Respiratory Syncytial Virus Circulation in Seven Countries With Global Disease Detection Regional Centers

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Background. Respiratory syncytial virus (RSV) is the leading cause of lower respiratory tract infections in young children globally, with the highest burden in low- and middle-income countries where the association between RSV activity and climate remains unclear.

Methods. Monthly laboratory-confirmed RSV cases and associations with climate data were assessed for respiratory surveillance sites in tropical and subtropical areas (Bangladesh, China, Egypt, Guatemala, Kenya, South Africa, and Thailand) during 2004–2012. Average monthly minimum and maximum temperatures, relative humidity, and precipitation were calculated using daily local weather data from the US National Climatic Data Center.

Results. RSV circulated with 1–2 epidemic periods each year in site areas. RSV seasonal timing and duration were generally consistent within country from year to year. Associations between RSV and weather varied across years and geographic locations. RSV usually peaked in climates with high annual precipitation (Bangladesh, Guatemala, and Thailand) during wet months, whereas RSV peaked during cooler months in moderately hot (China) and arid (Egypt) regions. In South Africa, RSV peaked in autumn, whereas no associations with seasonal weather trends were observed in Kenya.

Conclusions. Further understanding of RSV seasonality in developing countries and various climate regions will be important to better understand the epidemiology of RSV and for timing the use of future RSV vaccines and immunoprophylaxis in low- and middle-income countries.

Keywords. respiratory tract infections; respiratory syncytial virus infections; climate; seasons; humans.

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Respiratory syncytial virus (RSV) is a leading cause of lower respiratory tract infection among young children. Nearly all children have been infected by RSV by their second birthday [1]. In 2005, RSV was associated with an estimated 66 000–199 000 deaths among young children worldwide [2]. To reduce severe RSV-associated respiratory infections among high-risk populations and determine appropriate diagnostic testing, healthcare providers depend on surveillance to track RSV circulation [3]. RSV timing and intensity varies worldwide [2]. Temperature, rainfall, and humidity have been postulated to significantly impact RSV seasonality. For temperate climates, latitude and calendar month seem most influential [4–6]. Previous studies have described laboratory-confirmed RSV detections and weather in different geographical locations [7–12]. However, no studies have compared RSV seasonality and its association with climate in multiple sites globally using prospective surveillance for acute respiratory illness with standardized specimen collection and testing by reverse-transcription polymerase chain reaction (RT-PCR). Understanding worldwide RSV epidemics will be important to further define morbidity and mortality due to RSV, assist in timing prophylaxis, and guide RSV vaccine development. We report RSV seasonality data from 7 countries (2004–2012) that partner with the US Centers for Disease Control and Prevention (CDC).

METHODS

Study Sites

This study included RSV cases detected by RT-PCR by CDC Global Disease Detection (GDD) Centers in Bangladesh, China, Egypt, Guatemala, Kenya, South Africa, and Thailand. These centers conduct respiratory disease surveillance and laboratory testing through sites established by the GDD International Emerging Infections Program and Influenza Program in collaboration with local partners, as described in detail elsewhere [13, 14]. All countries included children aged <5 years, and 4 countries (Egypt, Guatemala, Kenya, and Thailand) included children and adults prospectively enrolled for acute respiratory illness surveillance in one or all of the following levels of healthcare: communities, hospitals, and clinics. Years of surveillance, age group, and patient source varied among sites for this study (Table 1).

