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Seasonality of Cryptosporidiosis: A Meta-Analysis Approach

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Abstract

Objectives—We developed methodology for and conducted a meta-analysis to examine how seasonal patterns of cryptosporidiosis, a primarily waterborne diarrheal illness, relate to precipitation and temperature fluctuations worldwide.

Methods—Monthly cryptosporidiosis data were abstracted from 61 published epidemiological studies that cover various climate regions based on the Köppen Climate Classification. Outcome data was supplemented with monthly aggregated ambient temperature and precipitation for each study location. We applied a linear mixed-effects model to relate the monthly normalized cryptosporidiosis incidence with normalized location-specific temperature and precipitation data. We also conducted a sub-analysis of associations between the Normalized Difference Vegetation Index (NDVI), a remote sensing measure for the combined effect of temperature and precipitation on vegetation, and cryptosporidiosis in Sub-Saharan Africa.

Results—Overall, and after adjusting for distance from the equator, an increase in temperature and precipitation predict an increase in cryptosporidiosis; the strength of relationship vary by climate subcategory. In moist tropical locations precipitation is a strong seasonal driver for cryptosporidiosis whereas temperature is in mid-latitude and temperate climates. When assessing lagged relationships temperature and precipitation remain strong predictors. In Sub-Saharan Africa, after adjusting for distance from the equator, low NDVI values are predictive of an increase in cryptosporidiosis in the following month.

Discussion—In this study we propose novel methodology to assess relationships between disease outcomes and meteorological data on a global scale. Our findings demonstrate that while climatic conditions typically define a pathogen habitat area, meteorological factors affect timing and intensity of seasonal outbreaks. Therefore, meteorological forecasts can be utilized to develop focused prevention programs for waterborne cryptosporidiosis.

Keywords

Keywords cryptosporidiosis; seasonality; temperature; precipitation; Normalized Difference Vegetation Index (NDVI); meta-analysis

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Introduction

The World Bank recently stated that worldwide 4 billion people live without adequate wastewater disposal and 2.4 billion live without proper sanitation, given these conditions diarrhea accounts for 4% of all deaths worldwide (WHO, 2008). A substantial fraction of diarrheal illnesses in developing and developed countries is caused by protozoa such as *Cryptosporidium*. *Cryptosporidium* is transmitted through water contaminated with human or livestock feces (Hunter and Thompson, 2005; Clark, 1999) or via human to human transmission (Dillingham et al., 2002; Griffiths, 1998). Currently, there are approximately 14 recognized species of *Cryptosporidium* of which two most affect humans, *C. hominis* and *C. parvum* (Sopwith et al., 2005). Though cryptosporidiosis infection (CPI), infection due to the parasite *Cryptosporidium*, is self-limiting in immuno-competent people, it can prove to be life threatening to immuno-compromised individuals, such as those with HIV/AIDS and the malnourished (Hawker et al., 2000; Griffiths, 1998). Children are the most susceptible to CPI and those less than 5 years of age have been shown to have the highest prevalence (Griffiths, 1998; Lima and Guerrant, 1992). Prevalence rates are higher in developing countries, 0.5–10%, compared to those in developed countries, 0.1–2% (Griffiths, 1998). Cryptosporidiosis infections in young children in developing countries lead to failure to thrive, severe persistent diarrhea, and increased mortality (Agnew et al., 1998; Checkley et al., 1997; Molbak et al., 1993).

CPI typically manifests itself through a low endemic level and well-pronounced seasonal outbursts, indicating a strong effect of meteorological and environmental factors. Studies conducted in tropical climates note an increase in incidence during warm, rainy season (Perch et al., 2001; Newman et al., 1999; Adegbola et al., 1994) and studies conducted in temperate climates note increases in the spring and fall (Naumova et al., 2005; Naumova et al., 2000; Shepherd et al., 1988). Our recent study demonstrated that in the temperate climate of Massachusetts, CPI peaks about six weeks after ambient temperature reached its annual maxima (Naumova et al., 2007). There is strong evidence that the concentration of *Cryptosporidium* oocysts increases in drinking water and surface water sources after heavy rainfall due to runoff (Muchiri et al., 2009; Lake et al., 2005; Alterholt et al., 1998; LeChevallier et al., 1991). However, variation in the rates of CPI cannot be explained by source of drinking water alone (Hughes et al., 2004). Recreational facilities, such as swimming pools, which are often used in the warmer months of the year, have also been associated with outbreaks of CPI (Dziuban et al., 2006; Craun et al., 2005; Yoder et al., 2004; Kramer et al., 1998). Based on this evidence, temperature and precipitation need to be assessed as drivers of seasonal patterns of CPI.

