Impact of Ambient Humidity on Child Health: A Systematic Review

Jinghong Gao¹, Yunzong Sun², Yaogui Lu¹, Liping Li¹*

1. Injury Prevention Research Center, Shantou University Medical College, No. 22 Xinling Road, Shantou, Guangdong, 515041, China, 2. Department of Public Health, Shantou University Medical College, No. 22 Xinling Road, Shantou, Guangdong, 515041, China

Abstract

Background and Objectives: Changes in relative humidity, along with other meteorological factors, accompany ongoing climate change and play a significant role in weather-related health outcomes, particularly among children. The purpose of this review is to improve our understanding of the relationship between ambient humidity and child health, and to propose directions for future research.

Methods: A comprehensive search of electronic databases (PubMed, Medline, Web of Science, ScienceDirect, OvidSP and EBSCO host) and review of reference lists, to supplement relevant studies, were conducted in March 2013. All identified records were selected based on explicit inclusion criteria. We extracted data from the included studies using a pre-designed data extraction form, and then performed a quality assessment. Various heterogeneities precluded a formal quantitative meta-analysis, therefore, evidence was compiled using descriptive summaries.

Results: Out of a total of 3797 identified records, 37 papers were selected for inclusion in this review. Among the 37 studies, 35% were focused on allergic diseases and 32% on respiratory system diseases. Quality assessment revealed 78% of the studies had reporting quality scores above 70%, and all findings demonstrated that ambient humidity generally plays an important role in the incidence and prevalence of climate-sensitive diseases among children.

Conclusions: With climate change, there is a significant impact of ambient humidity on child health, especially for climate-sensitive infectious diseases, diarrhoeal diseases, respiratory system diseases, and pediatric allergic diseases. However, some inconsistencies in the direction and magnitude of the effects are observed.
Introduction

“Warming of the climate system is unequivocal”, according to the United Nations Intergovernmental Panel on Climate Change, and is expected to continue for the next several decades [1]. Even if the concentrations of all greenhouse gases and aerosols remain constant at year 2000 levels, a further warming of about 0.1°C per decade would be expected [1, 2].

Climate warming will change rainfall patterns, and increase humidity and risk of floods, although a geographical and temporal heterogeneity in the occurrence of these changes is expected [3, 4]. There is strong consensus among expert scientists that with climate change, meteorological factors (e.g. temperature, humidity) are affecting and will increasingly influence human health [5–8]. Humidity along with other weather factors can affect the incidence and distribution of infectious diseases by influencing the reproduction, development and population dynamics of vectors [9, 10]. Increasingly warm and humid climates have been observed to be associated with increasing atmospheric levels and density of aeroallergens, indicating that ambient humidity may indirectly affect the incidence and prevalence of allergic diseases [11, 12]. In addition, humidity also plays a great role in the transmission of viral diseases, such as influenza [7, 13].

Compared with adults, children are inherently sensitive to climate change because they are physiologically and metabolically less effective at adapting to ambient humidity and other weather-related exposures. Their relatively immature immune systems increase the risk of serious consequences from a variety of infectious diseases [14]. In 2000, the World Health Organization estimated that climate change contributed to more than 150,000 deaths and 5.5 million lost disability-adjusted life years worldwide and more than 88% of this burden occurs in children under the age of 5 years [15]. According to a 2012 report of the World Health Organization, pneumonia, diarrhoeal disease and malaria, all of which are climate-sensitive diseases, are three of the leading causes of death among children under age five. For example, malaria is a climate-sensitive illness to which children are particularly vulnerable, currently causing 350–500 million illnesses annually, and more than 1 million deaths, with children experiencing disproportionately high levels of both morbidity and mortality (75% of malaria deaths occur in children younger than 5 years of age) [16].

However, although pediatric health care professionals have written about the effects of climate change on child health, relatively limited research has been conducted specifically on the impact of ambient humidity on child health. To our knowledge, almost all of the studies investigating the association between climate change and child health mainly focus on temperature or rainfall, while ambient humidity is usually considered as a dispensable and alternative variable.

Additionally, to date, no systematic review has specifically focused on the relationship between ambient humidity and child health. In order to fill this knowledge gap, the primary objective of this review is to improve our understanding of how humidity, both directly and indirectly, can influence child
health and to promote additional research in this field by presenting and summarizing the findings of all relevant studies related to the impact of ambient humidity on child health.

Methods

Data sources and search strategy
Relevant peer-reviewed journal databases (PubMed, Medline, Web of Science, ScienceDirect (Elsevier), OvidSP and EBSCO host) were searched using the following MeSH (Medical Subject Headings) terms and keywords: “climate change”, “humidity”, “wet”, “dew point”, “child”, “infant”, “adolescent” and “pediatric”. The search terms and keywords were adapted to suit the requirements of each database to facilitate a comprehensive search. After selection of the full text, the references of the identified articles were reviewed and the necessary hand search was performed to recover potentially relevant studies not included in the major databases.

The search sought to identify journal articles published in English up to March 2013. In accordance with the Convention on the Rights of the Child proclaimed by the United Nations, we defined children as the group of people 0–18 years of age [17].

Inclusion criteria
The following eligibility criteria were used in this study:

- Types of studies: the present review only included peer-reviewed original articles. Thus, reviews, books, meta-analyses and conference abstracts were excluded.
- Target population: only the studies involving children between 0–18 years of age were considered.
- Research factors: only studies in which humidity was one of the exposure indicators of interest were considered.
- Outcome measures: the reported results of the included studies should have included at least one quantitative effect estimate associated with humidity. An outcome measure was reported as either: percent change, regression coefficient, correlation coefficient, relative risk or odds ratio. We also required P-values or 95% confidence intervals (CIs) to have been reported.

Study selection and data extraction
Three of the authors (Gao, Sun and Lu) independently assessed the potential relevance of all publications, identified during the database search, based on the information provided in the titles and abstracts. When reviewers disagreed, a discussion was held to obtain consensus. After screening by titles and abstracts,
the full texts of the remaining articles were then obtained and critically reviewed by the first author.

We extracted data, from the final selected references, using a pre-designed data extraction form. The quantitative estimates of each study that met the eligibility criteria were carefully retrieved and the following key characteristics were captured: study region, target population, study design, humidity exposure variable, health outcomes and adjustment of confounders. All data extraction was performed by the first author (Gao) and cross-checked by another researcher (Sun). Any errors identified were corrected through discussion among all authors.

Quality assessment
To date, the use of quality assessment tools to appraise observational studies included in systematic reviews is less well established than in reviews of randomized controlled trials, and there is no existing generally accepted quality assessment tool for observational and cross-sectional studies [18, 19]. Therefore, the STROBE method (Strengthening the Reporting of Observational Studies in Epidemiology), a guideline for reporting observational studies, was selected and adapted for our purpose to describe the reporting quality of the final identified articles [20, 21].

As in a previous systematic review, an adapted version of the STROBE checklist (Table 1) was used to create a binomial scoring system (e.g. criterion met = 1, criterion not met = 0). Final score percentages were based on the number of reporting quality criteria met divided by the number of criteria that were relevant during the quality assessment [22]. During this process, studies that controlled for potential confounding factors and included an outcome measure, such as relative risk, odds ratio or regression coefficient, were given higher quality ratings. Meanwhile, studies were given lower quality ratings if they did not include adjustment of confounders or only included outcome measures such as an estimated slope coefficient from simple linear regression or a correlation coefficient for which only the $P$-value was given. As no accepted gold standard exists for judging the quality of observational studies, in the present review we did not exclude any identified studies based on the quality assessment, which used an adapted version of the STROBE checklist.