Between 1 and 7 years of data were available from 2004–2012 for 7 countries. Each country contributed RSV data (RSV type not specified) from 1–5 surveillance sites for a total of 16 distinct geographic areas grouped into 3 distinct climate indicator groups. Several sites changed their surveillance practices during the study period, which influenced enrollment. Kenya sites in Kibera and Lwak increased collection of respiratory specimens from eligible patients during the 2009 H1N1 influenza pandemic response, and in the Kibera site, surveillance procedures were changed during 2009 to allow collection of respiratory specimens from all eligible children aged <5 years, whereas previously specimens had only been collected from the first 5 eligible children per day. South Africa data were from sites in Pretoria for 2006–2012, where specimens were collected by attending physicians from patients with suspected RSV infection, whereas data from Soweto during 2009–2012 were collected as part of systematic sentinel surveillance with clinical case definitions. Data from Bangladesh were obtained from children aged <5 years through community-level surveillance for pneumonia and influenza in Dhaka during 2004–2007; the data for 2010–2011 were based on hospital surveillance for influenza and other respiratory viruses from 4 sentinel sites in geographically diverse locations of the country. RSV data from Bangladesh were not available for 2008–2009 for this analysis. The following data were excluded from the seasonal analysis but included in the Supplementary Figure 1: Guatemala in 2008 had low case counts because surveillance was conducted at only one site; a site in Guatemala city was temporarily added in response to the H1N1 influenza outbreak; during 2012, Guatemala had too few RSV detections to analyze because the RSV season began in 2012 but peaked in 2013 (2013 data not available); Kenya did not provide data before March 2007; therefore we cannot determine if the RSV season was underway in March or if RSV circulated at epidemic levels throughout the year. Additional details on inclusion criteria and enrollment for each site is described elsewhere [15–22].

Climate Data

Weather observation data for each of the GDD sites came from the National Oceanographic and Atmospheric Administration's National Climatic Data Center in Asheville, North Carolina, and were reported as standard (English) measurements. National Climatic Data Center weather stations located within 0.01 degree of latitude (approximately 0.69 miles) and longitude (approximately 0.69 miles) of the geographic center of each site with no missing data for the weather parameters over the years studied were selected to approximate weather conditions (Figure 1). From the daily Global Surface Summary of the Day data, we calculated monthly average minimum and maximum temperatures and total monthly precipitation (inches). Relative humidity was calculated based on the August-Roche-Magnus approximation using daily dew point and mean temperature [23]. Relative humidity, more commonly conceptualized than dew point, is the measure of air moisture described in this study. Each geographical area is shown in Figure 2 and grouped by broader climate indicators derived from the Köppen classification [24]: hot moderate (South Africa, Guatemala, China, and Kenya), moist tropical (Bangladesh and Thailand), and arid (Egypt); however, some countries had sites from two climate groups (Figure 1 and Table 1). Köppen climate zones vary greatly in

Table 1. Description of the Surveillance Sites and Weather Stations

		Surveillance Specifics			Climate Specifics		
Country	Site Location	Data Source	Available Surveillance Period	Age Group	Weather Station Location	Climate Indicator[a]	Elevation (meters)
Bangladesh	Dhaka District	Households, 2 hospitals, 1 clinic	Apr 2004–Feb 2008	<5 y	Dhaka	Moist Tropical	39
	Bogra District	Four tertiary hospitals	Jan 2010–Dec 2011	≤5 y	Bogra		66
	Barisal District				Barisal		7
	Comilla District				Comilla		10
	Kishoreganj District				Kurmitola Dia		62
China	Jingzhou	4 hospitals, 1 clinic	Jan 2011–Dec 2011	<5 y	Jiangling	Moderate Hot	2638
Egypt	Damanhour District	3 Ministry of Health hospitals, 2 private hospitals, 3 outpatient clinics	June 2009–June 2012	>30 d	Alexandria/Nouzha	Arid	0
Guatemala	Santa Rosa municipality	2 hospitals, 10 clinics	Nov 2007–Dec 2011	All ages	Guatemala City	Moderate Hot	5102
	Quetzaltenango municipality		Jan 2009–Dec 2011		Qutezaltenango		7782
	Guatemala City municipality		Jan 2009–Oct 2012		Guatemala City		5102
Kenya	Lwak	Households, 1 hospital, 1 clinics	March 2007–Feb 2011	All ages	Kisumu	Moderate Hot	3717
	Kibera				Nairobi		5509
South Africa	Pretoria	2 academic hospitals	Jan 2006–July 2012	<5 y	Pretoria-Eendracht	Moderate Hot	4337
	Soweto	1 academic hospital	Feb 2009–Dec 2011		Johannesburg		5518
Thailand	Nakhon Phanom province	All hospitals in 2 provinces	Jan 2005–Dec 2011	All ages	Nakhon Phanom	Moist Tropical	453
	Sae Kaeo province				Aranyaprathet		177