It has been shown that long term climate change can affect seasonal patterns of infectious diseases by lengthening the transmission cycle and changing thresholds which determine seasonal peaks (Harvell et al., 2002). Therefore, understanding the seasonality of a disease and its variation from year to year is the first step to understanding the impact of long term climate change on disease patterns (Pascual et al., 2002). It is important to understand the environmental factors which underlie seasonal trends in order to properly predict long-term effects due to climate change. Assessment of long term effects, especially on a large spatial scale, is often limited by availability of data, for both exposure and outcome. Data acquired from remote sensing satellites can be advantageous for assessment of environmental exposures, as worldwide data for various time periods is readily accessible and provides a variety of information such as temperature, precipitation, vegetation, and chemical content in the atmosphere. Remote sensing data provides various products including spectral vegetation indices, land and sea surface temperature indices, atmospheric moisture indices, and rainfall indices (Hay, 2000).

Remote sensing products have been used for study of public health (Patz, 2005). For example, land surface temperature indices have been used to assess health impacts of urbanization (Kalnay and Cai, 2003), spectral vegetation indices have been used to determine the impact of floods due to deforestation (Cockburn et al., 1999), and sea surface temperature and height have been used to explain the seasonal pattern of cholera outbreaks (Lobitz et al., 2000). The Normalized Difference Vegetation Index (NDVI) is the most often applied for use in epidemiology (Cringoli et al., 2005) and has been shown to have predictive properties in studies on onchocerciasis in Ethiopia (Gebre-Michael et al., 2005), schistosomiasis in Brazil (Bavia et al., 2005), and West Nile Virus in New York City (Brownstein et al., 2002). NDVI is a measure of density of plant growth over the entire globe which is calculated from satellite image data. Very low values of NDVI (0.1 and below) correspond to barren areas of rock, sand, or snow. Moderate values represent shrub and grassland (0.2 to 0.3), while high values indicate temperate and tropical rainforests (0.6 to 0.8). NDVI is used as a proxy for both temperature and precipitation, as neither measure alone sufficiently captures seasonal changes in weather.

While seasonality of cryptosporidiosis is well described, the consistency of such behavior on a global scale has not been investigated in part due to limited data on the monthly incidence of CPI collected over a long time period and difficulty in assessing local information on meteorological parameters in remote areas. In this study, we assembled a set of time series representing monthly incidence of CPI from 61 studies conducted in locations world-wide, examined the relationships between CPI and meteorological factors, namely precipitation and ambient temperature. We also conducted a sub-analysis in studies conducted in Sub-Saharan Africa in which we evaluated the use of the Normalized Difference Vegetation Index for predicting seasonal increases in CPI. We developed a meta-analysis framework to assess the link between proxies for environmental exposure to protozoa via drinking and recreational water and CPI incidence, which includes normalization for the outcome and exposure variables, a mixed effect modeling procedure adapted to time series data, and visualization of joint effects of environmental proxies on health outcome.

Methods and Materials

Outcome Data

We conducted a meta-analysis of studies published on cryptosporidiosis infection from 1966 to May 2008. Literature was gathered using the OVIDMedline search engine. The keywords used in the search were *cryptosporidiosis*, *Cryptosporidium parvum*, or *Cryptosporidium*. These keywords were combined with *seasonality* and *seasons*, resulting in 173 citations. The disease keywords were also combined with key words for various geographic areas, such as *West Africa*, *East Africa*, *Africa*, *Caribbean*, and *North America*, resulting in a total of 1923 citations. All of the search results were imported into EndNote and duplicates were removed, resulting in a total of 1301 studies in the database. Studies were evaluated based on the following three criteria:

1. Studies must involve observational data on cryptosporidium in humans that are not immuno-compromised (i.e., HIV/AIDS patients);
2. Studies must include at least a full year of data to cover all seasons;
3. Studies must provide data on a daily, weekly, monthly or quarterly basis.

Studies which did not meet the criteria were excluded. Figure 1 demonstrates how the studies were classified and reasons for exclusion. A total of 138 studies met the study criteria of which 49 studies presented data in the published journal article. We contacted authors of 82 studies, since 7 studies were duplicates, and 12 were able to provide data in the requested format. CPI outcome data were collected from a total of 61 sites and were aggregated on a monthly basis.

