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Respiratory Syncytial Virus Surveillance in the United States, 2007–2012

Results from a National Surveillance System

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Background: Annual respiratory syncytial virus (RSV) outbreaks throughout the US exhibit variable patterns in onset, peak month of activity and duration of season. RSVAlert®, a US surveillance system, collects and characterizes RSV test data at national, regional, state and local levels.

Methods: RSV test data from 296 to 666 laboratories from 50 states, the District of Columbia and Puerto Rico (as of 2010) were collected during the 2007–2008 to 2011–2012 RSV seasons. Data were collected in early August/September to the following August/September each season. Participating laboratories provided the total number and types of RSV tests performed each week and test results. RSV season onset and offset were defined as the first and last, respectively, of 2 consecutive weeks during which the mean percentage of specimens testing positive for RSV was ≥10%.

Results: Nationally, the RSV season onset occurred in October/November of each year with offset occurring in March/April of the following year. The RSV season averaged 20 weeks and typically occurred earliest in the South and latest in the West. The onset, offset and duration varied considerably within the US Department of Health and Human Services regions. RSV activity in Puerto Rico was elevated throughout the 2-year period studied. Median onset in core-based statistical areas ranged from 2 weeks earlier to 5 weeks later than those in their corresponding states.

Conclusions: Substantial variability existed in the timing of RSV activity at all geographic strata analyzed. RSV actively circulated (ie, ≥10%) in many areas outside the traditionally defined RSV epidemic period of November to March.

Key Words: respiratory syncytial virus, surveillance, seasonality

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Respiratory syncytial virus (RSV) is the most common cause of lower respiratory tract illness in infants and young children. Premature infants and children who are immunocompromised or have cardiopulmonary disease are at high risk for developing severe RSV disease manifesting as bronchiolitis and/or pneumonia.[1] RSV disease is the leading cause of hospitalization in children <12 months in the United States[2–4] and may be a risk factor for asthma.[5–7] A key component to disease prevention and reducing RSV infections is accurately assessing RSV circulation.

There is a seasonal pattern to RSV circulation, with RSV outbreaks occurring annually in the United States between September to December and February to May. The onset, peak month of activity and duration of the season vary both annually and among geographic regions.[8–10] Surveillance data based on RSV testing conducted by local institutions, academic centers and the US Centers for Disease Control and Prevention (CDC) are used to define and characterize the RSV season. The CDC collects and reports surveillance data regarding respiratory viruses through the National Respiratory and Enteric Virus Surveillance System,[11] a passive, laboratory-based system that monitors the circulation of RSV.[10]

The RSVAlert® program (http://www.rsvalert.com), established in 2004, was developed to broaden RSV laboratory data collection and reporting in the United States.[12,13] The publicly available surveillance data generated from the RSVAlert program have been used to evaluate variability and patterns of the seasonal RSV epidemics from a temporal and geographic perspective in the United States [(ie, all 50 states, the District of Columbia (DC) and, beginning in 2010, Puerto Rico (PR)].[12,13] The primary purpose of this analysis was to describe seasonal RSV activity reported from participating laboratories during 5 RSV seasons (2007–2012) at the regional and national levels. Secondarily, this paper examined intra-state variability within systematically selected local regions in the United States.

MATERIALS AND METHODS

The RSVAlert program is based on active data collection (ie, sites report even when no testing occurs and are reminded to report if the weekly reporting deadline is missed) from participating laboratories of RSV testing performed as a part of routine clinical practice. Laboratories with 1 or more of the following characteristics are invited to participate in the program on an annual basis: the laboratory is part of the National Association of Children's Hospitals and Related Institutions; the laboratory is associated with a large children's hospital; the laboratory is associated with a hospital that contains a neonatal and/or pediatric intensive care unit; the laboratory had a high volume of RSV tests reported in prior years (≥10 tests per week during RSV peak season) and had good reporting compliance (ie, at least 70%) in prior years. Geographic representation is also taken into account during the annual enrollment process. Certain sites were asked to participate to ensure representation across states and local community areas.