[a] Broader grouping of Köppen classification.

shifts in any cardinal direction from a given point. By accounting for weather and climate zones, which correspond with shifts in longitude and latitude, our study provides an assessment of variables that could influence RSV transmission.

We described fluctuations in weather based on oscillations, peaks (crests), and lows (troughs). A climate oscillation (cycle) is a repetitive variation in time of weather patterns from one state to its counter-state (eg, cold to hot) in select climate regions. Weather parameters over time generally are curved, traverse waves, with peaks followed by lows [25]. Two weather parameters (eg, minimum and maximum temperatures) oscillate jointly when they follow similar patterns of increases and decreases over time [25]. For countries with average monthly precipitation exceeding 14 inches each month, we define the rainy season as months with above-average annual precipitation.

Analysis

We assessed RSV seasonality among countries and the relationship between RSV seasonality and climate descriptively. To allow site-to-site comparison and ensure discernibility of low RSV activity and outbreaks, the 12-month period of each year has been presented.

An RSV epidemic period was determined based on the RSV peak, onset, and offset. RSV peak was defined as the month in each year when the maximum number of acute respiratory illness cases with RSV detected occurred. RSV onset was defined as the first of 2 consecutive months when the number of RSV cases exceeded 10% of the number detected during the RSV peak month. Offset was defined as the last of 2 consecutive months when the number of RSV cases exceeded 10% of the number detected during the RSV peak month. To identify multiple RSV epidemic seasons within a year, such as biannual RSV activity, 2 RSV peaks had to occur with a nonpeak month in-between the peak months and the monthly proportion of acute respiratory illness cases positive for RSV had to drop below 10% between the peaks. This method resulted in RSV peak, onset, and offset months that correlated most closely with each epidemic period observed in our data, capturing ≥70% of