In cases where data were presented on a quarterly basis (5 studies) the outcome was equally divided over the months in the quarter. The selected studies were conducted in different populations. Of the 61 studies, 24 (39.3%) studies were conducted in children less than 5 years of age, 16 studies (26.2%) were conducted in children less than 15 years of age, 20 (32.8%) studies were conducted in the general population and 1 (1.6%) study was conducted in the elderly. Table 1 provides details for the selected studies, including study reference, study location, age of study population, latitude and longitude of the study site, and years over which the study was conducted.

Exposure Data

Based on each study site's longitude and latitude, we supplemented monthly relative prevalence data with time specific ambient temperature and precipitation, obtained from the National Climatic Data Center databases (1080 of 1728 observations = 62.5%). When time specific data were unavailable temperature and precipitation averages were used from Global Historical Climatology Network (648 of 1728 observations = 37.5%). Each study site was classified based on the Köppen Climate Classification with the total of 30 categories. Using the study sites' latitude and longitude information each study location was plotted on a map of Köppen Climate Classification and using a GIS spatial overlay each location was classified into a specific climate category. For the purposes of analysis we used only the four major classifications; moist tropical climates are classified as Climate A, arid and semiarid climates are classified as Climate B, humid mid-latitude areas are classified as Climate C and colder temperate areas are classified as Climate D. Figure 2 provides a map of study locations and the number of years for which data were available for analysis.

The studies selected for this analysis used different measures for cryptosporidiosis outcome. Of the 61 studies, 38 studies (62.3%) present outcome data as number of cases, 14 studies (23.0%) present outcome as percent positive stools, 8 studies (13.1%) present outcome as prevalence and one study (1.6%) presented the outcome as incidence. In order to standardize the different outcome measures used in each study the raw values were normalized into z-scores on a study-by-study basis. Monthly z-scores were also calculated for temperature and precipitation data in order to assess relative associations. For example, a rainy month in a tropical location such as Bangladesh will have different implications compared to a rainy month in a dry arid location such as Kuwait. The z-score was calculated using the mean and standard deviation for the complete duration of each study as follows:

$$Z_{ij} = \frac{x_{ij} - \bar{x}_i}{S_i}$$

where Z_{ij} is the z-score for x_{ij} , the actual value for outcome (CPI cases, prevalence or percent positive stools) or exposure (temperature, precipitation) for study i in month j and $\bar{x}_i$ and s_i are the mean and standard deviation for each study, respectively.

Overall Analysis: Temperature, Precipitation, and Cryptosporidiosis

We examined seasonal patterns in temperature, precipitation, and cryptosporidiosis by climate category. We investigated relationships between temperature, precipitation and CPI in each climate category using 2-D imaging with linear interpolation on the 3 neighboring data points, since the distributions of the predictor variables, z-score for temperature and precipitation, are essentially normal.

A linear mixed effects model was used to link the z-score of monthly CPI values with z-score of temperature and z-score of precipitation individually (Model 1). We examined the

relationships overall for all the study sites as well as for each climate category. The mixed effect regression model was defined as follows:

$$Z_{ij} = \beta_0 + \beta_1 x_{ij} + b_{0i} + b_{1i} x_i,$$

where Z_{ij} is the cryptosporidiosis z-score, and x_{ij} is the exposure of interest (temperature z-score, or precipitation z-score), the fixed effects: β_0 is the population intercept, β_1 is the population slope, and random effects: b_0 is the study intercept and b_1 is the study slope. The mixed effect models were also examined utilizing the lagged exposure values to assess whether increased CPI rates may be due to temperature and precipitation exposure from the previous month (Model 2). The regression models were also run adjusting for latitude or distance of the study site from the equator. We included the square of the study site's latitude and the interaction with the exposure in the regression model as a fixed effect for each individual exposure predictors to control for the site's distance from the equator (Model 3). By adjusting for the distance from the equator we can account, in part, for heterogeneity in the interaction between annual temperature and precipitation levels and overall climate characteristics. For example, in temperate climates the highest precipitation occurs in the warmer months whereas in tropical climates the highest precipitation occurs in the relatively cooler months. The mixed effect model adjusting for the sites distance from the equator was also run utilizing lagged exposure values (Model 4).