Data synthesis
Due to heterogeneity in the target populations, outcome measures and design of studies, we did not conduct an overall summary estimate (e.g. meta-analysis). Instead, we summarized the evidence in a descriptive synthesis.

Results
A total of 3787 records were identified from the electronic database searches, and 10 additional studies were retrieved by reviewing references. After screening by
Table 1. Adapted STROBE Statement—checklist of items that should be included in reports of observational studies (including additions/adaptations for accommodating meteorological data).

| Item No | Recommendation |
|---------|----------------|
| **Title and abstract** | 1 |
| (a) Indicate the study’s design with a commonly used term in the title or the abstract |
| (b) Provide in the abstract an informative and balanced summary of what was done and what was found |
| **Introduction** | |
| Background | 2 |
| Explain the scientific background and rationale for the investigation being reported |
| Objectives | 3 |
| State specific objectives, including any pre-specified hypotheses |
| **Methods** | |
| Study design | 4 |
| Present key elements of study design early in the paper |
| Setting | 5 |
| Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection |
| Participants | 6 |
| (a) Cohort study—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up |
| Case-control study—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls |
| Cross-sectional study—Give the eligibility criteria, and the sources and methods of selection of participants |
| (b) Cohort study—For matched studies, give matching criteria and number of exposed and unexposed |
| Case-control study—For matched studies, give matching criteria and the number of controls per case |
| Variables | 7 |
| Clearly define all meteorological variables, outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable |
| Data sources | 8* |
| For each variable of interest, especially meteorological and outcome variables, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group |
| Bias | 9 |
| Describe any efforts to address potential sources of bias |
| Study size | 10 |
| Explain how the study size was arrived at |
| Quantitative variables | 11 |
| Explain how quantitative meteorological and outcome variables were handled in the analyses, including how meteorological variables were handled before using for analysis, and what kind of statistical software(s), as well as its/their version number were used to complete related statistical analysis. If applicable, describe which groupings were chosen and why |
| Statistical methods | 12 |
| (a) Describe all statistical methods, including those used to control for confounders |
| (b) Describe any methods used to examine meteorological and outcome subgroups and interactions |
| (c) Explain how missing data of meteorological variable and outcome were addressed |
| (d) Cohort study—If applicable, explain how loss to follow-up was addressed |
| Case-control study—If applicable, explain how matching of cases and controls was addressed |
| Cross-sectional study—If applicable, describe analytical methods taking account the sampling strategy |
| Item No | Recommendation |
|---------|----------------|
| (e) | Describe any sensitivity analyses |
| **Results** | |
| Participants | 13* |
| (a) | Report numbers of individuals at each stage of the study—e.g. numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed |
| (b) | Give reasons for non-participation at each stage |
| (c) | Consider use of a flow diagram |
| Descriptive data | 14* |
| (a) | Give characteristics of study participants (e.g. demographic, clinical, social) and information on exposures and potential confounders. Summarize meteorological characteristics of the study area (if applicable) |
| (b) | Indicate the number of participants with missing data for each variable of interest, especially meteorological and outcome variables |
| (c) | **Cohort study**—Summarize follow-up time (e.g. average and total amount) |
| **Outcome data** | 15* |
| **Cohort study**—Report numbers of outcome events or summary measures over time |
| **Case-control study**—Report numbers in each exposure category, or summary measures of exposure |
| **Cross-sectional study**—Report numbers of outcome events or summary measures |
| **Main results** | 16 |
| (a) | Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g. 95% confidence interval). Make clear which confounders were adjusted for and why they were included |
| (b) | Report category boundaries when meteorological or continuous variables were categorized |
| (c) | If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period |
| **Other analyses** | 17 |
| Report other analyses done—e.g. correlation analysis, analyses of subgroups and interactions, and sensitivity analyses |
| **Discussion** | |
| Key results | 18 |
| Summarise key results with reference to study objectives |
| Limitations | 19 |
| Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias |
| Interpretation | 20 |
| Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence |
| Generalizability | 21 |
| Discuss the generalizability (external validity) of the study results |

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.*

doi:10.1371/journal.pone.0112508.t001
titles and abstracts, 76 articles were selected for examination of the full text. Finally, 37 papers remained for inclusion in this systematic review (Fig. 1). Then quality assessment and data synthesis were performed to obtain the key results presented and summarized in Table 2. Among the 37 studies, 24% (9/37) involved infectious diseases, 32% (12/37) were on respiratory system diseases, and 35% (13/37) were focused on asthma and other allergic diseases. Nearly 73% (27/37) of the studies were conducted in high-income countries or regions. According to the adapted STROBE checklist, the reported quality scores ranged from 53.33% to 88.89%, with the majority of records (29/37) having scores above 70%, indicating a relatively high reporting quality of the articles. Studies using time-series analysis, Poisson regression or negative binomial regression were usually given higher scores.

**Gastrointestinal and other infectious diseases**

Studies found that ambient humidity plays an important role in the occurrence and prevalence of pediatric infectious diseases. A Brazilian study found that among the children hospitalized with community-acquired pneumonia, overall viral and Chlamydia trachomatis infections correlated with monthly mean relative humidity [23]. In Taiwan, a study identified a positive association between daily mean relative humidity and the incidence of enterovirus 71 (EV71) infections...
| Author(year)\(^a\) | Study region | Target population | Study design and analysis method | Humidity | Target outcome | Statistical indicator and effect estimate | Adjustment for confounding factors (quality score%) |
|-------------------|--------------|-------------------|---------------------------------|----------|----------------|----------------------------------------|---------------------------------------------|
| YÜKSEL et al. \(^b\) (1996) [47] | Izmir, Turkey | 21 children | Descriptive study, Daily | Total daily | \( r = 0.578 \) | No adjustments | 53.33 |
| Guo et al. \(^b\) (1999) [48] | Taiwan | 331,686 | Descriptive study, Daily | Asthma | Boys: \( R^2 = 0.57 \), \( \beta = 0.37 \) | Adjusted for age, history of atopic eczema and parental education | 64.29 |
| Checkley et al. \(^b\) (2000) [31] | Lima, Peru, | 57,331 children | Time-series study, Daily mean | Daily hospital | \( RR = 0.97 \) | No adjustments | 71.43 |
| Weiland et al. \(^b\) (2004) [53] | Western Europe | Children aged | Multilevel linear, Monthly mean | Prevalence rates | 1) 13–14 years old children: \( \beta = 0.13 \) (95% CI:0.04–0.23), adjusted for gross national product per capita (GNP) 2) 6–7 years old children: \( \beta = 0.09 \) (95% CI:0.02–0.15) | Adjusted for gross national product per capita (GNP) | 60.00 |
| Hashimoto et al. \(^b\) (2004) [55] | Tokyo, Japan | 5559 children | Multiple logistic, Daily mean | Number of emergent | \( \beta = 0.075 \), adjusting for calendar month and day of the week | No adjustments | 74.07 |
| Viegas et al. \(^b\) (2004) [33] | Buenos Aires, Argentina | 18,561 children | Spearman's rank, Monthly mean | Respiratory viruses | No adjustments | 62.96 |
| Lapeña et al. \(^b\) (2005) [34] | Leon, Spain | 167 children | Case-control study, Weekly | Admission with lower \( r = 0.15 \), \( P = 0.045 \) | No adjustments | 72.41 |
| Author(year)a | Study region | Target population | Study design and analysis method | Humidity | Target outcome | Statistical indicator and effect estimate | Adjustment for confounding factors | Reporting quality(%) |
|--------------|--------------|-------------------|---------------------------------|----------|---------------|------------------------------------------|----------------------------------|---------------------|
| Priftis et al. b (2006) [44] | Athens, Greece | 18950 children aged 0–4 years | Multiple regression analysis | Monthly mean | Admission rates for asthma | $\beta = 1.106, P < 0.05$ | 75.86 |
| Al-Toum et al. b (2006) [35] | Amman, Jordan | 200 Children aged under 2 years | Descriptive study | Relative | Prevalence of RSV | $r = 0.86, P < 0.05$ | 62.96 |
| Xirasagar et al. b (2006) [52] | Taiwan | 27275 Children aged 0–14 years | Cross-sectional study | Relative | Admission rates | $r = -0.290, P < 0.01$ | 70.97 |
| Ye’ et al. b (2007) [28] | Kossi, Burkina Faso | 676 children aged 6–59 months | Descriptive study | Daily mean | Incidence of clinical | $\beta = -23.2151$ | 75.86 |
| Kurt et al. b (2007) [45] | Turkey | 25843 children aged 6–15 years | Cross-sectional study | Relative | Allergic diseases | Adjusted for age, rural/urban sex, | 78.57 |