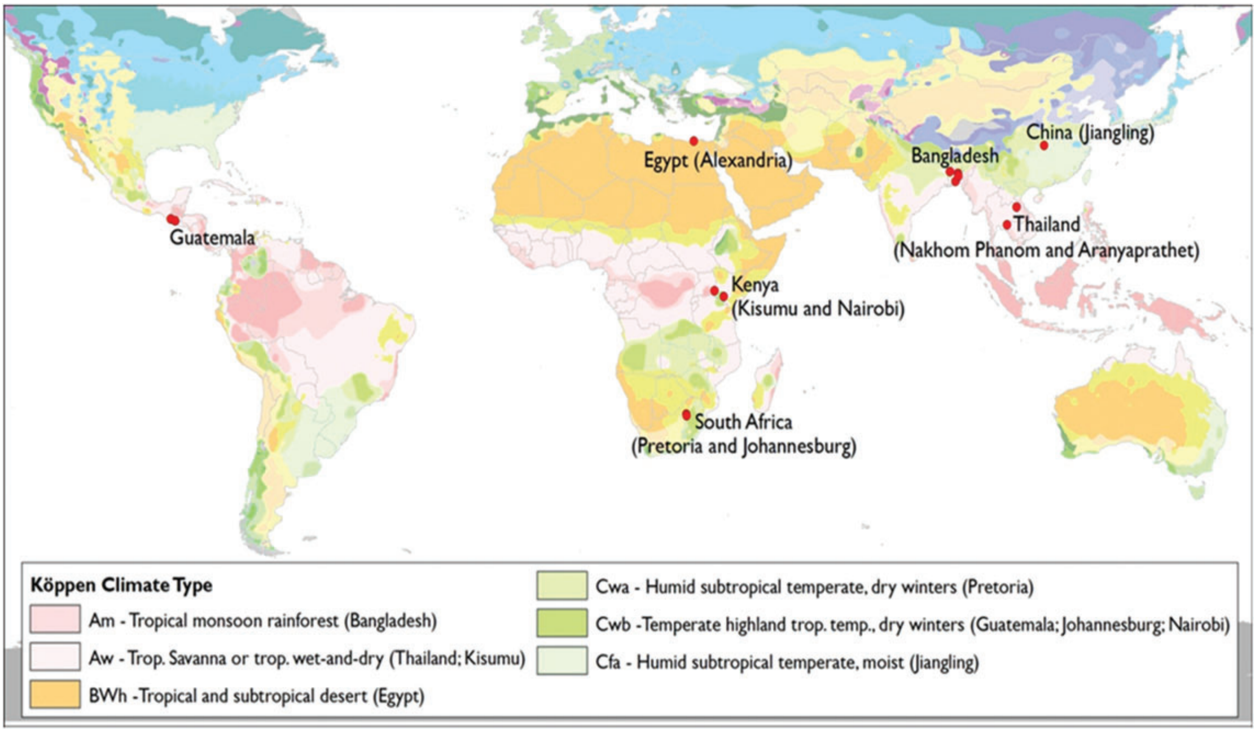

Figure 1. Climate zones of International Emerging Infections Program site's corresponding weather stations. See Table 2 correspondence between sites and stations.

RSV cases during each epidemic period. For each country, monthly RSV case totals and average monthly weather data were graphically summarized (Figure 2). All analyses were performed using SAS for Windows version 9.2.

RESULTS

RSV Seasonality

Multiple sites within the same country fell within different climate groups (Figure 1 and Table 1) but were similar in RSV circulation and weather over the time period analyzed. Therefore, multiples sites in Bangladesh, Guatemala, South Africa, and Thailand were combined, and results are presented by country. RSV seasonality between Lwak and Kibera sites in Kenya differed during 2009–2010; therefore, they are presented separately. One RSV epidemic period was observed in each country during each year, with 2 exceptions (Supplementary Figure 1): two distinct RSV epidemic periods, separated by 1 month, occurred in Egypt (during February–June 2010 and August 2010–February 2011) and in Bangladesh (during November 2005–March 2006 and May–August 2006). In Bangladesh, these two RSV epidemic periods were followed by 12 months with no RSV epidemics (September 2006–August 2007). Because of the absence of 2009 data from Bangladesh, the season onset could not be determined for other possible RSV epidemic periods during early 2010 in that country. Available data for 12 months from China was adequate to define onset and peak of 1 season but not offset. Of the countries analyzed, Thailand had the most consistent weather patterns and RSV surveillance over a 7-year period. The monthly number of RSV cases for Thailand and the other countries are shown in Figure 2.

Examining all countries combined, RSV season onsets occurred throughout January–December. Among countries with multiple years of data, the earliest calendar month of RSV season onset across all years occurred during the following months, by country: South Africa: (January), Kenya (February), Egypt (February), Guatemala (March), Bangladesh (May), Thailand (June), and China (September) (Supplementary Figure 1). RSV peaks occurred during January–December across all countries. RSV seasons lasted 3–9 months across all countries, with a median of 5 months. Bangladesh had the shortest seasons (median, 5 months) and Guatemala had the longest (median, 7 months).