Sub-Analysis: NDVI and Cryptosporidiosis

A sub-analysis was conducted to assess the use of the Normalized Difference Vegetation Index (NDVI) as a predictor for seasonal CPI increases. NDVI data was collected for 13 of the 14 studies conducted in Sub-Saharan Africa; NDVI data was not collected for one study because the study did not provide detail on the years in which the data were collected and the authors did not respond to requests for this information. NDVI data were obtained from the Famine Early Warning System (FEWS) Africa Data Dissemination Service (FEWS Network, 2008). The FEWS-NET NDVI data are a product from the NASA's Global Inventory Modeling and Mapping Studies (GIMMS) group, which provides 8 km resolution NDVI for every 10 days (Tucker et al., 2005; Pinzon et al., 2004). We used ESRI's ArcMap 9.1 software and Python scripts to extract NDVI statistics for each city's study area. A study area was defined by determining the bounding coordinates for the study location using the aerial imagery within Google Earth. The study area should avoid large water bodies, such as rivers, lakes, or oceans since these can skew NDVI measurements. The NDVI data were imported into ArcMap and the raw pixel data values were divided by 250 to recover the NDVI range of -1 to 1. ArcToolbox's Zonal Statistics function was used to calculate summary statistics for the minimum, maximum, mean, and standard deviation of all the NDVI pixel values within each defined study area. These summary statistics were then aggregated on a monthly basis.

The studies conducted in Sub-Saharan Africa fell into two climate categories, Climate A, arid and semiarid climates, and Climate C, humid mid-latitude areas. We examined the relationship between temperature, precipitation, and NDVI for all studies using the 2-D imaging linear interpolation method. The same four linear mixed effects models were used to link the z-score of monthly CPI values with NDVI. We examined the relationship synchronized (Model 1), with lagged NDVI (Model 2), adjusting for distance of the study site from the equator (Model 3), and adjusting for the sites' distance from the equator and utilizing lagged NDVI (Model 4).

Results

Overall Analysis: Temperature, Precipitation, and Cryptosporidiosis

Initial descriptive analysis illustrates the average values of temperature and precipitation for all study sites and also for each climate subcategory (Table 2). All study sites provide 1722 months of data; on average, each study site had 28 months of data. Studies located in tropical climate zone (Climate A) have the highest average monthly mean temperature with low variability and the highest monthly mean precipitation with the most variability. The arid/semi-arid (Climate B) has the lowest rainfall of all climate categories. The mid-latitude climate (Climate C) and cold temperate climate (Climate D) have similarly temperate temperatures however Climate C is less variable.

Visual analysis of seasonal patterns of temperature, precipitation, and CPI demonstrates differences by climate category (Figures 3–6). Panels A, B, and C in each figure show the temperature, precipitation and cryptosporidiosis z-score for each study over a year. Panel D shows the relationship of CPI z-score to temperature and precipitation z-score for all studies in that climate group. In the tropical climate zone (A) temperature demonstrates subtle seasonality and precipitation peaks biannually. In this climate zone CPI has high variability though it demonstrates a strong relationship with both temperature and the first peak in precipitation (Figure 3). The arid/semiarid region (Climate B) exhibits strong seasonality in temperature however, there is no seasonality seen in precipitation or CPI (Figure 4). Due to the fact that one study in this climate zone is from southern hemisphere, we see a six month shift in the seasonal pattern of temperature for that study. In the mid-latitude climate (Climate C) temperature demonstrates a clear seasonality. Again, as in the arid/semi arid climate zone, precipitation does not exhibit a seasonal pattern however; there is a slight peak in CPI in the spring (Figure 5). The patterns for temperature and precipitation in the cold temperate climate (Climate D) mimic those seen in the humid mid-latitude climate (Climate C). However, CPI demonstrates a slight seasonal peak in the fall which is associated with relatively higher precipitation (Figure 6).