For each year analyzed, collection of surveillance data began in August or early September to the following August/September, with the exception of May 2010 to August 2010 when data were not collected due to a program reduction. Participating laboratories

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provided the total number of diagnostic RSV tests performed each week and the type of test performed [ie, antigen detection, virus isolation or polymerase chain reaction (PCR)]. If multiple (ie, confirmatory) tests were performed, laboratories were asked to report the initial test type and result. RSV test data from the previous week (ending on Saturday) were aggregated (weekly) according to national, state and local geographic regions. Data from each year were analyzed for seasonal trends at the national, regional, state and local levels. To characterize seasonal patterns on a large scale, data were stratified by the 4 census regions (Northeast, Midwest, South and West) and the 10 regions defined by the US Department of Health and Human Services (HHS). Data from Florida (FL) and PR were analyzed separately due to their uncharacteristically longer season durations.

To examine RSV seasonality at local levels, a sample of core-based statistical areas (CBSAs, formerly known as metropolitan statistical areas) were systematically selected for comparison. CBSAs consist of metropolitan (urban core of ≥50,000 people) and micropolitan (urban core of ≥10,000 to <50,000 people) statistical areas. Each area consists of ≥1 county and any adjacent counties with a high degree of social and economic integration with the urban core (as measured by commuting ties).[14]

States with ≥6 CBSAs reported in RSVAlert across all 5 seasons that each contained ≥2 participating laboratories within the CBSA (California, FL, Texas, North Carolina, New York (NY), Ohio (OH), Pennsylvania, South Carolina, Michigan and Washington) were identified. After excluding FL because it is examined in more detail elsewhere, 3 states were randomly selected by first assigning a random order rank 1–9 and then using a random number generator from 1 to 9 to determine that CBSAs within NY, North Carolina and OH would be reviewed. Within these states, trends between CBSAs with ≥2 participating laboratories were assessed. For this assessment, the most populous CBSA in a state was identified and designated as the index CBSA. Two additional CBSAs were selected for comparison to the index CBSA based on proximity to the index CBSA. The proximal CBSA was the most populous CBSA within 150 miles of the index CBSA. The distal CBSA was

TABLE 1. RSVAlert Program Characteristics

Data Collection Periods	Laboratories, n	CBSAs Covered, n	States Participating, n	Test Types Collected
September 8, 2007, to August 30, 2008	626	200	50 (+ DC)	Antigen, VI, PCR
September 6, 2008, to August 29, 2009	666	200	50 (+ DC)	Antigen, VI, PCR
September 5, 2009, to May 1, 2010*	647/296†	197/99†	50 (+ DC)	Antigen, VI, PCR
August 14, 2010, to August 6, 2011	480	190	50 (+ DC, PR)	Antigen, VI, PCR
August 13, 2011, to August 4, 2012	479	191	50 (+ DC, PR)	Antigen, VI, PCR

*Data were not collected from May 2010 to August 2010.
†Reduced laboratory site and CBSA counts reflect program reduction beginning January 2010.
VI, virus isolation.

