature and humidity changed only minimally. The temperature model adjusted for humidity in the 0–14 years age group with three harmonics yielded the following values: below threshold (17·6%, 95% CI 9·8–26·0); above threshold (7·8%, 95% CI 2·2–13·7); corresponding values for 12 harmonics were: below threshold (24·4%, 95% CI 18·0–31·2); above threshold (9·8%, 95% CI 5·0–14·9). The humidity model adjusted for temperature in 0–14 years age group with three harmonics yielded 2·3% (95% CI –1·4 to 5·8);

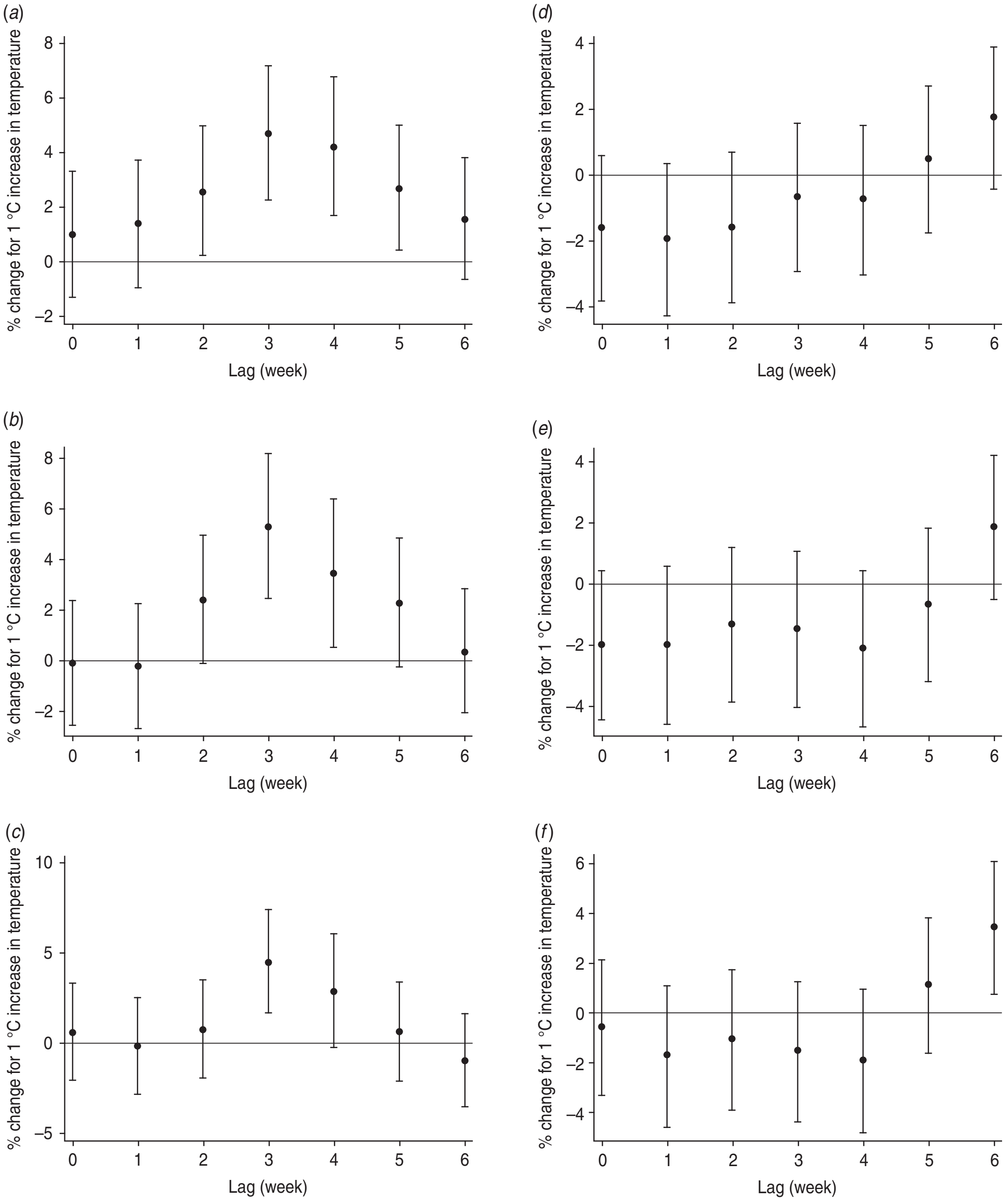

Fig. 3. Percent change (and 95 % confidence intervals) in the number of infectious gastroenteritis cases for temperature [per 1 °C increase (*a–c*) below the threshold and (*d–f*) above the threshold] at each lag (unconstrained distributed lag models) by age [(*a*, *d*) 0–4 years age group, (*b*, *e*) 5–9 years age group, (*c*, *f*) 10–14 years age group].

corresponding values for 12 harmonics were 3·8 % (95 % CI 0·9–6·7).

DISCUSSION