The results of the regression models for the individual exposure variables and lagged exposure variables are shown in Table 2. Overall, when assessing synchronized relationships (Model 1), temperature and precipitation z-score are significant predictors of CPI z-score. The relationships vary by climate subcategory. In tropical climates (A), a one unit increase in precipitation z-score results in 1.5 times higher increase in the cryptosporidiosis z-score compared to a similar increase in temperature z-score. In the arid/semiarid areas (Climate B), none of the variables can reliably predict the temporal changes in CPI. In the more temperate climates (C and D) only temperature was a significant predictor for cryptosporidiosis z-score. When the variables were lagged (Model 2), overall temperature and precipitation z-score remained significant predictors of CPI z-score. Temperature z-score is a stronger predictor when assessing lagged relationships and relationship with precipitation decreases compared to the synchronous relationship. This was also seen in the tropical climate (A). Again, in the temperate climates (C and D), temperature z-score was a significant predictor of CPI z-score the following month. Overall, in all studies, adjusting for latitude or distance of the study site from the equator did not affect the relationship with temperature (Model 3); the highest levels of CPI were seen in high temperature months regardless of latitude (Table 2). For precipitation the relationship remains significant however, the relationship gets weaker as the site is closer to the equator. The relationships were not significant when adjusting for latitude and lagging the exposure variables (Model 4). Both synchronous models, with and without adjustment for latitude of the study site, demonstrate that the highest levels of cryptosporidiosis are seen in warm and wet months.

Sub-Analysis: NDVI and Cryptosporidiosis

For studies conducted in Sub-Saharan Africa we conducted a sub-analysis utilizing NDVI data. Initial descriptive analysis illustrates the average values of NDVI for study sites in Sub-Saharan Africa and also by climate subcategory (Table 3). The 13 studies conducted in Sub-Saharan Africa provided 302 months of data; on average each study site had 23 months of data. These studies were only in the tropical and humid mid-latitude climates and the average NDVI values were about equal in both climate categories.

Figure 7 demonstrates the relationship between NDVI, temperature, and precipitation for study sites in Sub-Saharan Africa. Panel A shows the actual temperature and precipitation values and Panel B shows the z-scores for temperature and precipitation. Higher NDVI values are associated with higher precipitation. When assessing synchronized (Model 1) and lagged (Model 2) relationships NDVI overall, for all studies, was not significant (Table 3). NDVI was a significant predictor of cryptosporidiosis z-score only in the humid mid-latitude climate (C). When assessing lagged (Model 2) relationships NDVI was significant in both the tropical (Climate A) and the humid mid-latitude (Climate C) areas. In the humid mid-latitude areas an increase in NDVI predicts an increase in cryptosporidiosis z-score the following month. Whereas, in tropical climates an increase in NDVI predicts a decrease in cryptosporidiosis z-score the following month. Adjusting for distance from the equator (Model 3) demonstrated that the effect of NDVI is more pronounced as the study site is farther from the equator. These relationships held when assessing lagged effects of NDVI and controlling for distance from the equator (Model 4).

Discussion

The seasonal patterns in cryptosporidiosis infection can be substantially affected by seasonal variations in exposure level associated with water quality and access to water, as well as wildlife and agricultural activities which in turn can be affected by meteorological characteristics such as temperature and precipitation. While, outbreaks of waterborne diseases have been shown to be associated with increased precipitation (Curriero et al., 2001) our study assesses associations for overall seasonal patterns. Our results provide a quantitative link between the incidence of cryptosporidiosis and meteorological parameters on a global scale, and illustrate a strong potential for NDVI as a suitable proxy for exposure to *Cryptosporidium*, especially in the humid mid-latitude climate zones. In warm and wet locations expected precipitation can serve as a reliable predictor for incidence of cryptosporidiosis. Extreme meteorological events, such as heavy rainfall, droughts, and heat waves, may substantially alter a seasonal pattern in disease incidence.

There are two species of *Cryptosporidium* which most affect humans, *C. hominis* (previously referred to as *C. parvum*, genotype 1) and *C. parvum* (previously referred to as *C. parvum*, genotype 2) (Morgan-Ryan et al., 2002). The host reservoir for *C. hominis* is humans and the host reservoir for *C. parvum* are cattle, livestock and humans (Hunter and Thompson, 2005). Few studies conducted in the United Kingdom have assessed the difference in seasonal pattern between the species and found that *C. parvum* peaks in the late spring whereas *C. hominis* peaks in the fall (Sopwith et al., 2005; McLauchlin et al., 2000). Studies have also reported differing geographical range for the two species (Learmonth et al., 2004; McLauchlin et al., 2000). Findings regarding differences between the species are fairly recent, and only two of the studies utilized in our analysis specify the difference between species. Therefore, we were not able to address differing seasonal patterns based on species and combined both species in our dataset. Future studies which assess seasonality of CPI should address the differences by species in order to fully understand this variation.