Note: RSV = Respiratory Syncytial Virus; ARIMA = Autoregressive Integrated Moving Average; OR = Odds Ratio; CI = Confidence Interval.
| Author(year) and period | Study region | Target population | Study design and analysis method | Humidity | Target outcome | Statistical indicator and effect estimate | Adjustment for confounding | Reporting quality % |
|-------------------------|--------------|-------------------|---------------------------------|----------|---------------|-------------------------------------------|--------------------------|------------------|
| D’Souza et al. (2008) b | 3 Australian cities 0–5 years | Time–series study and log-linear | relative humidity | Weekly mean | Weekly admissions | IRR 0.98 (95% CI: 0.97–0.99) | Adjusted for trend, previous season and period | 76.00 |
| Omer et al. (2008) b | Lombok island, aged 0–2 years | Negative binomial regression and relative humidity | Daily mean | Daily number of RSV cases | IRR 1.06 (95% CI: 1.03–1.10) | No adjustments | 85.71 |
| Noyola, D. E. and Mandeville, P. B (2008) b | San Luis Mexico, aged 0–18 years | Regression | Weekly mean | Weekly number of RSV cases | β = 0.035, P = 0.0027 | Temperature, light precipitation | 61.29 |
| Nastos et al. (2008) b | Athens, Greece 0–4 years | Poisson GLM regression | Monthly mean | Monthly number of childhood asthma | β = 0.0273, P < 0.0001 | No adjustments | 76.92 |
| Lee et al. (2008) b | Taiwan 1995–1996 children aged | Cross-sectional study and Logistic regression | Monthly mean | Prevalence of flexural eczema | (95% CI: 1.04–1.27) | Adjusted for age, parental education | 78.13 |

...
| Author(year)a | Study region | Target population | Study design and analysis method | Humidity | Target outcome | Statistical indicator and effect estimate | Adjustment for Reporting and confounding factors | Quality(%) score |
|--------------|--------------|------------------|---------------------------------|----------|---------------|------------------------------------------|-----------------------------------------------|----------------|
| du Prel et al. b (2009) [40] | Mainz, Germany aged 0–16 years 2001–2006 | Multiple time series analysis humidity | Mean | Hospitalization | Human rhinovirus | Correlations among meteorological parameters were controlled for | 77.78 |
| Murdoch and Jennings (2009) [41] | Christchurch, New Zealand Children aged <5 years 1995–2006 | Ecological study, monthly incidence rates of IRR, regression analysis daily mean 9am humidity >75% 1-month lag | | Incidence rates of | IRR=1.87, P=0.04 | No adjustments | 80.77 |
| Mireku et al. b (2009) [51] | Detroit, America Children aged 1–18 years 2004–2005 | Time-series study, intraday additive model change | | The counts of | β=0.10, P=0.04 | Adjusted for | 73.08 |
| Charland K. M. et al. b (2009) [57] | 37 paediatric hospitals in USA 2000–2005 | Bayesian hierarchical dew point of influenza visits (95% CI: 1−0.20 to 0.031) | | The peak week | β=−0.085, | Population type, latitude, longitude, solar radiation and temperature | 74.19 |
| Garcia-Marcos et al. (2009) [50] | Coastal areas, Spain Children aged 6–7 years and 13–14 years 1994–2002 | Poisson regression mean relative humidity | | Adjusted prevalence | (95% CI: 1.12–1.46) | No adjustments | 81.48 |
| Connelly et al. b (2010) [59] | Kansas, USA 25 children | Multilevel model daily thrice | | Probability of | β=0.02, P=0.01; | Controlling for | 74.07 |
| Author(year) | Study region | Target population (number, age) | Study design and analysis method | Reported humidity variable | Reporting and effect estimate | Statistical indicator | Adjustment for confounding factors | Reporting quality (% score) |
|-------------|--------------|---------------------------------|---------------------------------|---------------------------|-----------------------------|---------------------|-------------------------------|---------------------------|
| Chou et al. (2010) | Taiwan | 290331 children Time-series study, Poisson regression | Monthly mean humidity | Changes in the child’s relative humidity | OR | 5.02 | -0.033, P = 0.004 | 84.62 |
| Tchidjou et al. (2010) | Cameroon, 1306 children | Time-series, Monthly mean humidity | Relative number of diarrhea (no lag) | Relative changes in the child’s monthly morbidity | Adjusted for seasonality and trend, and autocorrelation | IRR | Adjusted for 80.00 |
| Konstantinou et al. (2011) | Greece | 180 children | Correlation | Monthly mean humidity | Adjusted for 72.00 |
| Zacarias, Majlender (2011) | Mozambique, 42185 children | Time-series | Bayesian hierarchical models | Monthly mean humidity | Adjusted for 94.00 |
| Loh et al. (2011) | Singapore | 42185 children | Time-series | Monthly mean humidity | Adjusted for 94.00 |
| Author(year)a and period | Study region | Target population (number, age) | Study design and analysis method | Humidity | Target outcome | Statistical indicator and effect estimate | Adjustment for confounding factors score | Reporting |
|-------------------------|-------------|---------------------------------|---------------------------------|----------|---------------|--------------------------------------------|----------------------------------------|-----------|
| Onozuka, Hashizumeb (2011) | Fukuoka, Japan | almost aged 0–5 years, and Relative upper and lower 2003–2008 | ARIMA model | humidity | respiratory tract | 2) LRT: β=−0.760, Information Criterion | the lowest Akaike’s Information Criterion | 25 |
| Arnedo Pena et al. b (2011) | Spain | Japan aged<15 years, Negative binomial Relative 1% 2000–2008 | Logistic regression, Mean | humidity | increase in humidity for 0–2 weeks lag | inter-annual variations, | 56 |
| Onozuka, Hashizumeb (2011) | Fukuoka, Japan | 61736 children, Relative 2000–2010 | Time-series study, Weekly mean | Number of hand, foot, and mouth disease | % change: 1% increase in humidity with 0–3 weeks lag | Adjusting for seasonal, | 27 |
| Onozuka, Hashizumeb (2011) | Fukuoka, Japan | 423142 children, Relative 2000–2008 | Time-series study, Weekly mean | Number of infectious gastroenteritis per 1% | % change: 3.9%, | Adjusting for seasonal, | 26 |