Weather Patterns

Comparing meteorological data, sites in Egypt, Kenya, South Africa, and China were drier than those in Bangladesh and Thailand, which were hot and humid with heavy rainfall and monsoons (>59 inches of annual rainfall) (Supplementary Table 1). Guatemala sites, particularly those in Guatemala City

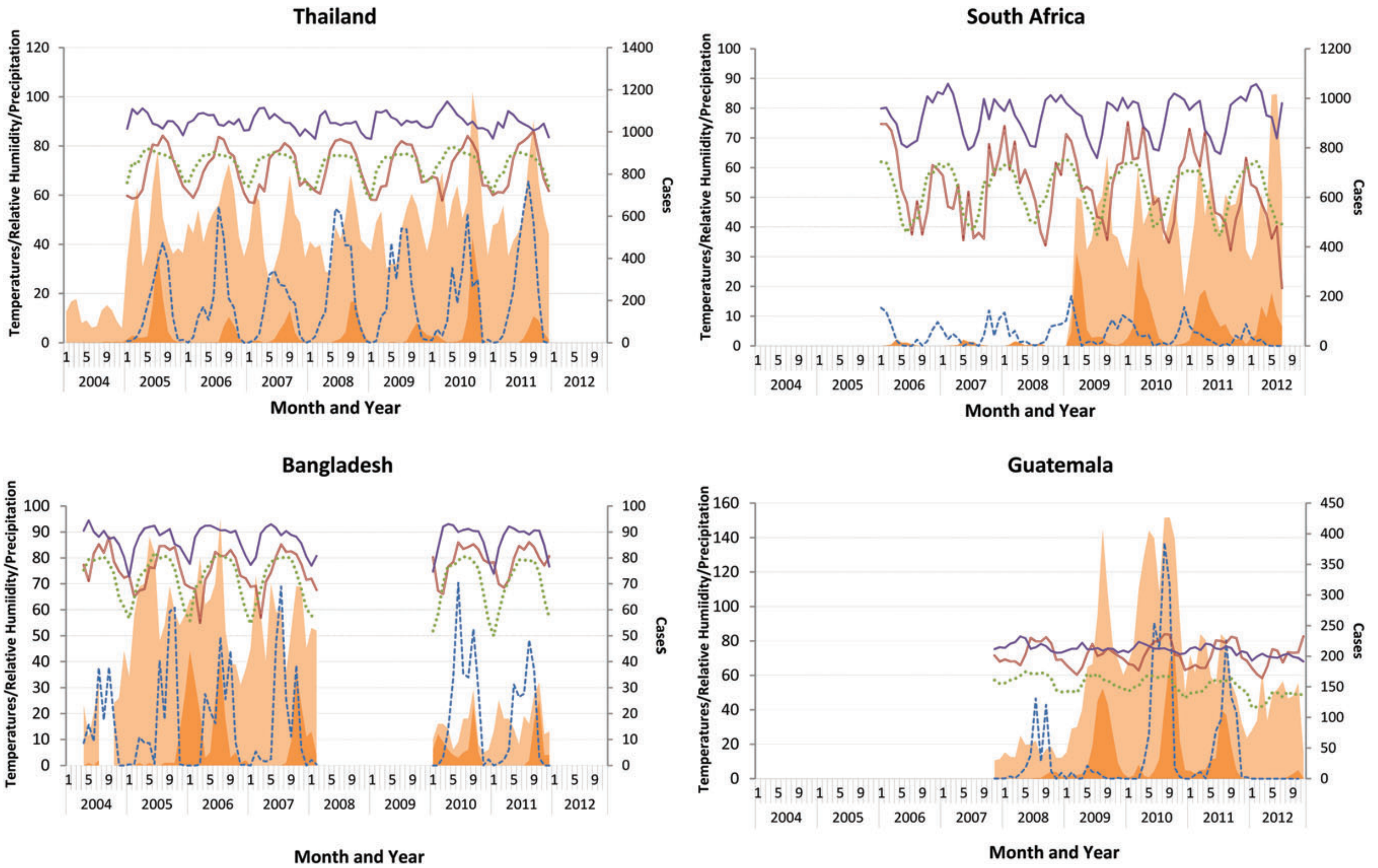

Figure 2. Laboratory-confirmed cases of respiratory syncytial virus (RSV) and weather measurements in combined sites by month, Thailand (2 provinces), South Africa (2 sites combined), Bangladesh (5 districts combined), Guatemala (3 sites combined), Kenya (2 separate sites), Egypt, and China, 2004–2012. RSV positives (dark orange), total number of patients tested for RSV (light orange), precipitation in inches (blue), percentage relative humidity (red), minimum temperature (green), and maximum temperature (purple) in degrees Farenheit. * Weather data extracted from weather station located in Kisumu. † Weater data extracted from weather station located in Nairobi.