In this study we adapted the Köppen Climate Classification for public health data by using only the four primary categories. This classification scheme is based on thirty years of data and is extremely complex and has several criteria. Therefore, utilizing these broad primary categories may cause grouping of different types of data. For example, in our data there are two distinct groups in temperature for studies in the arid/semi-arid climate zone (Climate B), those with the higher temperatures are classified in the subcategory BWh and those with the lower temperatures are classified in the subcategories BSh and BSk. The secondary classification for the arid/semiarid climate zone is based on yearly average temperature however, in our analysis they were grouped together. Also, the particular year of meteorological data we are considering may not conform to the normal thirty year average and therefore may demonstrate a seasonal pattern unlike other studies in the same category. However, using the more detailed classification would not be feasible as we would not have a sufficient number of studies per category for comparison.

The suggested approach of normalization of the outcome and exposure variables offers clear advantages for the analysis of CPI. Since each study expressed monthly level of cryptosporidiosis using different measures, by using the z-score we gain compatibility between the data types, which is crucial in merging data from several sources, however, there is a loss of data specificity. The primary limitation of this analysis is a small number of published studies that present seasonal data on CPI. This had several repercussions in the study overall. Due to the small number of studies, we were not able to stratify the analysis by age. Again, due to the small number of available studies, the studies covered a large time span (1982–2006) and it was difficult to gather time specific temperature and precipitation data for each study. For the studies in which averages were used temperature and precipitation may not represent the weather specific to the year for which CPI data is available.

This study also demonstrated the utilization of NDVI as a proxy for environmental exposure to the protozoa *Cryptosporidium*. Preliminary analysis demonstrated that the various data sources for NDVI may not be comparable (Jagai et al., 2007). We used the FEWS-NET NDVI because it has been calibrated to take into account several issues including, volcanic ash from an eruption in S. Africa in 1991, intra-sensor degradation, and inter-sensor degradation (FEWS Network, 2008). The FEWS-NET data is also spatially and temporally smoothed to remove clouds and subpixel cloud contamination and is inter-calibrated with another high resolution satellite which has a landcover sensor on board. Therefore, we found these data to be the most reliable for use in this sub-analysis. Our data set included only 13 studies in Africa for which NDVI data were extracted. A larger sample would have provided more data in each of the climate subcategories to understand more clearly the differences by category. Since NDVI was strongly associated with precipitation of a study location, we believe that remote sensing data and indices reflecting vegetation water content in particular can be very useful for predicting the incidence of waterborne infections on a large geographical scale. Continued interest in the use of remote sensing for public health research (Patz, 2005) may lead to the development of new products which supersede NDVI and may be more appropriate for this type of analysis. Further research must be conducted to understand how NDVI and other remote sensing data can be used for all locations worldwide in a comparable manner and to examine the validity and comparability from different sources, various satellites, and over time. Remote sensing data, such as NDVI, can be beneficial as an early warning system to predict higher rates of waterborne diseases in particular areas.

In this study, as an extension of previous research (Naumova et al., 2007), we proposed novel methodology to capitalize on previously published data to assess the relationships between meteorological characteristics and disease outcomes. The methodology utilized in this study can be applied to a variety of water-borne diseases and infections caused by thermo-sensitive pathogens. Our study confirms previous studies which demonstrate an increase in CPI during

warm and rainy seasons (Perch et al., 2001; Newman et al., 1999; Adegbola et al., 1994). Temperature and precipitation are significant predictors of incidence of cryptosporidiosis, particularly in the tropical climates. Given the climate change predictions of increases in temperature and variability in precipitation (Patz et al., 2000) it is necessary to understand how these meteorological characteristics drive the seasonal patterns of disease. The meteorological characteristics can then be used to focus and target prevention programs. This is critical in the case of cryptosporidiosis as this pathogen is resistant to conventional water treatment practices (Betancourt and Rose, 2004). This study demonstrates that while climatic conditions typically define a habitat area of a pathogen, meteorological factors affect timing and intensity of infectious outbreaks. Weather forecasting on a local and global scale can be useful for disease forecasting, so public health measures for disease prevention can be better targeted and focused.

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Figure 1.
Flow chart of selection of studies utilized in the analysis including inclusion and exclusion criteria.

Figure 2.

Map of Köppen Climate Classification with study locations marked. The size of the marker indicates the number of years of data utilized in this analysis from each location.

Figure 3.