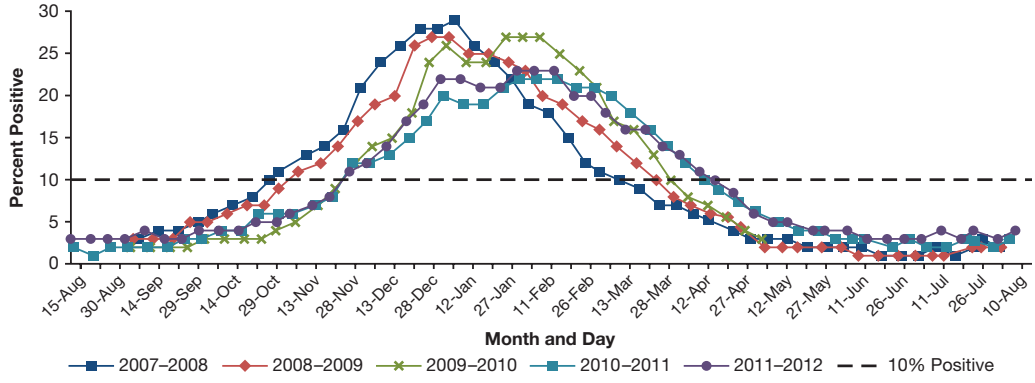

FIGURE 1. Proportions of RSV tests that were positive over 5 seasons, 2007–2008 through 2011–2012. Data from August 13 to August 6 of the following year are displayed for each season. If data collection for the RSVAlert program began or ended outside those weeks within a given season, data from those weeks are not displayed.

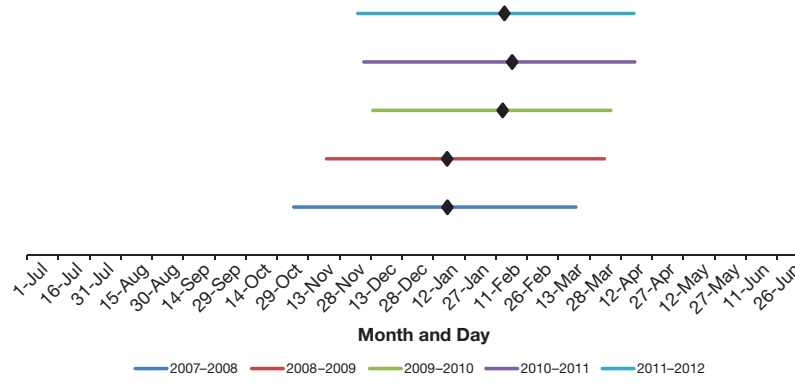

FIGURE 2. RSV season characteristics based on RSV antigen, PCR and virus isolation test results, national level (including FL and PR). Black diamonds represent RSV season peak week.

TABLE 2. Onset, Offset and Duration of Significant RSV Activity by Region and Season

Season	National*	National (Without FL or PR)	FL	Northeast	Midwest	South	West
2007–2008							
Onset	October 27, 2007	November 10, 2007	July 28, 2007	November 3, 2007	November 24, 2007	October 27, 2007	December 8, 2007
Offset	March 8, 2008	March 8, 2008	February 2, 2008	February 16, 2008	March 22, 2008	February 16, 2008	March 29, 2008
Duration, weeks	20	18	28	16	18	17	17
2008–2009							
Onset	November 8, 2008	November 15, 2008	July 12, 2008	November 15, 2008	December 13, 2008	November 1, 2008	December 6, 2008
Offset	March 21, 2009	March 21, 2009	February 7, 2009	March 21, 2009	March 28, 2009	February 28, 2009	March 28, 2009
Duration, weeks	20	19	31	19	16	18	17
2009–2010							
Onset	November 28, 2009	November 28, 2009	August 22, 2009	November 21, 2009	December 12, 2009	November 14, 2009	December 26, 2009
Offset	March 27, 2010	March 27, 2010	March 6, 2010	March 13, 2010	March 27, 2010	March 13, 2010	April 3, 2010
Duration, weeks	18	18	29	17	16	18	15
2010–2011							
Onset	November 27, 2010	December 4, 2010	September 25, 2010	November 27, 2010	December 25, 2010	November 27, 2010	December 11, 2010
Offset	April 9, 2011	April 9, 2011	March 19, 2011	March 26, 2011	April 23, 2011	April 2, 2011	April 2, 2011
Duration, weeks	20	19	26	18	18	19	17
2011–2012							
Onset	November 26, 2011	November 26, 2011	August 13, 2011	November 19, 2011	December 17, 2011	November 26, 2011	December 31, 2011
Offset	April 7, 2012	April 7, 2012	March 3, 2012	March 17, 2012	April 21, 2012	March 24, 2012	April 28, 2012
Duration, weeks	20	20	30	18	19	18	18

*Includes FL and PR.

the most populous CBSA between 150 and 300 miles of the index CBSA.