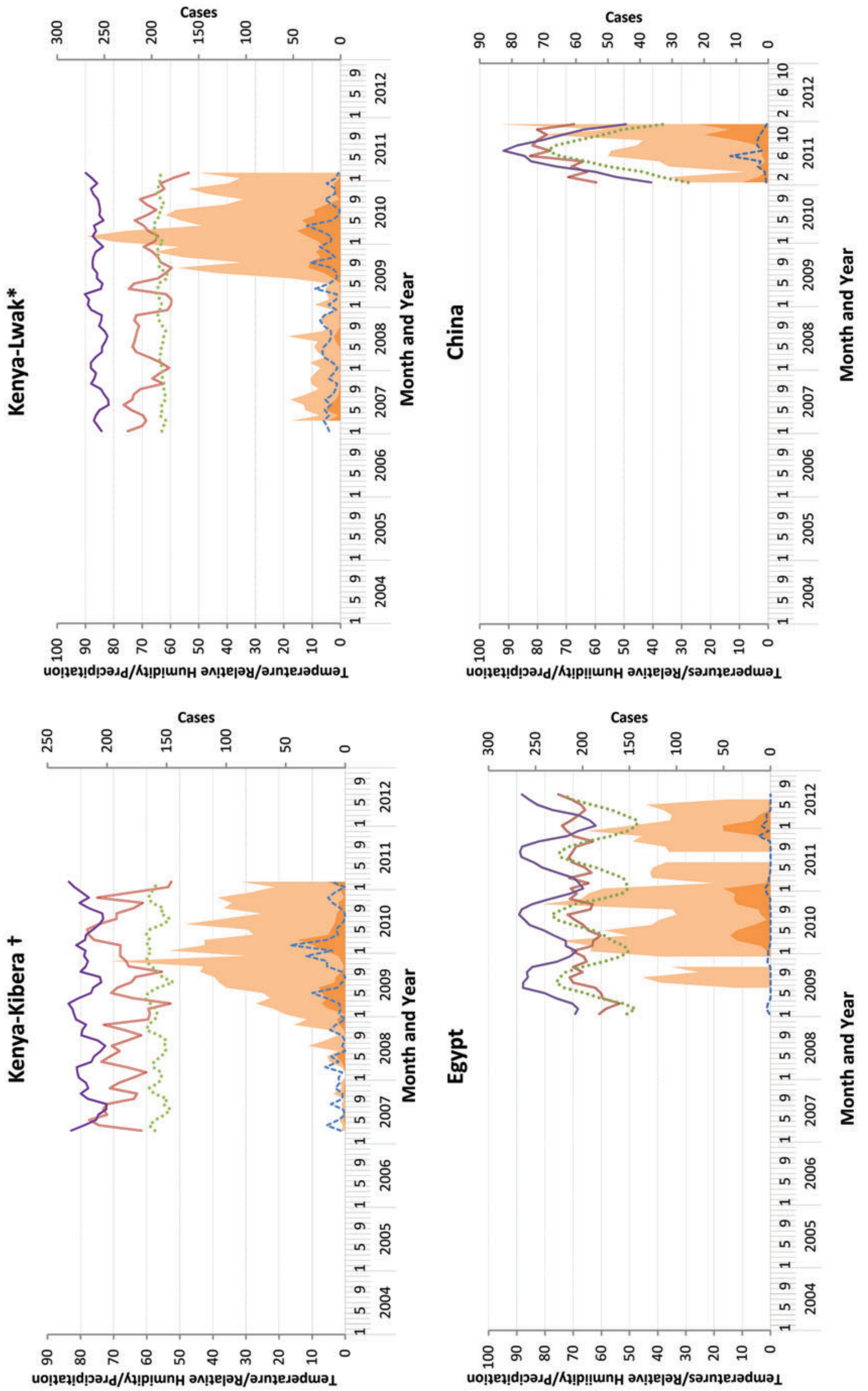

Figure 2 continued

and Quetzaltenango, also had periods with heavy rainfall but are at higher altitudes and were cooler than sites in Bangladesh and Thailand. In the China and South Africa sites, temperatures during the winter months dropped below freezing during some of the years observed.

Association Between RSV Activity and Weather

RSV onset occurred during periods of high rainfall and humidity (above-average precipitation and relative humidity) in Thailand, South Africa, and China (Figure 2 and Supplementary Table 1). In South Africa and China, RSV onset occurred within 1 month of the precipitation and relative humidity peak. Only in Thailand did the RSV onset occur during months with above-average minimum temperature. RSV onset did not appear to coincide consistently with patterns of rainfall, relative humidity, or temperature in Bangladesh, Egypt, Guatemala, or Kenya.

The RSV peak occurred during humid and warm months (above-average relative humidity and minimum temperature) in Bangladesh, Guatemala, and Thailand, countries with higher annual rainfall (annual precipitation >14 inches on average each month). In Bangladesh, 4 of 5 RSV peaks occurred during the rainy season (5 contiguous months of above-average precipitation based on the rainy season definition described in the Methods), which were characterized by above-average temperature and relative humidity. The remaining RSV peak in Bangladesh occurred during a cool period during 2006, the year with 2 RSV epidemics. In Guatemala, 2 of 3 RSV peaks occurred within 1 month of the relative humidity and precipitation peaks. These patterns were not always consistent, such as in 2009 in Guatemala when average monthly precipitation was <10 inches and a rainy season was less evident.

