RSV Hospitalizations in Arizona 2004-2008

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Abstract

Background: Respiratory syncytial virus (RSV) is a leading cause of lower respiratory tract infections in infants and young children and is a major cause of respiratory illness in immune compromised adults and the elderly. Yet, the epidemiology of RSV infections is not well characterized. In Arizona, current surveillance consists of weekly summarization of lab-confirmed data by the Arizona Department of Health Services (ADHS). A retrospective analysis of hospitalized RSV cases in Arizona was conducted to examine trends and demographics. Information gained will contribute to our understanding of RSV infections in Arizona.

Methods: Hospital Discharge Data from 2004 to 2008 were analyzed. Patients with ICD-9-CM codes for any RSV-related illness (466.11, 480.1, and 079.6) in the primary or secondary diagnosis fields were selected. Population-based hospitalization rates were calculated and mean length of stay was determined for the following variables: gender, ethnicity, age, county of residence, and insurance type. Multivariate analyses were performed.

Results: From January 2004 to December 2008, there were 10,424 residents hospitalized in Arizona due to RSV. Ninety-one percent of the total hospitalizations were in children < 2 years of age, 6% in 2-5 years of age, and 3% in >5 years of age. Fifty-four percent were male and 46% were female. Infants less than 3 months of age were more likely to have higher length of stays in the hospital than all other age groups (4.2 days, $p<0.001$). Hispanics had the highest rates of RSV hospitalizations (56.3 per 100,000), followed by American Indian/Alaskan Native (47.2 per 100,000) and Blacks (34.3 per 100,000). By county, Graham County had the highest rate (71.3 per 100,000), followed by Navajo County (58.2 per 100,000) and Coconino County (49.7 per 100,000).

Conclusion: The information gained will increase our understanding of RSV infections in Arizona and may lead to the development of enhanced education and prevention strategies.

Introduction

Respiratory syncytial virus (RSV) is the leading cause of lower respiratory tract infections in infants and young children and is a major cause of respiratory illness in immune compromised adults and the elderly. Yet, the epidemiology of RSV infections in Arizona is not well characterized. In Arizona, analyses of RSV infections are limited to descriptions of cases by age, gender, and geographical location. For this study, a descriptive analysis of inpatient RSV cases identified from the Arizona Hospital Discharge Database (from 2004 to 2008) was performed to examine hospitalization trends over time and space and compare length of stay by patient demographics.

Background

RSV is the most common cause of swelling and mucus buildup in the lungs (bronchiolitis) and inflammation in the lungs (pneumonia) in children less than one year of age in the United States (U.S.)(1). It is estimated that between 75,000 and 100,000 children are hospitalized with RSV every year in the U.S. (1). Most children are infected with RSV by the age of two (2). In Arizona, RSV infection rates can range anywhere from 13.2% to 34.1% (3). Other risk factors for serious infection include adults with severe immune compromised systems or with underlying heart and lung disease (4). Between 2-9% of elderly hospitalizations for pneumonia are caused by RSV (5). However, it is unclear if elderly hospitalizations are due to the frailty of the host body rather than a weak immune system (6). Immunity to RSV is oftentimes incomplete, and re-infection occurs in all ages (7).

RSV causes mild, cold-like symptoms in children and adults. Runny nose and decrease in appetite are common 4-6 days after exposure, followed by coughing, sneezing, and low-grade fever. Recovery typically occurs in 1-2 weeks. In more severe cases, children with pneumonia or bronchiolitis may need to be intubated and ventilated. No specific treatment is available to eliminate the virus from the body; instead therapy is geared towards treating the symptoms. Palivizumab, an antibody for the

prevention of RSV, can reduce the risk of hospitalization due to RSV, but due to its expense, it is currently recommended only for use in high risk infant groups (8).

Laboratory diagnosis is needed to distinguish RSV from other respiratory viruses that exhibit similar cold-like symptoms. The most common diagnostic methods are virus isolation in cell culture or direct examination of respiratory secretions by immunofluorescence microscopy. Serological tests to detect antibody levels can also be performed but require acute and convalescent-phase serum samples. The disadvantage to using cell culture or serological testing such as enzyme immunoassays (EIA) is that it may be days before results are available. When results are needed quickly to either start a severely ill patient on treatment or to prevent the spread of the virus, rapid diagnostic tests are preferred. Many rapid diagnostic EIA kits are available commercially to identify RSV antigen in respiratory secretions (9). The main advantage to the use of rapid test kits is time. Results can be available within minutes as opposed to days or weeks for cell culture or serological testing. However, the sensitivity and specificity of rapid test kits vary between commercial vendors.

The onset and duration of RSV seasons vary by location and by year. In the US, RSV seasons typically occur from November to April, with outbreaks lasting between 3-4 months. In temperate climates and desert climates, RSV outbreaks occur during the cold months. In tropical or subtropical climates, RSV outbreaks are associated with the rainfall. In temperate equatorial areas, RSV seasons are harder to define, with outbreaks occurring year round (10). In the US, the start of RSV season varies by location. For the 2007/2008 season, the start of the RSV season ranged from July (Florida) to mid-October (New York) to mid-December (Denver). The season offset ranged from late January (Florida) to early March (Kansas City) to early April (Chicago) (11).

Surveillance of RSV

Nationally, RSV is monitored by the National Respiratory and Enteric Virus Surveillance System (NREVSS), a voluntary, laboratory-based surveillance system maintained by the Centers for Disease

Control and Prevention (CDC). Laboratories report the number of viral tests performed (RSV included) and the total number positive by collection date. National, geographic, and state trends are updated weekly, and annual seasonal summary data are published in CDC's Morbidity and Mortality Weekly Report. For the 2009/2010 RSV season, a total of 634 laboratories from all 50 states and the District of Columbia participated in NREVSS RSV reporting (14).