RSV season onset was derived from the National Respiratory and Enteric Virus Surveillance System definition[10,15] and was the first of 2 consecutive weeks during which at least 2 of 10 specimens that were tested each week were positive for RSV or when at least 10% of ≥11 tests were reported to be RSV positive; season offset was defined as the last of 2 consecutive weeks when at least 2 of 10 specimens that were tested each week were positive for RSV or when at least 10% of ≥11 tests were reported RSV positive. Percentage positivity for a given week was calculated using the following formula:

$$(\text{Positive tests} \div \text{Total tests}) \times 100$$

RESULTS

National Results

RSV test data from 296 to 666 laboratories in all 50 states and DC were collected during the 2007–2008 through 2011–2012 RSV seasons (Table 1). Data collection and reporting from PR began with the 2010–2011 season. Weekly proportions of positive RSV tests in each of the 5 seasons are displayed in Figure 1. Across the 5 seasons, the total number of tests ranged from 527,653 to 678,649 and the total number of positive tests ranged from 67,819 to 84,094. Season onset and offset varied by up to 5 weeks over the 5 seasons. The median peak week was the week ending January 28 and occurred as early as the week ending January 3 and as late as February 5. Evaluation of the RSV season nationally showed that the duration of the RSV season ranged from 18 weeks in 2009–2010 to 20 weeks in 2007–2008, 2008–2009, 2010–2011 and 2011–2012 (Fig. 2). When data from FL and PR were excluded, the mean duration of the RSV season was shortened by 1 week over the 5 seasons with the onset time each season occurring during the same week or 1–2 weeks later (Table 2).

Regional Results

The RSV season typically began and ended earliest in the South and latest in the West over the 5 seasons studied (Table 2). Across the 4 census regions (Northeast, Midwest, South and West), the median onset varied across a 4-week period and the median offset varied between the groups by 3 weeks. The median peak in each of the groups varied over a range of 6 weeks. RSV activity peaked as early as the week ending December 29 (2007–2008 RSV season) in the South and as late as the week ending March 5 (2010–2011 RSV season) in the Midwest. The season duration ranged from 15 weeks (West in 2009–2010) to 19 weeks (Northeast in 2008–2009; Midwest in 2011–2012 and South in 2010–2011) and averaged 17–18 weeks in the 4 regions.

As shown in Figure 3, onset, offset, peak and duration of the RSV seasons varied considerably between the HHS regions and FL compared with the national season characteristics. Across the 13 geographic groups (10 HHS regions, FL, national and national without FL and PR), the median onset varied across a 19-week period and the median offset varied between the groups by 6 weeks. The median peak in each of the groups varied over a range of 12 weeks. In Florida, an extended season was observed in each of the 5 seasons studied. The mean duration of the 5 RSV seasons in FL was approximately 29 weeks, 9 weeks longer than the national average (not including FL or PR) within the same period (Table 2). RSV activity in FL peaked as early as the week ending October 18 (2008–2009 RSV season) and as late as the week ending January 2 (2009–2010 RSV season).

State and Local Trends

Several state and local trends were observed. In PR, where data collection began in the 2010–2011 season, the mean percentage