Note: a) indicates authorship details, b) indicates study methodology, and Table 2. Cont. indicates continuation of data from previous page.
| Author(year) | Study region | Target population | Study design and analysis method | Humidity | Target outcome | Statistical indicator | Adjustment for confounding factors | Reporting quality(%) |
|-------------|--------------|------------------|----------------------------------|----------|---------------|----------------------|-------------------------------------|----------------------|
| Wang et al. (2012) | 15 states | 1459 children | Multivariable | Daily mean | Hospital admission | OR=0.9, P=0.04 | Adjusting for pressure | 76.67 |
| | in USA | <2 years of age | logistic regression | dew point | (95% CI: 0.8–0.996) | altitude, wind speed, and temperature | | |
| Khor et al. (2012) | Kuala Lumpur, aged 0–5 years | 10269 children | Multiple | Monthly mean | Monthly number of respiratory syncytial virus cases | β=-1.070, P=0.001 | No adjustments | 74.07 |
| Chang et al. (2012) | Taiwan | 1914 children | Case-crossover | Daily mean | Incidence of Enterovirus 71 | IRR=1.08, P<0.001 | Adjusted for seasonal, temporal trends and annual variations | 68.97 |
| Turkish Neonatal (2012) | Turkey | 3464 children | Correlation analysis | Monthly mean | Hospitalization with r=0.627, P<0.001 | Trends and seasonality | 73.08 |

**Abbreviations:** GAM, generalized additive model; GLM, generalized linear models; ARIMA models, autoregressive integrated moving average modeling; r, correlation coefficient; β, regression coefficient; R², coefficient of determination; RR, relative risk; OR, odds ratio; IRR, incident rate ratio; CI, 95% confidence interval; RSV, human respiratory syncytial virus; IA, influenza virus A.

*These included articles are ordered by the date of publication and the first word of their titles.

*In these studies there is more than one meteorological factor that was investigated and analyzed, respectively or simultaneously.*

*[N]: N is the specific citation number of the related study included in the present review.*

doi:10.1371/journal.pone.0112508.t002
among children under 15 years of age (IRR = 1.08, 95% CI: 1.05–1.10), with seasonal and annual trends being controlled [24].

In Japan, one study indicated that for each 1% increase in the weekly mean relative humidity, the number of mumps cases increased by 1.4% (95% CI: 0.5–2.4%) among children [25]. In another Japanese study, the weekly number of hand, foot, and mouth disease cases increased by 4.7% (95% CI: 2.3–7.1%), in children between 0–4 years of age, for each 1% increase in relative humidity [26]. An additional study investigated the relationship between weather variability and infectious gastroenteritis (IG) in children. However, the results indicated that for every 1% decrease in weekly mean relative humidity, the number of IG cases increased by 3.9% (95% CI: 2.8–5.0%) [27].

Existing studies suggest that ambient humidity has a significant impact on malaria risk and diarrhoeal diseases among children. A prior study found that the clinical malaria risk increased non-linearly with the increase in mean relative humidity of the previous month [28]. A Mozambican study reported that humidity was a significant predictor of malaria incidence, with every additional 1% increase in relative humidity level leading to a 5% increase in risk of malaria incidence [29]. In Taiwan, a study examining the relationship between climate variations and diarrhea-associated morbidity found that there was a significant negative correlation between relative humidity and the morbidity of diarrhea in 0- to 14-year-old children (β = −0.033, P = 0.004) [30]. Another study performed in Peru indicated that an increase of 1% in mean relative humidity was associated with a 3% decrease in the number of diarrhoeal admissions [31]. The results of an Australian study showed that higher humidity in the previous week was associated with a decrease in rotavirus diarrhoeal admissions among children hospitalized for rotavirus diarrhoea after controlling for season [32].

**Respiratory system diseases**

Many pediatric respiratory system diseases are sensitive to relative humidity. An Argentinean study reported that respiratory syncytial virus (RSV) and influenza virus A had a positive correlation with mean monthly relative humidity among children hospitalized due to acute lower respiratory viral infections [33]. Another study found that low absolute humidity presented a protective effect on the admission of infants who had lower respiratory tract infection (LRTI) due to RSV [34]. In a study conducted in Jordan, a significant positive correlation between the prevalence of RSV infection and relative humidity was identified among hospitalized children [35]. A similar study in Indonesia indicated that for children hospitalized with clinical pneumonia, a 1% rise in mean relative humidity was associated with a 6% increase in RSV cases [36]. An additional study of children hospitalized with LRTI in Turkey reported that the number of RSV infection cases positively correlated with relative humidity, similar to results reported by Noyola and Mandeville for Mexico [37, 38]. Another retrospective study was performed in Malaysia to investigate the viral etiology of children who were admitted with viral
respiratory tract infections. However, the results showed that monthly RSV cases were inversely correlated with relative humidity [39].

In Germany, a study found that human rhinovirus positively correlated with relative humidity among children who were hospitalized with acute respiratory tract infections (ARIs) [40]. Another study in New Zealand showed that the number of days per month with a mean 9 AM humidity >75% positively correlated with the incidence of invasive pneumococcal disease in children [41]. The results of a study in Cameroon showed that high relative humidity was directly associated with an increase in the frequency of hospitalization from ARIs [42]. However, in one Singapore study, of 42155 children presenting in the hospital with one of five common paediatric diseases, both upper respiratory tract infections and LRTI were negatively correlated with relative humidity [43].

Dermatopathy and pediatric allergic diseases
Childhood asthma and other pediatric allergic diseases are important adverse consequences of humidity. In Greece, the results of a study showed that relative humidity was an implicated meteorological variable for younger asthmatic children [44]. A study performed in fourteen cities in Turkey found that asthma, wheezing and allergic rhinitis were associated with higher mean yearly outdoor humidity among school children [45]. Another study reported an interesting finding that relative humidity was significantly associated with the incidence of acute urticaria in childhood. However, the humidity accounted for different effects in the two study cities. Specifically, decreasing incidence was found for humidity increases in Norwich, Britain, while the inverse was observed in Heraklion, Greece [46].

In one Turkish study of 21 bronchial asthma children, results indicated that increasing relative humidity leads to an increase in total daily complaints of asthma patients [47]. A study reported that winter humidity was positively associated with the prevalence of asthma in Taiwanese middle-school students [48]. A positive relationship between mean monthly relative humidity and childhood asthma admissions (CAAs) was reported in Greece. For this study, a 10% increase in humidity was related to a 31% increase in the probability of having a CAA [49]. In addition, an analysis, carried out exclusively within the coastal region of Spain, showed that relative humidity constituted a significant risk factor for wheezing in both the 6–7 and 13–14 age groups [50]. A retrospective study performed in America indicated that a 10% intraday increase in humidity one or two days before admission was associated with approximately 1 additional emergency department visit for asthma [51].

On the contrary, a study in Taiwan indicated that relative humidity was negatively correlated with asthma admission rates of pre-school and school-age children [52]. In Western Europe, a positive relationship between the lowest monthly mean relative humidity and prevalence rates of asthma symptoms was found among children [53]. Another similar study conducted among school children in Taiwan indicated that the lowest monthly mean relative humidity is
positively related to eczema [54]. An additional study conducted in Japan reported that the number of emergency visits for childhood asthma per night increased significantly when climate conditions showed a rapid decrease from higher humidity [55]. A study in Spain also showed that relative humidity was negatively associated with asthma in the 13–14 age group [56].

Others
Dew point, another measure of ambient humidity, is the temperature at which water vapor in the air becomes saturated and water droplets begin to form. To date, relative humidity and dew point are two widely used indicators for the amount of moisture in air. Accordingly, some other studies also investigated the association between ambient humidity and child health by choosing dew point as the indicator. A negative association between the peak week of child-related influenza visits and dew point was reported by Charland and colleagues, although the relationship was not significant [57]. In another study, Wang et al. found that a higher dew point was associated with a lower risk of hospital admission among children [58].