Under Arizona Administrative Code (A.A.C.) R9-6-204, laboratory-confirmed cases of RSV must be reported to the Arizona Department of Health Service's Office of Infectious Disease Services (ADHS OIDS) within five working days after obtaining a positive test result. Reports include name, address and phone number (if available), birth date, specimen type, date of collection, type of test, results, and health care provider contact information. Summary data are compiled weekly and are available on the ADHS website (http://www.azdhs.gov/phs/oids/epi/flu/index.htm).

In Arizona, all state-licensed non-federal and non-tribal hospitals are mandated to report hospital inpatient and emergency department discharge records to ADHS under Arizona Revised Statute (A.R.S) 26-125.05 and A.A.C. Title 9, Chapter 11, Articles 4 & 5. In addition to more detailed patient demographic information, Hospital Discharge Database (HDD) records include procedure codes, billing codes, costs, and provider information. Information obtained can be used to enhance our understanding of RSV.

Methods

Data Collection Methods

For this study, inpatient HDD records for the years 2004 to 2008 were obtained from ADHS. Subjects were identified by their International Classification of Diseases (ICD) code, 9th edition. Patients with the following primary or secondary ICD diagnosis codes were included in the study: 466.11 (RSV bronchiolitis), 480.1 (RSV pneumonia), and 079.6 (RSV not otherwise specified). Out-of-state patients and patients with no known addresses were excluded from the study. Data were de-identified before

analysis. For these selected patients, the following variables were utilized and included in the analysis file: age, race, gender, county of residence, length of hospital stay, insurance type, and total charges. Records were de-duplicated based on the medical record number such that any repeat patient visits within 90 days were counted as one case.

Age in days was calculated from the admission date and birth date. One additional categorical variable was created using the age in days variable. Age was separated into three-month intervals. A length of stay variable was calculated by subtracting the date of admission from the date of discharge. Payer source was consolidated into four categories: AHCCCS (which includes Health Care Group, AHCCS Medicaid, Children's Rehab Services), federal insurance (includes Medicare, CHAMPUS/TRICARE, Indian Health Services, Medicare Risk), Private Insurance (includes Self Pay, Commercial Indemnity, HMO, PPO, Workers Compensation), and Other Payment (includes Charity, Foreign National, and Other). Counties were grouped into four geographical regions: Central Region (Gila, Maricopa, and Pinal Counties), Northern Region (Apache, Coconino, Navajo, and Yavapai Counties), Southern Region (Cochise, Graham, Greenlee, Pima, and Santa Cruz Counties), and Western Region (La Paz, Mohave, and Yuma Counties).

Season onset, as defined by NRVESS, is the first two consecutive weeks during which the mean percentage of specimens testing positive for RSV antigen is $\geq$ 10%, and season offset as the last of two consecutive weeks during which the mean percentage of positive specimens is $\geq$ 10% (13, 14). RSV season onsets and offsets for hospitalizations could not be determined using NRVESS criteria because it was unknown how many of the cases were laboratory-confirmed as RSV. Instead, for the purpose of this study, hospitalized season onset was defined as the first of two consecutive weeks during which there were more than two hospitalizations. Season offset was defined as the last of two consecutive weeks during which there were more than two hospitalizations. The measure of two hospitalizations was chosen due to some counties having fewer cases, making it difficult to assess seasonality. Season onsets and offsets were then computed for each of the five seasons.

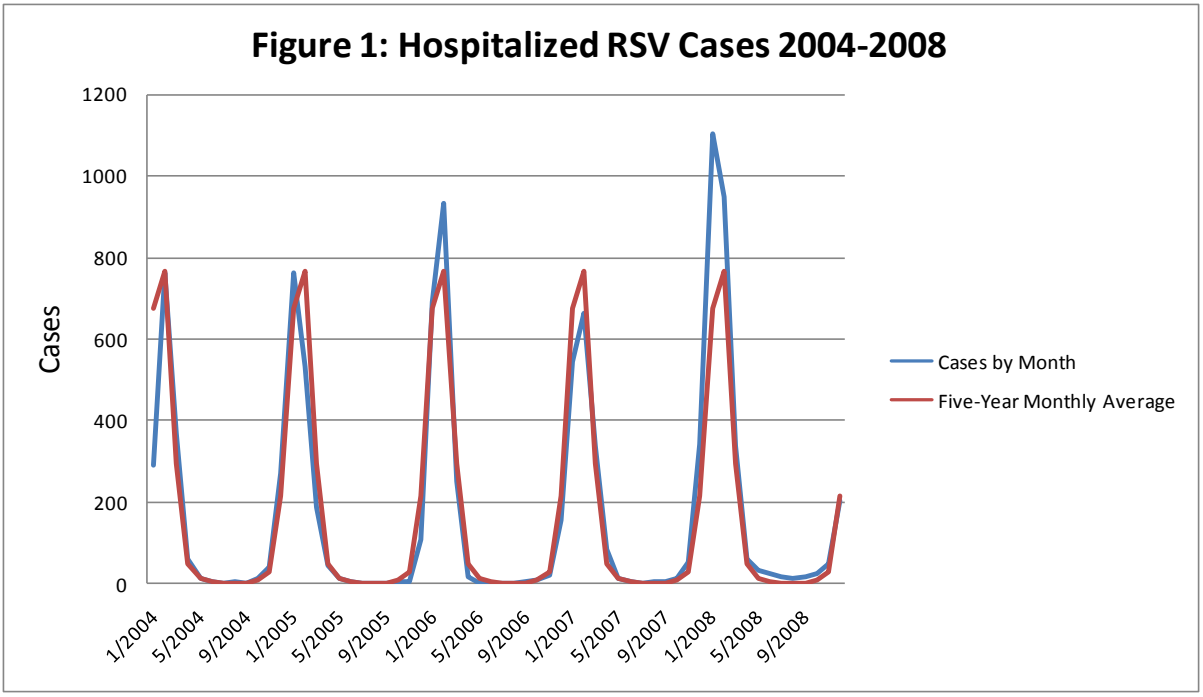
Inpatient HDD records were also obtained for comparison for children ≤ 2 years of age with the following ICD-9 coding: 480.9 (viral pneumonia unspecified), 480.2 (pneumonia due to parainfluenza), 480.0 (pneumonia due to adenovirus), and 079.8 (adenovirus) for years 2004 to 2008. Total counts by year and ICD-9 coding were tabulated for these non-RSV records. No other demographic variable was used for these diagnostic codes.