Our results yielded several notable findings. Most importantly, the results suggest the presence of a significant positive association between the number of IG cases and temperatures below a threshold after adjusting for potential confounding by humidity, seasonal patterns, and between-year variations. In addition, the results also suggest the presence of a significant negative association between the number of IG cases and temperatures above a threshold. An inverse association between relative humidity and the number of IG cases was also observed.

The number of patients documented weekly revealed distinct winter and spring peaks. A previous

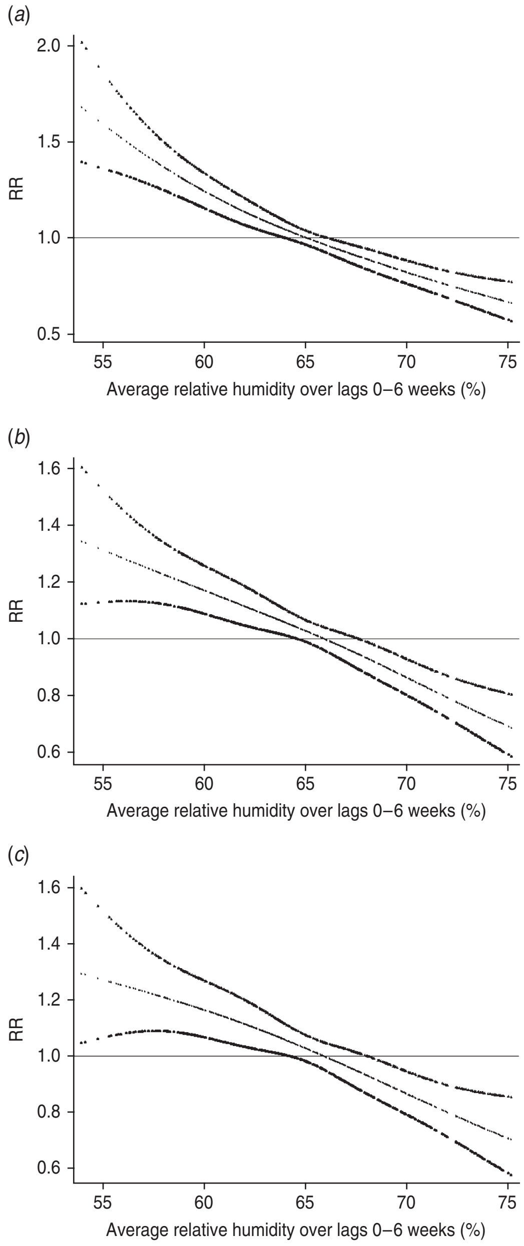

Fig. 4. Relationship between relative risk (RR) of infectious gastroenteritis (IG) (scaled to the mean weekly number of IG cases) and relative humidity over lags of 0–6 weeks (shown as a 3 D.F. natural cubic spline). Relationship adjusted for temperature, seasonal variations, and between-year variations by age: (*a*) 0–4 years age group, (*b*) 5–9 years age group, (*c*) 10–14 years age group. The centre line in the graph shows the estimated spline curve, and the upper and lower lines represent the 95 % confidence limits.