In addition, ambient humidity may also play a role in other diseases among children. For instance, the results of an American study showed a positive association between relative humidity and the likelihood of headache among children [59].

Discussion
The purpose of the present systematic review was to summarize key findings related to the effects of ambient humidity on child health, and identify the relationship between humidity exposure and common pediatric diseases. The systematic review of the 37 included publications performed herein demonstrates that ambient humidity generally plays a significant role in the incidence and prevalence of childhood climate-sensitive diseases, especially for gastrointestinal, respiratory system, and allergic diseases. Considering the expected continuation of climate change, the adverse influence of ambient humidity on children may become increasingly serious. However, some inconsistencies or even contradicting directions and magnitudes of the effects were also observed.

Almost 73% of the final included studies were conducted in high-income countries or regions, indicating that more attention should be paid to the developing countries of Asia and Africa. Because of low-income, a large population and poor infrastructure, people in these countries are usually more vulnerable to climate-sensitive diseases. The results of the quality assessment indicate that the combined application of advanced statistical methods, such as time-series analysis combined with Poisson regression, usually tends to provide more reliable results (higher quality ratings), since adjustments could be made for potential confounders, including long-term trends, seasonality and air pollution.
Impact of ambient humidity on child health

Because of their physiologic, metabolic and cognitive immaturity, and greater sensitivity to certain exposures, children are often the most vulnerable to adverse health effects from environmental hazards [14, 16]. In addition, more expected future years of life will expose them to newly developing or worsening environmental hazards [7]. In general, child vulnerability to environmental hazards (e.g. humidity) can be potentially explained by their unique modality of physiological, metabolic, behavioral, and self-care ability [60, 61]. Therefore, with global climate change, children are likely to suffer disproportionately from weather factors [60, 62]. It is thought that if children are adversely affected by meteorological factors (e.g. humidity), their long-term health may also be adversely impacted [63].

Findings from the present review suggest that the occurrence and prevalence of childhood climate-sensitive infectious diseases are significantly associated with ambient humidity. It is predicted that climate change will lead to more frequent and abundant rainfall, increasing temperature and higher concentrations of water vapor, which will cause favorable conditions of ambient humidity and concomitantly favor increases in the occurrence and development of infectious diseases [3, 4, 10]. For example, ambient humidity together with temperature can influence the population dynamics of vectors, persistence and survival of pathogens, seasonal activity of microorganisms, and duration of the life cycle of parasites, and therefore impact the occurrence and prevalence of various infectious diseases [10, 63, 64].

Ambient humidity can affect tick abundance and seasonal tick activity. It has been reported that the host seeking activity of I. ricinus depends on the relative humidity, and below a relative humidity threshold of 86%, the tick dehydrates and cannot continuously seek a host [65, 66]. In Sweden, a study found that the number of days with levels of relative humidity above 86% correlates positively with the incidence rate of erythema migrans [67].

For gastrointestinal infectious agents such as rotaviruses and EV71, changes in ambient humidity have been reported to facilitate viral resistance, thereby enhancing the virulence and increasing the efficiency of transmission through contaminated air, fomites and environmental surfaces [68, 69]. A laboratory-based study suggested that the stability of enteroviruses in external environmental conditions is dependent on temperature and humidity, and another study reported that raising the relative humidity to 80% results in a rapid loss of infectivity, suggesting that humidity might be an important environmental determinant of rotavirus infectivity [68, 70]. This perhaps can explain why the relative humidity has a linear inverse relationship with the number of cases of rotavirus diarrhea previously reported in a study of 3115 rotavirus diarrhoea cases in 0- to 2-year-old Bangladesh children [71]. However, a study performed in China suggested that the number of hand, foot, and mouth disease infections is positively correlated with ambient humidity [72].

Malaria is a climate-sensitive vector-borne illness. Meteorological factors (e.g. temperature, humidity) have considerable impact on Anopheles vector abundance
and the extrinsic cycles that the parasites perform inside mosquitoes. Thus, meteorological factors may affect malaria incidence and constitute driving forces for malaria epidemics [73]. A study in China suggested that moderate temperature and relative humidity increase the longevity of the adult mosquito so that it can transmit infection for a longer period of time [74]. In India, a study found a higher positive correlation between monthly malaria parasite incidence and ambient humidity [75].

Many studies demonstrate the effects of relative humidity on pediatric respiratory tract infections. In tropical and subtropical areas (e.g. Singapore, Malaysia), it has been suggested that high humidity and temperature prolong the activity and stability of microorganisms in large-particle aerosols, and permit year-round transmission of the microorganisms [5, 76]. A study reported that relative humidity is positively associated with RSV activity, with more RSV infection occurring when humidity increases [77]. However, a converse conclusion was found in an Argentinean study, which concluded that humidity provides a protective effect against respiratory infections [78].

The possible effects of ambient humidity on childhood asthma and other allergic diseases are of particular concern due to this population’s greater susceptibility. Meteorological factors (humidity, temperature) can influence both biological and chemical components of air and might induce negative effects on respiratory allergic diseases. With climate change, ambient humidity is likely to impact asthma, hay fever and other allergic diseases via its influence on the concentration and distribution of pollens, mould spores, house dust mites, and other aeroallergens [79, 80]. Moreover, changes in the outdoor humidity, resulting from climate change, is important not only because of its own effects, but also because of its influence on indoor humidity, which results in infestation of homes with house dust mites, growth of fungal spores and home dampness, and is associated with the incidence of allergic diseases [12, 79, 81]. A study conducted among school children in Spain indicates that humidity significantly influences the occurrence of atopic eczema [82]. Youssefagha and colleagues indicate that upper-air relative humidity ≥50% and higher dew point (>−1.9) are significantly associated with exacerbation of asthma among children [83]. Another study performed in Japan also suggests that asthmatic children frequently visit the emergency department during early mornings with high absolute humidity [84].

However, in this review, some studies also report a negative association between ambient humidity and pediatric allergic diseases [52, 56]. The reasons for the inconsistencies among different studies are possibly due to regional differences and local characteristics, such as geographical environment, type of climate, vegetation condition, air quality, socio-economic status, and the acclimatization and adaptation of the local populations [63, 79, 80]. Additionally, study design, subgroups of children and method of analysis may also contribute to the controversies.

As mentioned above, different studies may present inconsistencies in the direction and magnitude of the effects of ambient humidity, with other studies even concluding that the occurrence of relevant climate-sensitive diseases appears
to be unrelated to humidity [36, 39, 85, 86]. This discrepancy can be explained by the following possible reasons: firstly, relative humidity can affect microorganisms in different ways. Some microorganisms tend to be more invasive in increased humidity, while others develop better in lower humidity [10]. Similar effects of ambient humidity on the concentration and distribution of aeroallergens have also been reported [87]. Secondly, there is a geographical, meteorological and temporal heterogeneity in the different studies. The occurrence of different effects suggests that geographical sites, regional variability and acclimatization of the local population may play a role in determining the exposure–response relationship. Thirdly, among various studies, whether or not one takes into account potential confounding factors and what kind of confounder is adjusted for existing differences, can make a difference in the conclusions. Moreover, even mutual confounding factors among different studies are likely to vary between regions, which implies that regional differences and local characteristics may modify the effects of weather factors [25, 27, 71]. Lastly, the date of the study conducted, the limited study duration and participants, and the different age groups of the study population may also play a role in the discrepancy. Future research taking these factors into account will be appreciated.