Data Analysis

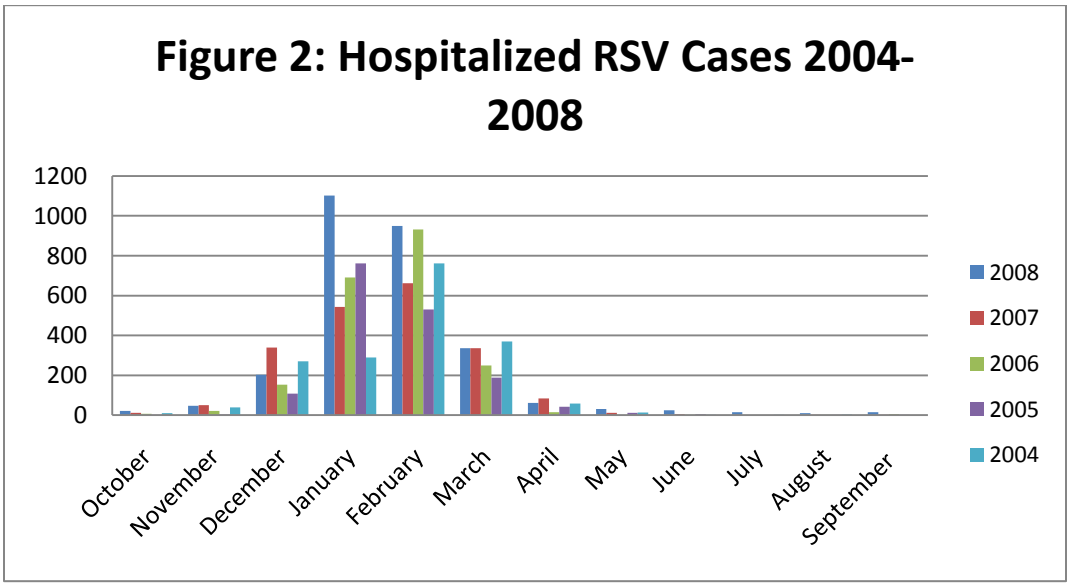
Descriptive analyses were conducted to describe the distribution of RSV infections in Arizona by age, county of residence, race/ethnicity, payer type, length of hospital stay, and total charges. Hospitalization rates were expressed as the number of hospitalized RSV patients per 100,000 residents. Population denominators were obtained from the Arizona Health Status and Vital Statistics website at www.azdhs.gov/plan/index.htm. Hospitalization rates were calculated by dividing the number of persons hospitalized for RSV by the estimated populations by year and by group. Five-year hospitalization rates were then calculated by taking the mean of the individual years. Hospitalization rates and 95% confidence intervals were calculated for race/ethnicity and county of residence. Mean length of stay was calculated for age, race/ethnicity, gender, and county of residence. One-way ANOVA was used to determine statistically significant differences between length of stay and the categorical variables. Statistical analyses were performed with SAS version 9.2 (SAS Institute Inc., Cary, NC).

Results

From January 2004 to December 2008, there were 10,960 patients hospitalized in Arizona with a primary or secondary diagnosis of RSV. Five hundred thirty-six cases were excluded due to unknown or out-of-state residency for a total of 10,424 cases. The seasonality of RSV hospitalizations has been consistent, with no dramatic shifts over the five-year period (Figure 1). The greatest number of RSV-related hospitalizations occurred in the 2007/2008 season (2,868 hospitalizations from November to May).



Based on NRVESS surveillance data, RSV season onset in Arizona is typically from November to mid-December. RSV season offset is typically from mid-March to early April (13, 14). In the five-year period examined here, hospitalizations in the HDD generally start to increase in November or December, the season peaks in January or February, and season offset is in March or April (Figure 2).



Using our definition for hospitalized season onset and offset, the Central Region had the earliest onset dates and the longest season duration of all the regions. The Western Region had the shortest season duration (Table 1). Over the five-year period, the 2007/2008 RSV season was the longest in duration for all regions.