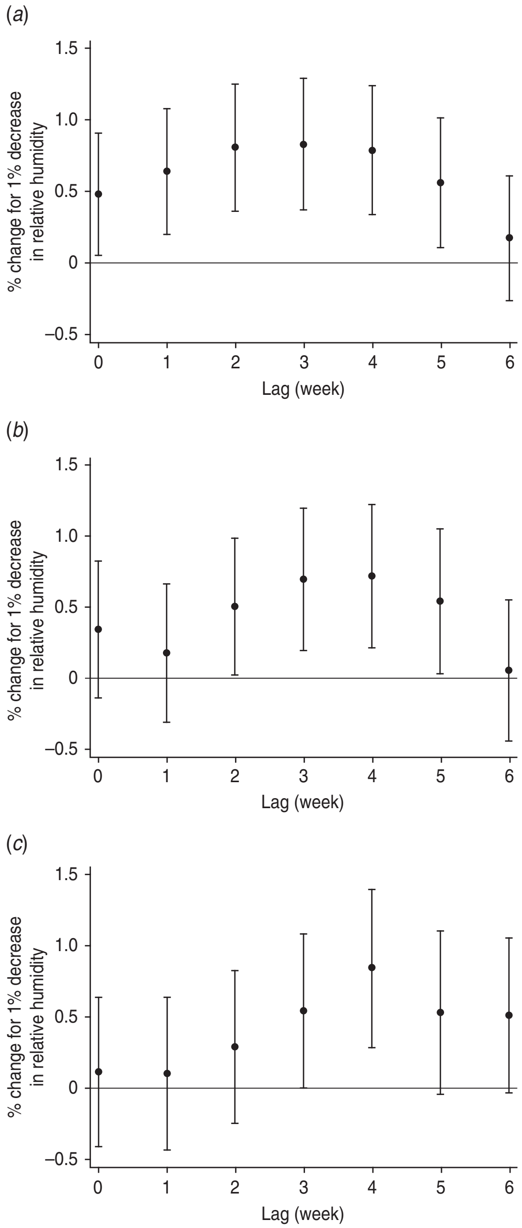

Fig. 5. Percent change (and 95 % confidence intervals) in the number of infectious gastroenteritis cases for relative humidity (per 1 % decrease) at each lag (unconstrained distributed lag models) by age: (*a*) 0–4 years age group, (*b*) 5–9 years age group, (*c*) 10–14 years age group).

study conducted in Japan found that norovirus and rotavirus were mainly detected in samples from IG patients, but the peak time of norovirus detection was earlier than that of rotavirus [23]. Moreover, several studies conducted in Japan, UK, and Canada reported that norovirus was more prevalent in the winter period [24, 25]. Thus, our results suggest that norovirus might peak in winter and rotavirus might peak in spring, which is consistent with previous findings [23–25].

The number of IG cases increased with a 1 °C increase below the threshold (13 °C); in contrast, the number of IG cases decreased with a 1 °C increase above the threshold (13 °C). These results might be due to differences in the pathogens between norovirus and rotavirus infections, as indicated by their different seasonal patterns. Previous studies have indicated that rotavirus is the leading cause of childhood diarrhoea and that at least 30–60% of hospital admissions for acute gastroenteritis in children are the result of rotavirus infection [26–30]. Moreover, several studies have suggested that more cases of rotavirus diarrhoea occur at lower temperatures [15, 17, 31]. With regard to norovirus infections, previous epidemiological studies have indicated that norovirus-associated outbreaks peak in winter, and the fewest cases of the disease (both sporadic cases and outbreaks) are reported in the warm season [32, 33]. We did not have access to information about specific pathogens of IG, which could confound the relationship between temperature and IG cases. However, our results suggest that the effects of temperature below 13 °C may be related to rotavirus infections, whereas the effects of temperature above 13 °C may be related to norovirus infections.