Strengths and limitations
This systematic review begins to address the current knowledge gap in the relationship between ambient humidity and child health. This is the first attempt to synthesize, using a systematic approach, the existing evidence of humidity-related health outcomes, across different countries, among children between 0–18 years of age. According to Table 2, almost all of the final included journal articles (34/37) were published after the year 2000, and were of relatively high reporting quality (the majority of records having a reporting quality above 70%). The findings in Table 2 suggest that ambient humidity has been playing a significant role in weather-related health outcomes. Unfortunately, children are usually the most susceptible subpopulation. The present review is crucial because this literature provides details of the current state of studies that examine the effects of humidity on child health and proposes directions for the future research.

Despite targeting the reporting quality of observational studies, many items of the STROBE checklist were no doubt selected due to evidence of association with susceptibility to bias. Thus experts have suggested that the STROBE statement provides a suitable starting point for development of a quality assessment tool [20, 88]. Just as the MOOSE (Meta-analysis Of Observational Studies in Epidemiology) guidelines are being used to assess quality, although they were actually developed as reporting guidelines, in this review, we tried to describe the reporting quality of the final identified articles by using an adapted version of the STROBE checklist [18, 89]. After the quality assessments, studies that applied credible and convincing statistical methods and outcome measures often obtained higher quality scores at the same time (Table 2), indicating that the adapted STROBE checklist can describe the reporting quality of the final identified articles
well. This novel quality assessment tool is innovative and potentially ground-breaking in terms of its contribution to relevant environmental and meteorological literature reviews [22].

However, regarding the results of this systematic review, some limitations should be acknowledged. First, this review is limited by its emphasis on papers published in English in peer-reviewed journal databases, so we may have missed potentially useful studies. Second, despite the highly sensitive and comprehensive nature of the search strategy employed, it is unlikely that all existing studies have been identified, and publication bias cannot be entirely excluded. Third, the adapted version of the STROBE checklist was initially implemented to describe the reporting quality of weather-related studies, so the validity and reliability of the checklist for our purposes have not been completely tested and formally evaluated. However, in this review, the tool was used only to describe the reporting quality, and the quality scores were not included as part of the relevance criteria. Fourth, it has been reported that temperature and relative humidity are not independent of one another, so the effects of relative humidity may be confounded by temperature. However, in our review, the majority of studies adjusted for potential confounding factors (e.g. temperature) when analyzing the impact of humidity on child health, and studies that conducted no adjustments were given lower quality ratings. Additionally, relative humidity is a popular indicator that has been widely used in current research and meteorological monitoring. Therefore, it is helpful and of practical significance to choose relative humidity rather than absolute humidity or water vapor pressure as the exposure variable. Finally, the data extraction and quality assessment were not performed independently by more than one reviewer, which may have led to subjective errors and introduced bias. However, in the present review, due to the explicit inclusion criteria, specially pre-designed data extraction form, definite exposure variable and health outcome, and the adapted quality assessment tool, the authors were able to ensure the integrity of the review, and to be unbiased during the conduction of assessment.

**Conclusion**

In summary, this study demonstrates that due to various inherent and unique characteristics, children are often susceptible to ambient humidity. We find that with climate change, there is a significant impact of humidity on child health, especially for climate-sensitive infectious diseases, diarrhoeal diseases, respiratory system diseases, and pediatric allergic diseases. However, the humidity-related effects on child health are various and complex. Ambient humidity continues to impact children unequally and in different ways, with impacts ranging from direct and indirect, and negative and positive. In this review we find that the influence of humidity on child health involves heterogeneous and even converse effects among different study regions, research designs, health outcomes, adjustments of potential confounding factors (e.g. air pollution, seasonality, interaction with
other meteorological factors), and subgroups of children, which suggests that further studies focusing on the association between ambient humidity and child health are needed to deal with the aforementioned problems.

Current increasing interest in the relationship between climate change and child health may provide an ideal opportunity to employ various epidemiological and statistical methods to further explore the impact of ambient humidity on child health. Such research and epidemiologic evidence can inform the local health officials and policy-makers to make and implement necessary preparations (mitigation and adaptation), ultimately contributing to better health outcomes for a humidity-impacted population.

Supporting Information

S1 Checklist. PRISMA checklist.
doi:10.1371/journal.pone.0112508.s001 (DOCX)

Acknowledgments

We thank Ms. Jan Bian and Dr. Stanley Lin for providing language help, and proofreading our manuscript for mistakes and grammatical errors.

Author Contributions

Conceived and designed the experiments: JG LL. Performed the experiments: YS YL. Analyzed the data: YS YL. Wrote the paper: JG YS YL LL. Study selection, data extraction and quality assessment: JG YS YL. Development of methodology: LL.

References

1. IPCC (2007) Climate change 2007: synthesis report. Cambridge University Press Cambridge, UK.
2. Pachauri R, Reisinger A (2007) Climate Change 2007: Synthesis Report. Contribution of Working Groups I, II and III to the Fourth Assessment Report of the Intergovernmental Panel on Climate Change. Intergovernmental Panel on Climate Change.
3. Harvell CD, Mitchell CE, Ward JR, Altizer S, Dobson AP, et al. (2002) Climate warming and disease risks for terrestrial and marine biota. Science (New York, NY) 296: 2158–2162.
4. Nakai S, Itoh T, Morimoto T (1999) Deaths from heat-stroke in Japan: 1968–1994. International journal of biometeorology 43: 124–127.
5. Yusuf S, Piedimonte G, Auais A, Demmler G, Krishnan S, et al. (2007) The relationship of meteorological conditions to the epidemic activity of respiratory syncytial virus. Epidemiology and Infection 135: 1077–1090.
6. Nichols A, Maynard V, Goodman B, Richardson J (2009) Health, Climate Change and Sustainability: A systematic Review and Thematic Analysis of the Literature. Environmental health insights 3: 63–88.
7. Sheffield PE, Landrigan PJ (2011) Global Climate Change and Children's Health: Threats and Strategies for Prevention. Environmental Health Perspectives 119: 291–298.
8. Kan HD, Chen RJ, Tong SL (2012) Ambient air pollution, climate change, and population health in China. Environment international 42: 10–19.
9. El-Fadel M, Ghanimeh S, Maroun R, Alameddine I (2012) Climate change and temperature rise: Implications on food- and water-borne diseases. Science of the Total Environment 437: 15–21.

10. Mirski T, Bartoszcze M, Bielawska-Drozd A (2012) Impact of Climate Change on Infectious Diseases. Polish Journal of Environmental Studies 21: 525–532.

11. Reid CE, Gamble JL (2009) Aeroallergens, Allergic Disease, and Climate Change: Impacts and Adaptation. Ecohealth 6: 458–470.

12. Dapul-Hidalgo G, Bielory L (2012) Climate change and allergic diseases. Annals of Allergy Asthma & Immunology 109: 166–172.

13. Willem L, Van Kerckhove K, Chao DL, Hens N, Beutels P (2012) A Nice Day for an Infection? Weather Conditions and Social Contact Patterns Relevant to Influenza Transmission. Plos One 7: e48695.

14. Balbus JM, Malina C (2009) Identifying vulnerable subpopulations for climate change health effects in the United States. Journal of occupational and environmental medicine/American College of Occupational and Environmental Medicine 51: 33–37.

15. Tillett T (2011) Climate Change and Children’s Health Protecting and Preparing Our Youngest. Environmental Health Perspectives 119: 132–132.

16. Shea KM, Comm Environm H (2007) Global climate change and children’s health. Pediatrics 120: E1359–E1367.

17. Assembly UG (1989) Convention on the Rights of the Child. United Nations, Treaty Series 1577.

18. Mallen C, Peat G, Croft P (2006) Quality assessment of observational studies is not commonplace in systematic reviews. Journal of clinical epidemiology 59: 765–769.