Table 1: Season Onset and Offset of Hospitalized Cases by Region

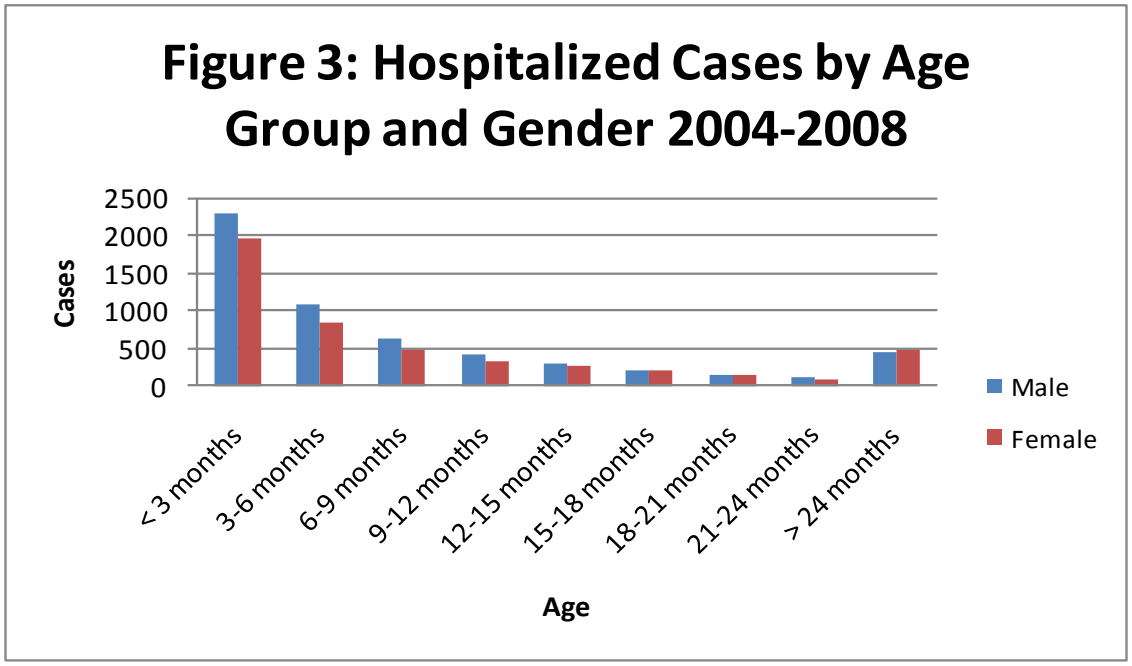
	04/05 SEASON		05/06 SEASON		06/07 SEASON		07/08 SEASON	
	onset week	offset week	onset week	offset week	onset week	offset week	onset week	offset week
Central Region (Gila, Maricopa, Pinal)	11/04	05/08	11/27	04/02	11/05	04/29	10/07	07/27
Northern Region (Apache, Coconino, Navajo, Yavapai)	01/02	04/17	12/25	03/26	12/10	04/08	12/09	04/06
Southern Region (Cochise, Graham, Greenlee, Pima, Santa Cruz)	11/21	03/27	12/11	03/26	10/15	04/08	12/02	05/18
Western Region (Lapaz, Mohave, Yuma)	11/14	02/06	01/15	03/12	12/10	02/18	12/23	02/24
NRVESS Region 9* (Arizona, California, Hawaii, Nevada)	12/18	03/26	not available	not available	12/16	03/31	11/24	03/29

Hospitalized season onset is the first two consecutive weeks of > 2 hospitalizations. Season offset is the last two consecutive weeks of > 2 hospitalizations

*NRVESS season onset is the first two consecutive weeks during which the median percentage of specimens testing positive for RSV antigen >10%. Season offset is last two consecutive weeks of >10%.

RSV Infections and Age and Gender of Patients

Fifty-four percent of the total cases were male and 46% of the cases were female (Figure 3). The largest number of hospitalizations occurred in the < 3 months age group.



Over 98% of the total cases were in children ≤ 14 years of age (Table 2).

Table 2: Age Breakdown of RSV Cases

Age Groups	Cases	% of Total
< 1	8038	71.11%
1-14	2221	21.31%
15-19	3	0.03%
20-44	30	0.29%
45-64	56	0.54%
65+	76	0.73%

RSV and Race/Ethnicity

Over the five-year period, Hispanics had the highest numbers of hospitalizations (45%), followed by whites (39%) and Native Indian/Alaskan natives (7%) (Figure 4). By rate, Hispanics had the highest average hospitalization rate at 56.0 hospitalizations per 100,000 and whites had the lowest at 20.8 hospitalizations per 100,000 (Table 2).

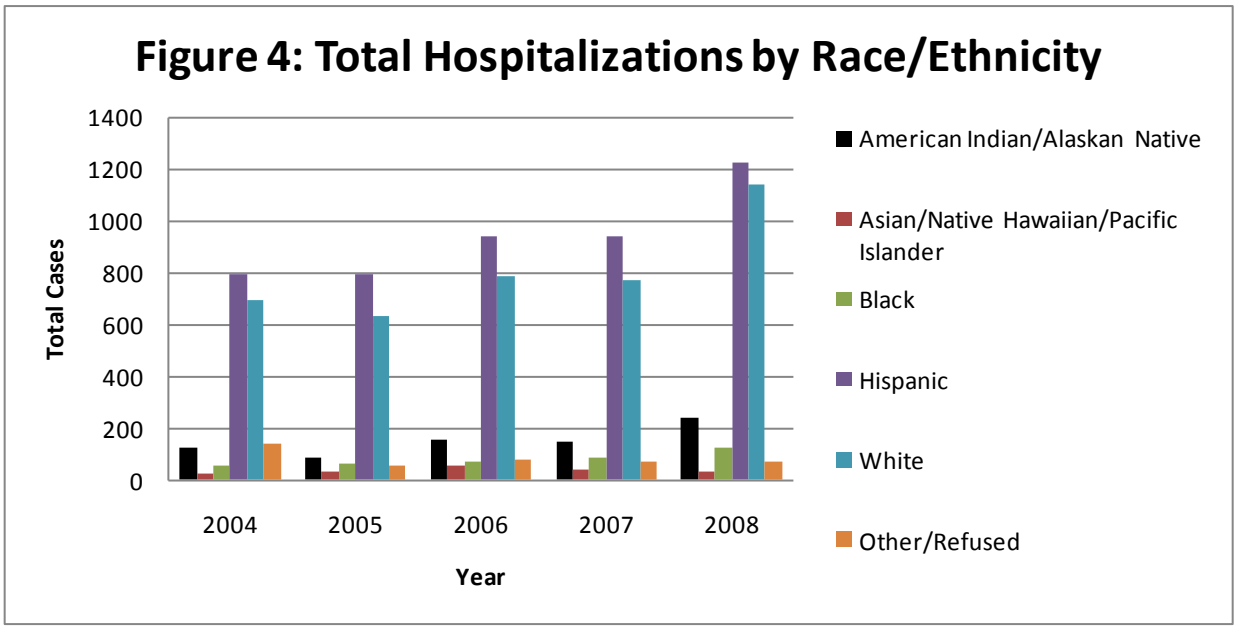


Table 2: Hospitalized RSV Rates by Race/Ethnicity and Year per 100,000

	2004	2005	2006	2007	2008	Average (95% CI)
White	18.4	16.1	20.6	20	28.8	20.8 (14.8-26.8)
Black	28.7	32	28.2	32.4	47.8	33.8 (23.9-43.7)
American Indian/Alaskan Native	44.6	29.5	46.1	43.2	69.5	46.6 (28.8-64.4)
Asian	19.6	28.4	32.7	21.2	19.7	24.3 (17.0-31.6)
Hispanic	53.8	51.7	55.3	52.4	67	56.0 (48.2-63.8)

RSV Infections by County of Residence

Sixty-seven percent of RSV hospitalizations were among residents of Maricopa County, followed by residents of Pima County (10.4%) and Pinal County (4.4%). The five-year average rate per 100,000 residents was calculated for all counties. Graham, Navajo, and Coconino Counties had the highest rates, followed by Maricopa, Apache, and Pinal Counties. Mohave County had the lowest rate (Table 3).