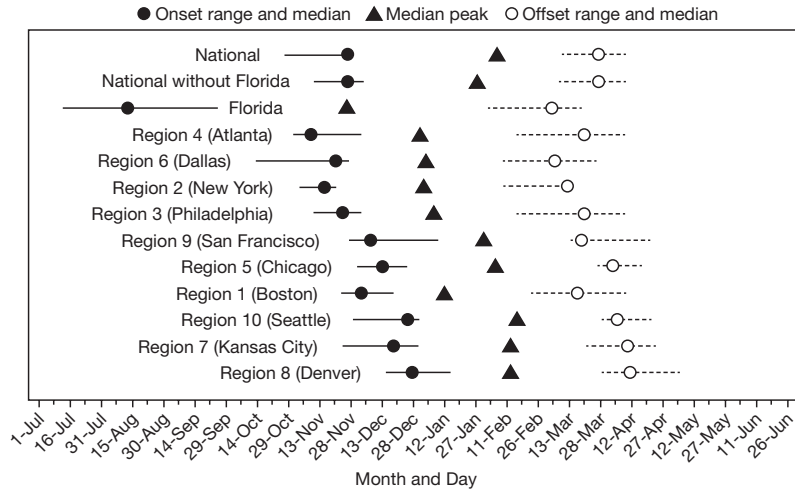

FIGURE 3. RSV season onset and offset range and median, national and HHS region levels* and FL, September 2007 to August 2012. HHS, US Department of Health and Human Services. Figure format source was taken from Mutuc and Langley.[10] *Listed by region number and headquarters city. Region 1 (Boston): Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island and Vermont. Region 2 (NY): New Jersey and NY. Region 3 (Philadelphia): Delaware, DC, Maryland, Pennsylvania, Virginia and West Virginia. Region 4 (Atlanta): Alabama, Georgia, Kentucky, Mississippi, North Carolina, South Carolina and Tennessee. Region 5 (Chicago): Illinois, Indiana, Michigan, Minnesota, OH and Wisconsin. Region 6 (Dallas): Arkansas, Louisiana, New Mexico, Oklahoma and Texas. Region 7 (Kansas City): Iowa, Kansas, Missouri and Nebraska. Region 8 (Denver): Colorado, Montana, North Dakota, South Dakota, Utah and Wyoming. Region 9 (San Francisco): Arizona, California, Hawaii and Nevada. Region 10 (Seattle): Alaska, Idaho, Oregon and Washington.

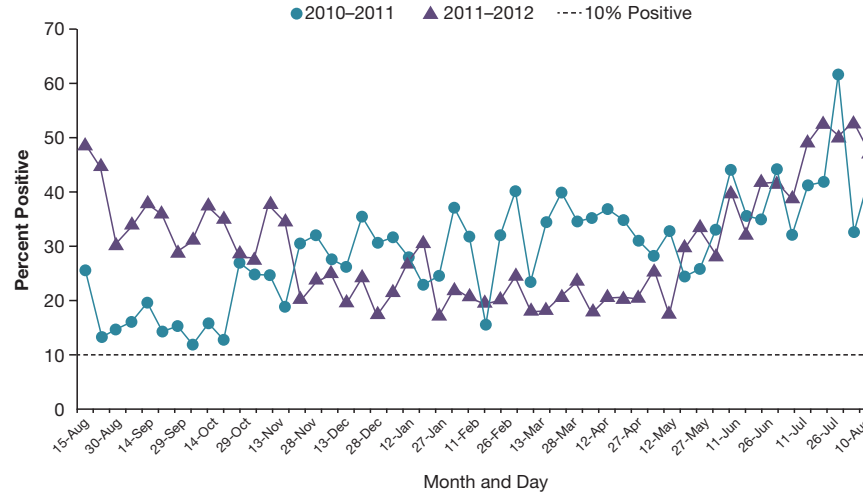

FIGURE 4. RSV activity in PR during the 2010–2011 and 2011–2012 seasons.

of specimens testing positive for RSV was ≥10% (range, 12–62%) throughout each of the 2 seasons studied (Fig. 4).