19. Rietmeijer-Mentink M, Paulis WD, Middelkoop M, Bindels PJ, Wouden JC (2013) Difference between parental perception and actual weight status of children: a systematic review. Maternal & Child Nutrition 9: 3–22.

20. von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, et al. (2007) The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. PLoS Med 4: e296.

21. Vandenbroucke JP, Von Elm E, Altman DG, Gotzsche PC, Mulrow CD, et al. (2007) Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration. PLoS medicine 4: e297.

22. Aimone AM, Perumal N, Cole DC (2013) A systematic review of the application and utility of geographical information systems for exploring disease-disease relationships in paediatric global health research: the case of anaemia and malaria. International journal of health geographies 12: 1.

23. Nascimento-Carvalho CM, Cardoso MRA, Barral A, Araujo-Neto CA, Oliveira JR, et al. (2010) Seasonal patterns of viral and bacterial infections among children hospitalized with community-acquired pneumonia in a tropical region. Scandinavian Journal of Infectious Diseases 42: 839–844.

24. Chang HL, Chio CP, Su HJ, Liao CM, Lin CY, et al. (2012) The association between enterovirus 71 infections and meteorological parameters in Taiwan. PLoS One 7: e46845.

25. Onozuka D, Hashizume M (2011) Effect of weather variability on the incidence of mumps in children: a time-series analysis. Epidemiology and infection 139: 1692–1700.

26. Onozuka D, Hashizume M (2011) The influence of temperature and humidity on the incidence of hand, foot, and mouth disease in Japan. The Science of the total environment 410–411: 119–125.

27. Onozuka D, Hashizume M (2011) Weather variability and paediatric infectious gastroenteritis. Epidemiology and infection 139: 1369–1378.

28. Ye Y, Louis VR, Simboro S, Sauerborn R (2007) Effect of meteorological factors on clinical malaria risk among children: an assessment using village-based meteorological stations and community-based parasitological survey. BMC Public Health 7: 101.

29. Zacarias OP, Majlender P (2011) Comparison of infant malaria incidence in districts of Maputo province, Mozambique. Malaria Journal 10: 93.
30. Chou WC, Wu JL, Wang YC, Huang H, Sung FC, et al. (2010) Modeling the impact of climate variability on diarrhea-associated diseases in Taiwan (1996–2007). The Science of the total environment 409: 43–51.

31. Checkley W, Epstein LD, Gilman RH, Figueroa D, Camara R, et al. (2000) Effects of El Niño and ambient temperature on hospital admissions for diarrhoeal diseases in Peruvian children. The Lancet 355: 442–450.

32. D’Souza RM, Hall G, Becker NG (2008) Climatic factors associated with hospitalizations for rotavirus diarrhoea in children under 5 years of age. Epidemiology and Infection 136: 56–64.

33. Viegas M, Barrero PR, Maffey AF, Mistchenko AS (2004) Respiratory viruses seasonality in children under five years of age in Buenos Aires, Argentina: A five-year analysis. Journal of Infection 49: 222–228.

34. Lapena S, Robles MB, Castanon L, Martinez JP, Reguero S, et al. (2005) Climatic factors and lower respiratory tract infection due to respiratory syncytial virus in hospitalised infants in northern Spain. European Journal of Epidemiology 20: 271–276.

35. Al-Toum R, Baidor S, Ayyash H (2006) Epidemiology and clinical characteristics of respiratory syncytial virus infections in Jordan. Journal of Tropical Pediatrics 52: 282–287.

36. Omer SB, Sutanto A, Sarwo H, Linehan M, Djelantik IGG, et al. (2008) Climatic, temporal, and geographic characteristics of respiratory syncytial virus disease in a tropical island population. Epidemiology and Infection 136: 1319–1327.

37. Turkish Neonatal S (2012) The seasonal variations of respiratory syncytial virus infections in Turkey: a 2-year epidemiological study. The Turkish journal of pediatrics 54: 216–222.

38. Noyola DE, Mandeville PB (2008) Effect of climatological factors on respiratory syncytial virus epidemics. Epidemiol Infect 136: 1328–1332.

39. Khor CS, Sam IC, Hooi PS, Quek KF, Chan YF (2012) Epidemiology and seasonality of respiratory viral infections in hospitalized children in Kuala Lumpur, Malaysia: a retrospective study of 27 years. BMC Pediatr 12: 32.

40. du Prel JB, Puppe W, Grondahl B, Knuf M, Weigl JA, et al. (2009) Are meteorological parameters associated with acute respiratory tract infections? Clinical infectious diseases : an official publication of the Infectious Diseases Society of America 49: 861–868.

41. Murdoch DR, Jennings LC (2009) Association of respiratory virus activity and environmental factors with the incidence of invasive pneumococcal disease. The Journal of Infection 58: 37–46.

42. Tchidjou HK, Vescio F, Boros S, Guemkam G, Minka E, et al. (2010) Seasonal Pattern of Hospitalization from Acute Respiratory Infections in Yaounde, Cameroon. Journal of Tropical Pediatrics 56: 317–320.

43. Loh TP, Lai FY, Tan ES, Thoon KC, Tee NW, et al. (2011) Correlations between clinical illness, respiratory virus infections and climate factors in a tropical paediatric population. Epidemiology and infection 139: 1884–1894.

44. Priftis KN, Paliatsos AG, Panagiotopoulos-Gartaganis P, Tapratzi-Potamianou P, Zachariaidou- Xypolita A, et al. (2006) Association of weather conditions with childhood admissions for wheezy bronchitis or asthma in Athens. Respiration 73: 783–790.

45. Kurt E, Metintas S, Basyigit I, Bulut I, Coskun E, et al. (2007) Prevalence and risk factors of allergies in Turkey: Results of a multicentric cross-sectional study in children. Pediatric allergy and immunology : official publication of the European Society of Pediatric Allergy and Immunology 18: 566–574.

46. Konstantinou GN, Papadopoulos NG, Tavladaki T, Tsekoura T, Tsilimigaki A, et al. (2011) Childhood acute urticaria in northern and southern Europe shows a similar epidemiological pattern and significant meteorological influences. Pediatric allergy and immunology : official publication of the European Society of Pediatric Allergy and Immunology 22: 36–42.

47. Yüksel H, Tanac R, Tez E, Demir E, Çoşker M (1996) Childhood asthma and atmospheric conditions. Pediatrics International 38: 606–610.

48. Guo YL, Lin YC, Sung FC, Huang SL, Ko YC, et al. (1999) Climate, traffic-related air pollutants, and asthma prevalence in middle-school children in Taiwan. Environmental health perspectives 107: 1001–1006.
49. Nastos PT, Paliatsos AG, Papadopoulos M, Bakoula C, Priftis KN (2008) The effect of weather variability on pediatric asthma admissions in Athens, Greece. The Journal of asthma: official journal of the Association for the Care of Asthma 45: 59–65.

50. Garcia-Marcos L, Batllés-Garrido J, Blanco-Quiros A, García-Hernandez G, Guillen-Grima F, et al. (2009) Influence of two different geo-climatic zones on the prevalence and time trends of asthma symptoms among Spanish adolescents and schoolchildren. International journal of biometeorology 53: 53–60.

51. Mireku N, Wang Y, Agar J, Reddy RC, Baptist AP (2009) Changes in weather and the effects on pediatric asthma exacerbations. Annals of Allergy Asthma & Immunology 103: 220–224.

52. Xirasagar S, Lin HC, Liu TC (2006) Seasonality in pediatric asthma admissions: the role of climate and environmental factors. European journal of pediatrics 165: 747–752.

53. Weiland SK, Husing A, Strachan DP, Rzehak P, Pearce N, et al. (2004) Climate and the prevalence of symptoms of asthma, allergic rhinitis, and atopic eczema in children. Occupational and Environmental Medicine 61: 609–615.