Table 3: Total Cases and Rates by County

Total cases by Year and County							Rate	
	2004	2005	2006	2007	2008	Average Cases per Year	Average rate (2004-2008) per 100,000 residents (95% CI)	
Apache	18	11	31	16	49	25	Apache	33.6 (8.1-59.2)
Cochise	49	24	40	22	39	35	Cochise	25.8 (15.3-36.4)
Coconino	70	64	75	41	80	66	Coconino	49.7 (35.5-63.9)
Gila	12	22	14	18	19	17	Gila	30.7 (21.7-39.7)
Graham	17	13	18	33	49	26	Graham	71.3 (20.5-122.2)
Greenlee	2	4	1	1	4	2	Greenlee	28.5 (6.2-50.8)
La Paz	6	1	7	6	7	5	La Paz	25.2 (10.6-39.8)
Maricopa	1170	1183	1393	1456	1830	1406	Maricopa	37.5 (28.6-46.4)
Mohave	41	14	22	23	24	25	Mohave	12.8 (6.5-19.1)
Navajo	56	31	91	49	98	65	Navajo	58.0 (26.4-89.7)
Pima	189	134	227	206	333	218	Pima	22.3 (13.0-31.6)
Pinal	52	69	63	100	173	91	Pinal	33.8 (11.3-56.3)
Santa Cruz	19	7	13	11	12	12	Santa Cruz	27.5 (15.6-39.5)
Yavapai	72	44	34	50	61	52	Yavapai	24.6 (16.0-33.3)
Yuma	50	37	46	17	41	38	Yuma	19.7 (11.5-27.9)

Average Length of Stay for RSV Infection

One-way analysis of variance (ANOVA) was used to test whether the mean length of stay (LOS) differs between individual variables. There were significant differences in LOS between age groups, with the < 3 months and > 24 months age groups having the highest mean LOS. Mean LOS by gender was significant, with females having a slightly higher LOS than males ($p<0.004$). Among payer groups, patients with federal insurance plans had longer stays than all other payers. Among the race/ethnicity groups, only the white and Hispanic groups had significantly different mean LOS (Table 4).

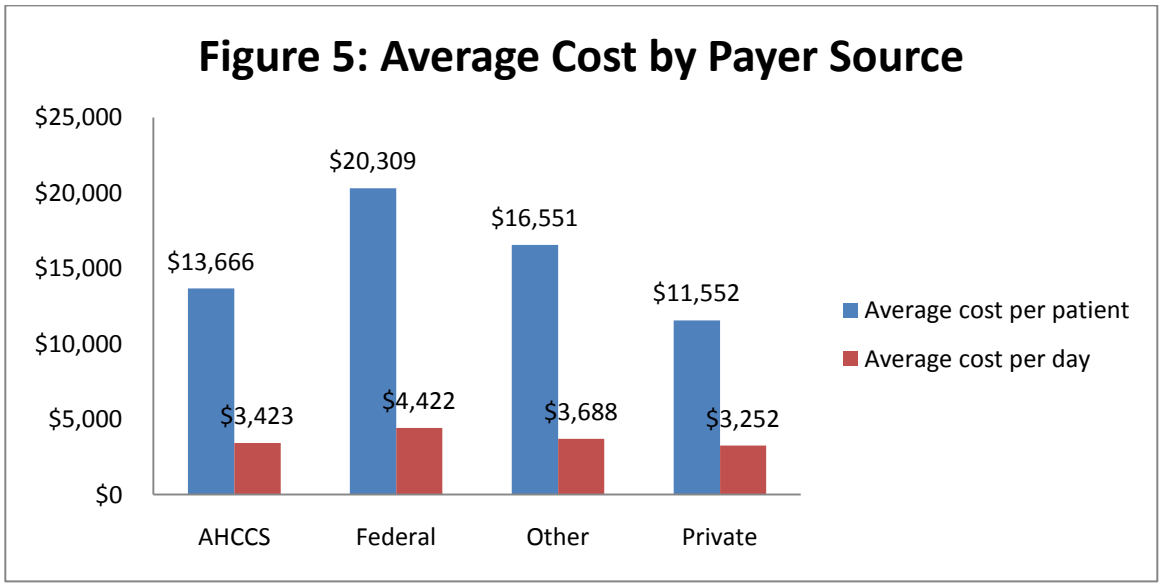
Table 4: Length of Stay

Variable	All Patients N = 10424 (% of total)	Mean Days in Hospital	Analysis
Age			
< 3 months	4253 (40.8%)	4.245	ANOVA, p<0.0001 *significant difference from < 3 month group at 0.05 level **significant difference from 12 months group at 0.05 level
3-6 months	1928 (18.5%)	3.632*	
6-9 months	1098 (10.5%)	3.648*	
9-12 months	726 (7.0%)	3.444*	
12-15 months	555 (5.3%)	3.668*	
15-18 months	421 (4.0%)	3.508*	
18-21 months	304 (2.9%)	3.664	
21-24 months	216 (2.1%)	3.593	
> 24 months	923 (8.9%)	4.07**	
Gender			
Female	4795 (46.0%)	4.014	ANOVA, p<0.0044
Male	5629 (54.0%)	3.815	
Payer Code			
AHCCCS	7141 (68.5%)	3.994	ANOVA, p<0.0001 significant difference for all groups except for federal-other and other-AHCCCS at 0.05 level
Federal	307 (2.9%)	4.593	
Other	242 (2.3%)	4.488	
Private	2434 (23.3%)	3.552	