When the median RSV season onsets from the CBSAs were compared with the median onsets of their respective states, results demonstrated onset differences between 1 week earlier and 8 weeks later than the median onset at the state level (Fig. 5). Average CBSA season durations ranged from 11 weeks shorter (the Youngstown-Warren-Boardman, OH-PA CBSA) to similar duration (the Dayton, OH CBSA) as their respective states. Among the 3 CBSAs that were analyzed in each state, the proximal CBSAs had a median onset that occurred from 3 weeks before (OH) to 6 weeks after (NY) the median onset of the index CBSAs. The average season duration for the proximal CBSAs was up to 3 weeks shorter (NY) to 6 weeks longer (OH) than the average season duration from the index CBSA. Differences similar to those between proximal and index CBSAs were observed between the distal and index CBSAs.

DISCUSSION

This report describes RSV activity reported during 5 RSV seasons (2007–2008 through 2011–2012) at the local (ie, CBSA), state, regional and national levels. Our results underscore the variability in annual RSV season characteristics by season and at all geographic levels.

At the national level, RSV season onset and offset varied across the seasons by 0–5 weeks while season duration varied by 0–2 weeks in length. The findings are similar to those reported for RSVAlert during the 2004–2005 through 2006–2007 RSV seasons, which showed the season onset and offset varied by 1–4 weeks and duration by 4–5 weeks.[12] Season onset and offset occurred later during 2009–2012 compared with 2007–2009, but this is not atypical; we previously reported onset occurring in the second half of November during the 2005–2006 RSV season.[12] Preliminary data

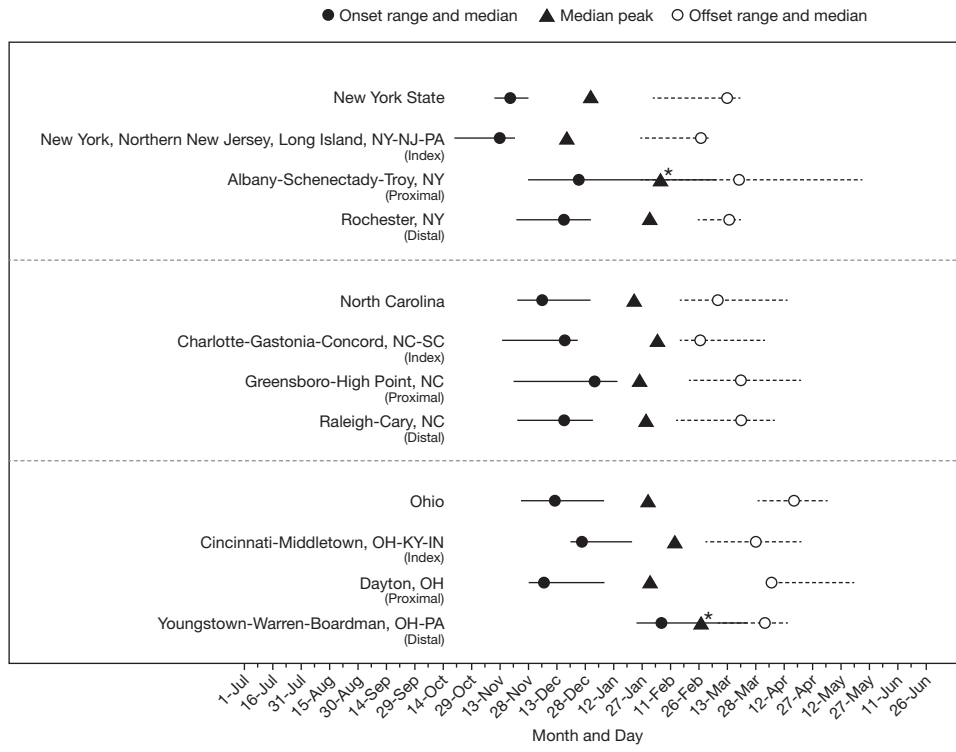

FIGURE 5. RSV season onset and offset range and median, CBSA level. *Median onset and offset ranges overlap.

from RSVAlert and the CDC[16] for the 2012–2013 RSV season also suggest a reversion to an earlier onset and offset, similar to that observed in the 2007–2009 RSV seasons. These observations highlight the variability in RSV season characteristics.