The inverse linear relationship that we identified between IG cases and relative humidity is consistent with previous findings in Australia [15], Peru [34], and Bangladesh [35]. Our study also revealed that the effect of relative humidity on IG was independent of ambient temperature. In Japan, a previous study suggested that rotavirus gastroenteritis was not associated with relative humidity [17]. The discrepancy could be due to the effects of seasonally varying factors and mutual confounding between weather factors, which we controlled for but the previous study did not. In addition, our finding of a negative association between cases of IG and relative humidity is more consistent with laboratory evidence. Therefore, our combined temperature and humidity results demonstrate the importance of weather variability on the prevalence of gastroenteritis infections.

When we conducted age-specific analyses, the most marked weather variability effect was observed for children aged <5 years, and the effect tended to decrease with age. A previous longitudinal study of serum antibodies to norovirus indicated that the prevalence of antibodies to norovirus was 7% in children aged <6 months; this increased to 80% in children aged 2–5 years [36]. Further, almost all children have serum antibodies to rotavirus by age 2 years, and rising antibody titres are significantly associated with increasing age [36, 37]. Finally, epidemiological longitudinal studies have indicated that the incidence of diarrhoea is highest in children aged 2–11 months, and the incidence declines progressively with age [38, 39]. Thus, our results probably reflect the acquisition of serum antibodies to norovirus and rotavirus by children as they grow and develop.

Using the distributed lag model, it would appear that the lag at 3 weeks is the strongest indicator based on temperature, but significant effects at other lags are also apparent. This could be related to the fact that temperature affects contamination earlier in the food production or distribution system [6, 12]. This suggests that temperature control during food production, processing, transport, preparation or storage may interact with ambient temperature, and thus have an impact on the risk of disease.

Methodologically, results of most previous studies extrapolating the weather–diarrhoea relationship from seasonal patterns of diarrhoea are still subject to influences by other factors that cause departures from the typical seasonal patterns. In contrast, our results are not subject to confounding bias by factors that might explain inter-annual or seasonal patterns. Although we did not have access to data about the specific causes of diarrhoea, a previous study has suggested that cases of bacterial diarrhoea increase during summer, and cases of rotavirus infections increase during winter [40]. Warmer weather may also be associated with behavioural patterns such as increased demand for water and less conscientious hygienic practices, which are known to promote diarrhoea transmission [31]. While other behavioural factors that are not related to weather variability may also affect the seasonality of diarrhoea, such as the consumption of certain foods during holidays and changes in the patterns of food availability, we had no evidence of these factors.

One possible concern is that surveillance data do not represent all cases in the community. This under-reporting can occur anywhere in the reporting chain, from the initial tendency of a patient to seek health care to the recording of the case in the disease registry. However, we have no reason to believe this would result in substantial bias, as the degree of under-reporting is not likely to vary over time. Another concern may be related to the fact that sentinel medical institutions were recruited on a voluntary basis, but this does not pose a threat to validity of the comparisons over time, which is the subject of this study.

Finally, we would like to refer to the practical implications of the present findings. Elucidation of the effects of weather variability on the epidemiology of infectious diseases is important for disease control by public health officials. The results of this study may help public health officials to predict epidemics and prepare for the effects of climate changes on the epidemiology of IG through implementation of preventive public health interventions. Such interventions might include alerting health workers, aggressive community-based campaigns to promote oral rehydration, increasing staff and the number of beds in oral rehydration units in hospitals, weather forecasts for early warning, and planning additional control programmes for IG.

In conclusion, this study demonstrated that the number of IG cases increased with temperatures below the threshold and with lower relative humidity, and the number decreased with temperatures above the threshold. In addition, it revealed that children aged <5 years are at greatest risk, and identified a progressive reduction in weather-related IG cases with age. Our findings highlight the importance of further investigations of how weather effects are associated with exposure to specific pathogens of IG.

NOTE

Supplementary material accompanies this paper on the Journal's website (http://journals.cambridge.org/hyg).

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DECLARATION OF INTEREST

None.

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