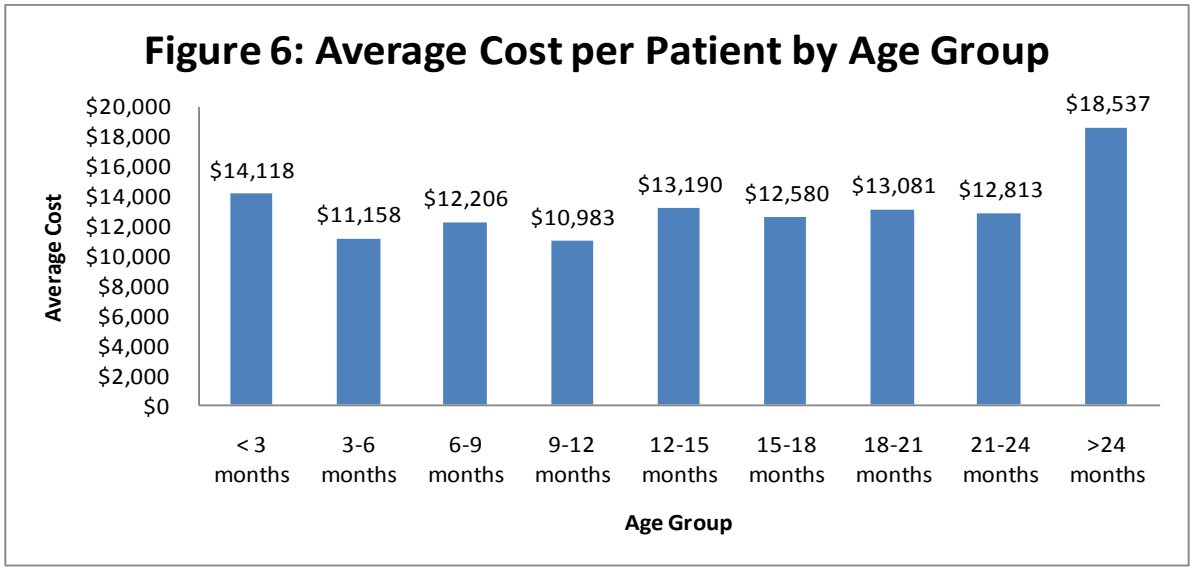
Race/Ethnicity			
American Indian/Alaskan Native	749 (7.2%)	3.959	ANOVA, p<0.0001 *significant difference for Hispanic and White at 0.05 level
Asian	53 (0.5%)	3.528	
Black	387 (3.7%)	4.075	
Hispanic	4684 (44.9%)	4.1*	
White	4020 (38.6%)	3.705*	
Native Hawaiian	125 (1.2%)	3.344	
Other	85 (0.8%)	3.212	
Refused	321 (3.1%)	3.766	

Average Cost of Hospital Stay for RSV patients

Patients with federal insurance, on average, had the highest cost among the four different payer sources at $20,309 per patient. Private insurance had the lowest cost per patient at $11,550 (Figure 5). This correlates with mean LOS by Payer Source. Patients with federal plans had longer LOS and higher cost than other payer groups. Private insurance patients had both the shortest LOS and the smallest cost of all the payer groups. Average cost per day was $4,422 for Federal plans, $3,423 for AHCCS, $3,688 for the Other payer group, and $3,252 for Private plans.



Age groups with the longest mean LOS (age groups < 3 months and > 24 months) also had the highest average cost per patient ($14,118 and $18,537) (Figure 6).



See appendix for additional charts and graphs.

Discussion

The purpose of this study was to conduct a descriptive analysis of RSV hospitalizations using HDD records. Our data show that children less than two years of age account for a majority of the patients hospitalized with a primary or secondary diagnosis of RSV (91% of total cases). Seasonally, RSV infections in Arizona typically start in November/December, peak in February, and end in March/April. Season duration varies by region. The Central Region (including Maricopa, Gila, and Pinal counties) had the earliest season onsets and the latest season offsets of all regions. The variability in region may be due to higher population densities in the Central Region and reporting differences by county. Densely populated counties such as Maricopa and Pinal have more hospitals reporting data than smaller counties. For 2009, Central Region hospitals represent 59% of the total number of hospitals reporting HDD data (15).

Among racial/ethnic groups, Hispanics had the highest rate of hospitalization for all years analyzed, followed by American Indians/Alaskan Natives, and blacks. Maricopa County, with the highest

number of Hispanics, had only the fourth highest rate. The counties with the highest rates (Graham, Navajo, and Coconino Counties) also had higher populations of American Indians/Alaskan Natives and Hispanics. In Graham County, American Indians/Alaskan Natives and Hispanics comprise 42.5% of the total population (5-year average) (13). In Navajo County this proportion was 55.9%, and in Coconino County 40.3% (13). For Maricopa County, American Indians/Alaskan Natives and Hispanics accounted for 29.2% of the total population. However, the counties with the highest percentage of American Indians/Alaskan Natives and Hispanics (Santa Cruz 80.7%, Apache 81.8%) did not have the highest rates (33.6 and 27.5 respectively).

To determine the burden of RSV hospitalization, mean LOS was calculated by age, gender, and payer source. Within these variables, there were statistically significant differences in LOS between various groups. The groups with the highest mean LOS were the < 3 month age group (4.2 days), females (4.0 days), patients with federal insurance plans (4.6 days), and Hispanics (4.1 days).

The information collected from HDD data can be used in conjunction with state surveillance data to provide a more complete picture of RSV infections in Arizona. One major drawback to using HDD for surveillance is that the data are not made available until months after the actual event, making it difficult to be used in real-time surveillance. Also by comparing number of patients hospitalized for RSV to the number of lab-reported tests reported to ADHS, there appears to be a discrepancy between the two data sets. For the 2007/2008 season, there were a total of 2,319 lab-confirmed cases reported to ADHS (14). For the same period, there were a total of 2,910 hospitalized cases. The data suggest that either lab-confirmed cases are under-reported or that hospitalized cases are misdiagnosed or not tested. Further investigation is needed.