Varying seasonal patterns of RSV activity were also observed between and within individual states. Analysis of CBSA-level data demonstrated a high degree of intra-state variability. Consistent with previous reports,[15,17,18] our findings suggest that RSV circulation is primarily a local phenomenon. For example, previous reports[10,19,20] have shown that the RSV season is longer in FL compared with all other states in the United States. In PR, RSV activity was year-round and lacked a discernable seasonal pattern (ie, the weekly percentage of specimens testing positive for RSV was ≥10% throughout the entire year in each of the 2 seasons studied). To our knowledge, this has not been reported elsewhere for RSV, although it is similar to other respiratory viruses, such as influenza, which have been shown to circulate seasonally in temperate regions of the world and aseasonally in tropical regions.[21,22] RSV activity in PR should be monitored in the future to substantiate the observations reported here.

A comparison of the current analysis with the data published by the CDC[9,10,19,20] for the 2007–2009 and 2010–2012 RSV seasons (2009–2010 RSV season data were not published separately) showed that nationally (including FL) our data differed by up to 1 week for onset or offset times and up to 2 weeks in duration. When the CDC data from the HHS regions were compared (across the 2007–2009 and 2010–2012 RSV seasons and all HHS regions), our data differed by up to 4 weeks for onset or offset times and up to 5 weeks in duration. Comparisons at the CBSA level were not available because those data are not reported by the CDC. The primary difference between the methods of the CDC analysis and the current analysis is that the CDC defines RSV seasonal onset, offset and duration based solely on antigen test results,[9,10,19,20] whereas RSVAlert uses the results of all RSV tests regardless of type (antigen, virus isolation and PCR). The minimal differences between the 2 approaches at the national level suggest that RSV test type does not significantly affect the determination of RSV seasonality. However, the larger differences at the regional level suggest that inclusion of all RSV test types may better characterize regional RSV seasonality. Differences between surveillance programs should be considered when comparing results.

The primary limitation of this analysis is the lack of standardization of clinical or laboratory methods across participating sites. The timing of RSV testing at individual sites may be influenced by provider perceptions of expected timing of RSV activity, which may bias RSV surveillance data patterns. The results of a large US study in 2006–2008 of infants presenting to emergency departments with lower respiratory tract illness or apnea suggested that RSV activity may be higher than generally appreciated in September to October in the MidAtlantic and Southeast regions.[23] Although the current analysis demonstrated an early onset of RSV activity in the Northeast and South, it did not demonstrate high levels of RSV activity before late October. This difference suggests that surveillance data obtained via general clinical practices (ie, without protocols regarding whom to test and when) may not fully capture RSV activity. Although the recruitment strategy focused on capturing pediatric data, it is likely that there is a low proportion of data from nonpediatric hospitals, especially if sites were contacted to ensure geographic representation. Results may also be subject to nonresponse bias because program participation is voluntary; the data may be influenced by a participation bias and thus may differ from the total population. Moreover, participating laboratories in the RSVAlert program varied from season to season, which may account for some of the observed variability in RSV season characteristics.

Strengths of the study include active data collection methods which allowed for more accurate, complete and timely data capture compared with methods that rely on voluntary reporting of

data. Moreover, our large and geographically diverse sample of participating laboratories allows for a robust description of US RSV activity. Finally, the ability to examine local geographic areas (ie, CBSAs) provides additional insight into the nuances of geographic patterns of RSV activity in the United States.

CONCLUSIONS

In summary, results from the RSVAlert program for 2007–2012 demonstrate substantial variability in the timing of RSV activity between and within geographic areas. This observation was noted at all geographic strata (census regions, HHS regions, states and CBSAs) over the 5 seasons studied. RSV actively circulated in many areas for periods of time that were either longer or shorter than the commonly described season (ie, onset in the fall and offset in the late winter or early spring). Local and regional variability in RSV circulation emphasizes the importance of local surveillance data in accurately assessing RSV activity.

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