Thailand had the most consistent associations between RSV season and weather. Thailand's 7 RSV peaks (and 6 of 7 RSV onsets) occurred during rainy seasons with above-average annual rainfall (>17.41 inches), relative humidity (>71%), and minimum temperature (>73°F). The RSV peaks occurred several months after peak precipitation, but still during the rainy season, which on average occurred during May–October. Maximum temperature in Thailand exhibited less seasonality and did not have an evident association with RSV onset.

In contrast, RSV peaks occurred consistently during cooler months (below-average minimum and maximum temperatures) in China and Egypt and during autumn (after warmest months and before the coolest) in South Africa. In South Africa and China, RSV peaks occurred within 1 or 2 months after temperature lows. Similarly, the number of RSV cases was also comparatively low during temperature peaks. In Egypt, RSV peaks occurred on average 2 months before temperature lows.

Guatemala was the only country where RSV offset had a consistent pattern with any of the weather parameters assessed, occurring during cooler months and consistently occurring on average 2 months before temperature lows.

Over the period of available RSV surveillance data, weather parameters in Kenya exhibited less seasonality and did not have evident associations with RSV onset, peak, or offset. Unlike the Kibera site, the Lwak site had RSV cases during 2009–2010 that did not separate into multiple distinct RSV epidemic periods based on our onset and offset definitions.

DISCUSSION

This study describes recent RSV seasonality in a global surveillance network with similar specimen collection and RT-PCR testing. We observed distinct annual epidemics of RSV in all countries that provided multiple years of data and biannual RSV peaks in 1 year in Egypt and Bangladesh. The peak and duration of these annual epidemics varied by country but were generally consistent from year-to-year within a country.