There are several limitations in this study. First, for a more accurate picture of RSV in Arizona, it is necessary to look at data beyond the hospital discharge record. The hospital discharge data provide only an overview of severe RSV infections, and do not reflect outpatient care, emergency room care, or

primary physician care. A comprehensive study including data collected from hospitals, clinics, and private physicians will be needed to accurately reflect the RSV burden in Arizona. In addition, the variables used in this study cannot be used to determine the severity of infection. The total cost is given for each patient; however, cost breakdowns given within HDD were not examined. The total cost variable only confirms that longer hospital stays correlated with higher costs. Second, the data set is comprised of patients with either a primary or a secondary diagnosis for RSV. It is unknown how many of these cases were laboratory-confirmed RSV cases or how many RSV cases were undiagnosed. Relying on specific RSV ICD9 coding for diagnosis may be subject to error. If a true RSV case is coded as pneumonia or unspecified bronchiolitis, it will not be included in our dataset. Therefore, our dataset may underestimate the true number of RSV hospitalizations or overestimate the number if laboratory confirmations were not obtained on all cases. Third, since the data set only contains RSV hospitalizations, this study is limited to a descriptive analysis. With 97% of the patients being less than five years of age, it would have been useful to include all hospitalizations (not just RSV) from that age group to the study. With a comparison group, we would have been able to look at predictors of length of stay and outcomes. Various studies have also reported on the effect of meteorological conditions on RSV epidemics. Humidity and temperature are the two main factors that affect seasonality (16, 17). Further research is necessary to determine if this is also true in Arizona.

Conclusions

Prior to this study, there was no summary data available for inpatient RSV hospitalizations. This analysis was able to identify the groups (by age and race/ethnicity) most likely to be hospitalized for RSV-related illness. The severity of hospitalization approximated by the mean length of stay was determined for each group. We identified two findings that warrant further research: the higher rates of hospitalization for Hispanics and American Indians/Alaskan Natives and the seasonality variation by region. In conjunction with lab-confirmed data, we will be able to more accurately predict season onset

and offset. The combined information can be used to develop RSV management strategies to ensure adequate treatment and health coverage for future RSV seasons. In addition, outreach programs can target high-risk population groups to educate them on RSV prevention and treatment. HDD data can be incorporated with lab-confirmed data to provide health care providers and public health agencies with a more accurate representation of RSV in Arizona.

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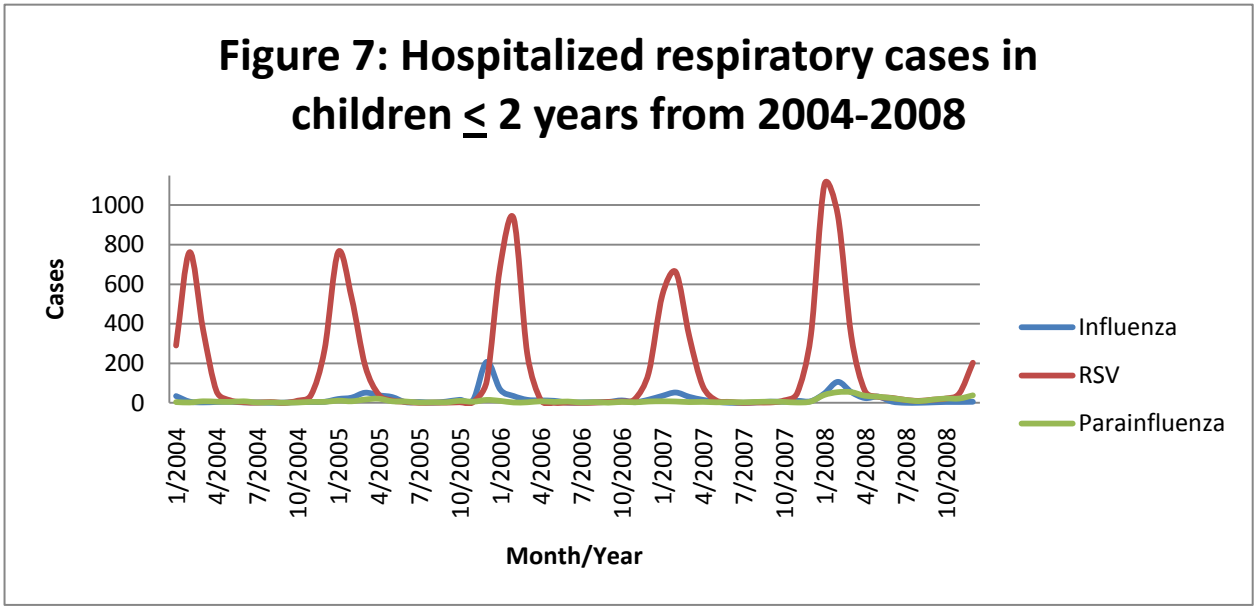
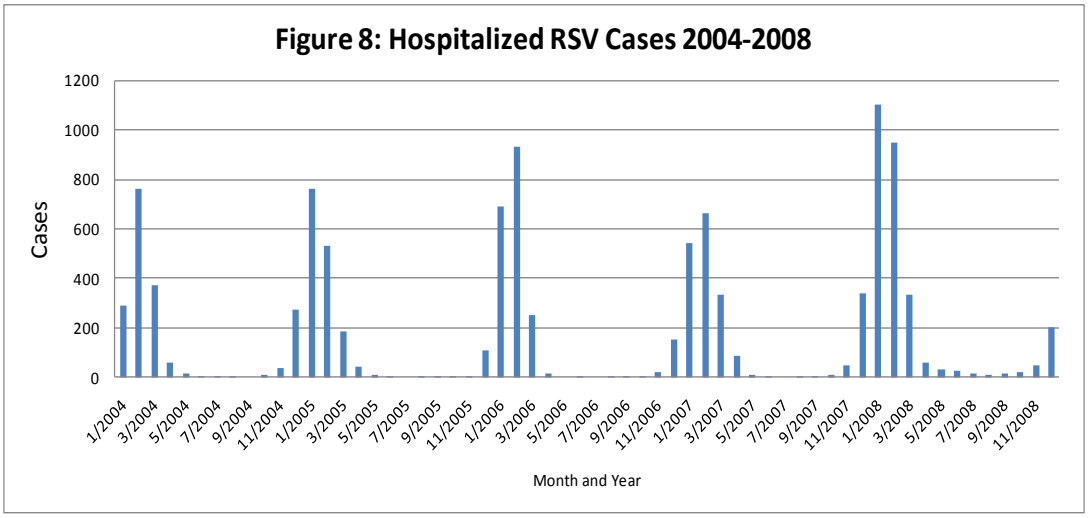
Appendix