54. Lee YL, Su HJ, Sheu HM, Yu HS, Guo YL (2008) Traffic-related air pollution, climate, and prevalence of eczema in Taiwanese school children. The Journal of investigative dermatology 128: 2412–2420.

55. Hashimoto M, Fukuda T, Shimizu T, Watanabe S, Watanuki S, et al. (2004) Influence of climate factors on emergency visits for childhood asthma attack. Pediatrics international: official journal of the Japan Pediatric Society 46: 48–52.

56. Arnedo-Pena A, Garcia-Marcos L, Fernandez-Espinar JF, Bercedo-Sanz A, Aguinaga-Ontoso I, et al. (2011) Sunny hours and variations in the prevalence of asthma in schoolchildren according to the International Study of Asthma and Allergies (ISAAC) Phase III in Spain. International Journal of Biometeorology 55: 423–434.

57. Charland KM, Buckeridge DL, Sturtevant JL, Melton F, Reis BY, et al. (2009) Effect of environmental factors on the spatio-temporal patterns of influenza spread. Epidemiol Infect 137: 1377–1387.

58. Wang VJ, Cavagnaro CS, Clark S, Camargo Jr CA, Mansbach JM (2012) Altitude and environmental climate effects on bronchiolitis severity among children presenting to the emergency department. Journal of environmental health 75: 8–15; quiz 54.

59. Connelly M, Miller T, Gerry G, Bickel J (2010) Electronic Momentary Assessment of Weather Changes as a Trigger of Headaches in Children. Headache 50: 779–789.

60. Shannon MW, Best D, Binns HJ, Forman JA, Johnson CL, et al. (2007) Global climate change and children’s health. Pediatrics 120: 1149–1152.

61. Xu Z, Etzel RA, Su H, Huang C, Guo Y, et al. (2012) Impact of ambient temperature on children’s health: a systematic review. Environmental research 117: 120–131.

62. Bernstein AS, Myers SS (2011) Climate change and children’s health. Current problems in pediatric and adolescent health care 40: 2–18.

63. Jensen P (2000) Host seeking activity of Ixodes ricinus ticks based on daily consecutive flagging samples. Experimental & applied acarology 24: 695–708.

64. Knülle W, Rudolph D (1982) Humidity relationships and water balance of ticks. Physiology of ticks: 43–70.

65. Bennet L, Halling A, Berglund J (2006) Increased incidence of Lyme borreliosis in southern Sweden following mild winters and during warm, humid summers. European journal of clinical microbiology & infectious diseases: official publication of the European Society of Clinical Microbiology 25: 426–432.

66. Sattar SA, Lloyd-Evans N, Springthorpe VS, Nair RC (1986) Institutional outbreaks of rotavirus diarrhoea: potential role of fomites and environmental surfaces as vehicles for virus transmission. The Journal of hygiene 96: 277–289.
69. Rohayem J (2009) Norovirus seasonality and the potential impact of climate change. Clinical microbiology and infection: the official publication of the European Society of Clinical Microbiology and Infectious Diseases 15: 524–527.

70. Rajtar B, Majek M, Polanski L, Polz-Dacewicz M (2008) Enteroviruses in Water Environment: A Potential Threat to Public Health. Ann Agric Environ Med 15: 199–203.

71. Hashizume M, Armstrong B, Wagatsuma Y, Faruque ASG, Hayashi T, et al. (2008) Rotavirus infections and climate variability in Dhaka, Bangladesh: a time-series analysis. Epidemiology and Infection 136: 1281–1289.

72. Zou XN, Zhang XZ, Wang B, Qiu YT (2012) Etiologic and epidemiologic analysis of hand, foot, and mouth disease in Guangzhou city: a review of 4,753 cases. The Brazilian journal of infectious diseases: an official publication of the Brazilian Society of Infectious Diseases 16: 457–465.

73. Krefis AC, Schwarz NG, Kruger A, Fobil J, Nkrumah B, et al. (2011) Modeling the Relationship between Precipitation and Malaria Incidence in Children from a Holoendemic Area in Ghana. American Journal of Tropical Medicine and Hygiene 84: 285–291.

74. Gao HW, Wang LP, Lian S, Liu YX, Tong SL, et al. (2012) Change in Rainfall Drives Malaria Re-Emergence in Anhui Province, China. Plos One 7.

75. Devi NP, Jauhari R (2006) Climatic variables and malaria incidence in Dehradun, Uttaranchal, India. Journal of vector borne diseases 43: 21–28.

76. Paynter S, Ware RS, Weinstein P, Williams G, Sly PD (2010) Childhood pneumonia: a neglected, climate-sensitive disease? Lancet 376: 1804–1805.

77. Meerhoff TJ, Paget JW, Kimpen JL, Schellevis F (2009) Variation of Respiratory Syncytial Virus and the Relation With Meteorological Factors in Different Winter Seasons. The Pediatric infectious disease journal 28: 860–866.

78. Amarillo AC, Carreras HA (2012) The effect of airborne particles and weather conditions on pediatric respiratory infections in Cordoba, Argentine. Environmental pollution (Barking, Essex : 1987) 170: 217–221.

79. Sheffield PE, Weinberger KR, Kinney PL (2011) Climate change, aeroallergens, and pediatric allergic disease. The Mount Sinai journal of medicine, New York 78: 78–84.

80. Bielory L, Lyons K, Goldberg R (2012) Climate Change and Allergic Disease. Current allergy and asthma reports 12: 485–494.

81. Nicolai T, Illi S, Von Mutius E (1998) Effect of dampness at home in childhood on bronchial hyperreactivity in adolescence. Thorax 53: 1035–1040.

82. Suarez-Varela MM, Garcia-Marcos Alvarez L, Kogan MD, Llopis Gonzalez AL, Gimeno AM, et al. (2008) Climate and prevalence of atopic eczema in 6-to 7-year-old school children in Spain. ISAAC PhASE III. International Journal of Biometeorology 52: 833–840.

83. Youssoufagha AH, Lohrmann DK, Jayawardene WP, El Afandi GS (2012) Upper-air observation indicators predict outbreaks of asthma exacerbations among elementary school children: integration of daily environmental and school health surveillance systems in Pennsylvania. The Journal of asthma: official journal of the Association for the Care of Asthma 49: 464–473.

84. Kashiwabara K, Itonaga K, Moroi T (2003) Airborne water droplets in mist or fog may affect nocturnal attacks in asthmatic children. The Journal of asthma: official journal of the Association for the Care of Asthma 40: 405–411.

85. Lee YL, Shaw CK, Su HJ, Lai JS, Ko YC, et al. (2003) Climate, traffic-related air pollutants and allergic rhinitis prevalence in middle-school children in Taiwan. The European respiratory journal: official journal of the European Society for Clinical Respiratory Physiology 21: 964–970.

86. Jusot JF, Adamou L, Collard JM (2012) Influenza transmission during a one-year period (2009–2010) in a Sahelian city: low temperature plays a major role. Influenza and other respiratory viruses 6: 87–89.

87. D’Amato G, Cecchi L (2008) Effects of climate change on environmental factors in respiratory allergic diseases. Clinical and experimental allergy: journal of the British Society for Allergy and Clinical Immunology 38: 1264–1274.

88. Sanderson S, Tatt ID, Higgins JP (2007) Tools for assessing quality and susceptibility to bias in observational studies in epidemiology: a systematic review and annotated bibliography. International Journal of Epidemiology 36: 666–676.
89. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, et al. (2000) Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. JAMA: the journal of the American Medical Association 283: 2008–2012.