Although the RSV activity observed among areas in our study may be influenced by weather patterns in general, the RSV peaks observed occurred during rainy seasons, after the precipitation peak in countries with higher annual temperatures and precipitation (Bangladesh, Guatemala, and Thailand). Other studies in tropical/subtropical areas have reported RSV seasons occurring during periods of high precipitation [10, 11], consistent with the hypothesis that rainy seasons prompt indoor crowding, thereby facilitating RSV transmission in tropical areas [26]. Conversely, we found that in countries with lower annual temperature and precipitation (China, Egypt) RSV peaks coincided with temperature lows, as reported by other studies [4, 12, 27]. Associations between cold temperatures and widespread RSV circulation in temperate climates have been well described [4, 28], whereas studies investigating the influence of weather on RSV epidemics in more extreme climate zones have been inconclusive [11, 27]. In Kenya, the duration of RSV seasons was long, but over the time period observed, there were no clear climate patterns that appeared to coincide with changes in RSV circulation. Other variables that likely influence RSV activity include environmental factors, social interactions, host susceptibility, and viral characteristics. Some studies have indicated that environmental factors such as solar radiation may influence RSV infectivity and that pollution may impact illness severity; others have postulated that indoor climate influences the route of RSV transmission [29–32]. We did not investigate these in our study.

Our study has several limitations. We cannot reach definitive conclusions about the association between RSV and climate factors, given the limited number of years and types of data available for analysis and the descriptive nature of our assessment. RSV activity observed in this study was limited to the catchment areas of participating surveillance sites and may not be representative of other areas. Also, the timing and availability of surveillance data varied by year and site, and data were aggregated by month, which limited our ability to conduct statistical modeling associations between climate parameters and RSV activity. However, at least 3 countries were represented in 7 of the 8 years analyzed. Differences or changes in surveillance protocols in the study sites during the study period may have affected the number and timing of RSV detections, particularly in areas with limited access to healthcare. Nevertheless, we retained all available years because the timing of RSV circulation trends was consistent over the study years. Finally, although the National Climatic Data Center is considered a reliable source of weather data, its data quality and completeness vary depending on the maintenance of weather monitors. However, we limited our analysis to weather stations with few gaps in data collection for the weather parameters used in our study during 2004–2012.

Despite these limitations, we found considerable heterogeneity in RSV circulation and weather patterns and their relative timing to one another, both within and among the countries contributing data to our study. Additional years of data and geographic areas would be needed to analyze the possible associations between RSV activity and Köppen-type climate groups or weather patterns.

In conclusion, we observed annual or biannual epidemics of RSV among different regions of the world. The timing of epidemic peaks varied among countries participating in our study, but from year to year, epidemics occurred generally during the same months within a country, and fluctuations in temperature and precipitation appeared to be associated with the timing of epidemics observed in surveillance sites of 6 of the 7 countries (Bangladesh, China, Egypt, Guatemala, South Africa, and Thailand). More data are needed to understand whether climate and other environmental factors and patterns of human behavior influence the timing and severity of RSV epidemics. Although it is challenging to assess causality from statistical associations, further surveillance and modeling would provide a better understanding of the dynamics of RSV circulation in low- and middle-income countries, which would help clinicians and public health authorities to better understand the contribution of RSV to acute respiratory illness in these countries and to allocate resources accordingly. Improved understanding of the seasonality and burden of RSV epidemics in these countries would also allow for the potential use of appropriately timed pharmaceutical and nonpharmaceutical interventions against RSV disease, such as future RSV vaccines, immunoprophylaxis, and good hygiene and infection control practices.

Supplementary Data

Supplementary materials are available at *The Journal of Infectious Diseases* online (http://jid.oxfordjournals.org/). Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyedited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author

Notes

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Potential conflicts of interest. All authors report no potential conflicts.

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