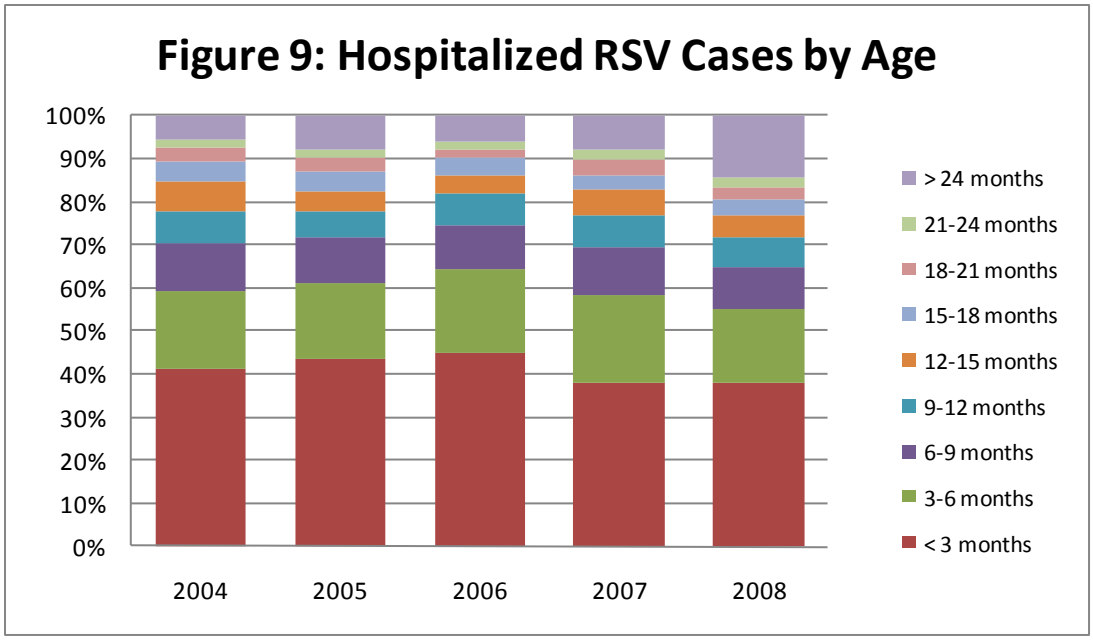
When RSV hospitalizations are compared to hospitalizations from other common respiratory viral infections (influenza, adenovirus, and parainfluenza), RSV is the leading cause of respiratory hospitalizations in children less than two years of age in Arizona (Figure 7).



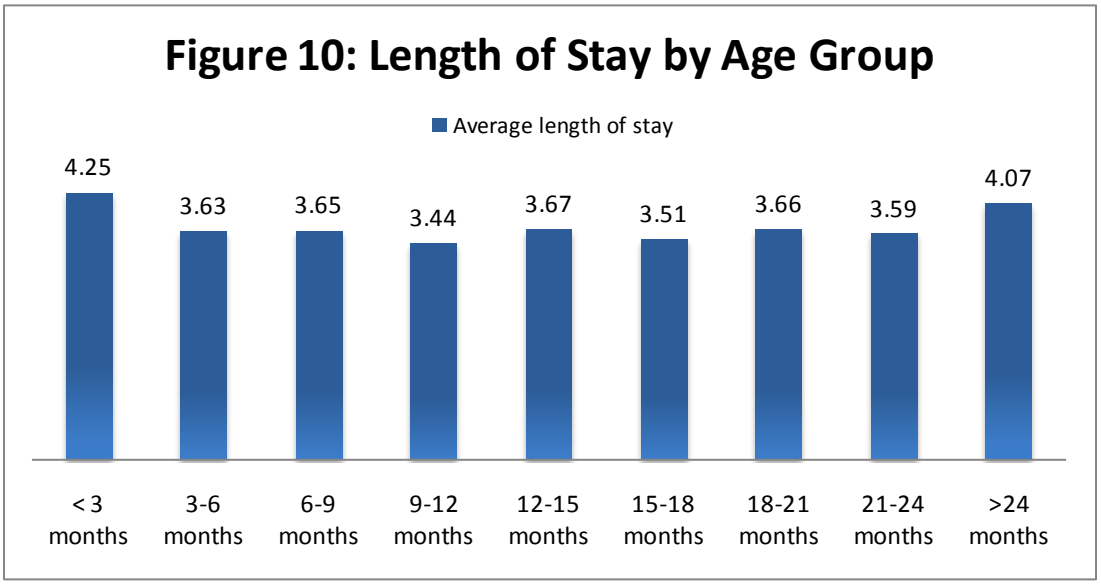
The total number of AZ cases analyzed was 10,424. The majority of the cases occurred in the months between December and March (Figure 8).



Over 91% of the total number of cases were in children ≤ 2 years of age (Figure 9).



The < 3 months and > 24 months age groups had the highest mean length of stay (Figure 10).



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