Meteorological characteristics of studies in Climate Category A (Tropical Climate). Monthly temperature z-score (Panel A), monthly precipitation z-score (Panel B), monthly cryptosporidiosis z-score (Panel C). For all Panel A–C the monthly mean is shown in blue and the annual mean is shown in red. Interpolation of cryptosporidiosis z-score in relation to precipitation and temperature z-score (Panel D).

Figure 4. Meteorological characteristics of studies in Climate Category B (Arid/Semi Arid Climate). Monthly temperature z-score (Panel A), monthly precipitation z-score (Panel B), monthly cryptosporidiosis z-score (Panel C). For all Panel A–C the monthly mean is shown in blue and the annual mean is shown in red. Interpolation of cryptosporidiosis z-score in relation to precipitation and temperature z-score (Panel D).

Figure 5. Meteorological characteristics of studies in Climate Category C (Humid Mid-Latitude Climate). Monthly temperature z-score (Panel A), monthly precipitation z-score (Panel B), monthly cryptosporidiosis z-score (Panel C). For all Panel A–C the monthly mean is shown in blue and the annual mean is shown in red. Interpolation of cryptosporidiosis z-score in relation to precipitation and temperature z-score (Panel D).

Figure 6. Meteorological characteristics of studies in Climate Category D (Cold Temperate Climate). Monthly temperature z-score (Panel A), monthly precipitation z-score (Panel B), monthly cryptosporidiosis z-score (Panel C). For all Panel A–C the monthly mean is shown in blue and the annual mean is shown in red. Interpolation of cryptosporidiosis z-score in relation to precipitation and temperature z-score (Panel D).

Figure 7. Interpolation of NDVI in relation to precipitation and temperature (Panel A) and precipitation z-score and temperature z-score (Panel B).

Descriptive statistics and regression results for overall analysis, for all studies and by climate category. Mean and standard deviation for temperature and precipitation, number of studies and number of months covered. Regression parameters for each of the four models for all studies and by climate category. Significant parameters ($p < 0.05$) are shown in bold.

Table 2

	Exposure Variable	All Studies	Climate A Moist tropical	Climate B Arid and Semiarid	Climate C Humid mid-latitude	Climate D Cold Temperate
Descriptive Statistics	Temperature (°C)	17.80 ± 9.07	26.44 ± 2.81	18.25 ± 8.32	13.54 ± 6.44	13.33 ± 9.98
	Precipitation (mm)	78.24 ± 95.47	119.90 ± 149.54	16.40 ± 22.63	63.60 ± 53.48	85.54 ± 52.17
	Studies	61	23	10	24	4
	Months	1722	487	245	564	426
Model 1 ^a	Temperature	0.167	0.175	-0.058	0.226	0.178
	Precipitation	0.172	0.325	0.145	0.062	0.071
Model 2 ^b	Temperature	0.215	0.288	-0.067	0.234	0.267
	Precipitation	0.091	0.157	0.086	0.048	0.024
Model 3 ^c	Temperature	0.151	-0.047	0.118	0.283	-0.309
	Precipitation	0.285	0.301	0.117	0.168	-0.280
Model 4 ^d	Temperature	0.244	0.098	0.002	0.379	-0.220
	Precipitation	0.162	0.256	-0.044	0.182	-0.774

^a Synchronous model

^b Model with exposure lagged by one month

^c Synchronous model adjusted for distance from the equator

^d Model with exposure lagged by one month and adjusted for distance from the equator

Table 3

Descriptive statistics and regression results for Sub-Saharan sub-analysis, for all studies and by climate category. Mean and standard deviation for temperature and precipitation, number of studies and number of months covered. Regression parameters for each of the four models for all studies and by climate category. Significant parameters ($p < 0.05$) are shown in bold.

	Exposure Variable	All Studies	Climate A Moist tropical	Climate C Humid mid-latitude
Descriptive Statistics	NDVI	0.36 ± 0.12	0.36 ± 0.13	0.34 ± 0.10
	Studies	12	8	4
	Months	302	218	84
Model 1 ^a	NDVI	0.214	-0.988	3.284
Model 2 ^b	NDVI	-0.938	-3.363	4.549
Model 3 ^c	NDVI	-1.635	-0.980	13.940
Model 4 ^d	NDVI	-4.514	-1.964	11.261

^aSynchronous model

^bModel with exposure lagged by one month

^cSynchronous model adjusted for distance from the equator

^dModel with exposure lagged by one month and adjusted for distance from the equator