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The Epidemiology and Clinical Characteristics of Young Children Hospitalized With Respiratory Syncytial Virus Infections in Guatemala (2007–2010)

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Abstract

Background: There have been few population-based studies from Central America on respiratory syncytial virus (RSV) infections in young children. We report population-based incidence rates and describe epidemiological and clinical characteristics of children <5 years old hospitalized with RSV infections in Guatemala.

Methods: Prospective, active hospital-based surveillance for acute respiratory infections in children <5 years old was conducted at 3 hospitals in Guatemala from November 2007 through July 2010. RSV hospitalization rates were calculated for areas where the catchment population could be defined. Comparisons were made between children who were RSV-positive and RSV-negative.

Results: RSV was detected in 549 (25%) of enrolled children. Overall, annual rates of RSV hospitalizations ranged from 5.9 to 45.9 and 2.0 to 13.7 per 1000 children <1 year old and <5 years old, respectively, but varied by location and calendar year. Rates generally decreased with age—children <6 months had rates up to 30 times higher than older children, but children >12 months old still had rates up to 5.5 per 1000 per year and accounted for 42% of deaths. Children with RSV infections were more likely to have signs of respiratory distress (85% versus 63%, $P < 0.001$) compared with those without RSV infections, but case fatality ratios were similar (3–4%).

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The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.

Conclusions: The large burden and severity of RSV infections in young Guatemalan children is similar in magnitude and age distribution to RSV disease burdens found in other developing countries and suggests that this population would benefit from prevention strategies, including vaccines against RSV that are currently under development.

Keywords

respiratory syncytial virus; Guatemala; children; acute respiratory infections

Severe acute lower respiratory infections (ALRIs) are the leading cause of death among young children, accounting for an estimated 18% of all deaths in children <5 years old worldwide.[1] Respiratory syncytial virus (RSV) is recognized as the most common cause of severe respiratory infections in industrialized and developing countries and an important cause of deaths among young children.[2] The disease burden and clinical manifestations of RSV infections have been described in many locations,[3–12] but there are few studies from Central America,[13,14] and none used molecular techniques to determine etiologies.

Guatemala is a lower middle income country with a population of approximately 14 million located on the Southern border of Mexico. About 51% of the population lives below the poverty line; the life expectancy is 70 years, and the literacy rate is 74%.[15] Most areas of Guatemala have a tropical or subtropical climate, with some mountainous regions experiencing more temperate conditions.[16] Guatemala is included in the “Countdown to 2015” initiative that tracks maternal and child deaths in the 68 countries where more than 95% of worldwide maternal and child deaths occur.[17] In 2008, an estimated 17% of deaths in children under 5 in Guatemala were attributed to pneumonia.[18]

Determining the epidemiology and clinical manifestations of RSV infections in specific populations is important for guiding global and local prevention strategies, especially because vaccines against RSV are currently under development.[19] The objectives of this study were to report population-based estimates of the incidence of RSV hospitalizations among children <5 years old in Guatemala and to describe epidemiological and clinical characteristics of children hospitalized with RSV infections.

MATERIALS AND METHODS

Surveillance Sites

Prospective, active hospital-based surveillance for acute respiratory infections (ARIs) was conducted at 3 hospitals in the departments of Santa Rosa, Quetzaltenango and Guatemala City. The hospital in Santa Rosa (elevation: 970 meters) is a regional government referral center located 50 km southeast of Guatemala City that provides services to surrounding urban and rural communities. It has 36 general admission and 4 intensive care unit (ICU) pediatric beds. The hospital in Quetzaltenango (elevation: 2330 meters) is a regional government referral center located 120 km northwest of Guatemala City that also provides general (48 beds) and ICU (22 beds) pediatric services to surrounding rural and urban communities. The hospital in Guatemala City (elevation: 1500 meters), the capital of the

country, serves salaried persons and their dependents aged <5 years old. It has 179 general admission and 10 pediatric ICU beds.

Surveillance Population, Laboratory Diagnostics and Case Definition

Surveillance nurses at each of the sites prospectively identified persons eligible for enrollment by reviewing ward registries and emergency department logs 7 days a week in Santa Rosa and Quetzaltenango and 5 days a week (Monday through Friday) in Guatemala City for upper or lower ARI-related admission diagnoses and chief complaints. Children <5 years old were eligible for enrollment if they were hospitalized and had (1) a sign of acute infection (fever ≥38.0°C, hypothermia, abnormal white blood cell count or differential) and (2) at least 1 sign or symptom of respiratory disease (tachypnea, cough, sputum production, hemoptysis, difficulty breathing or feeding, sore throat or abnormal lung exam). The specific criteria for each of these conditions have been previously described.[20,21]

Nasopharyngeal and oropharyngeal swab specimens were collected from enrolled patients. The nasopharyngeal/oropharyngeal swabs were combined in a single tube with viral transport media and placed into a cooler with ice packs for a brief period of time before being refrigerated at 4°C for up to 72 hours until they were sent to the laboratory at the Universidad del Valle de Guatemala where all testing was performed. Specimens were tested by real-time reverse-transcription polymerase chain reaction (rRT-PCR) assays for RSV, influenza virus types A and B, parainfluenza virus types 1–3, human metapneumovirus and adenovirus using qualified primer/probe reagents and protocols provided by the United States Centers for Disease Control and Prevention.[22]

For this analysis, an enrolled child was considered to be infected with RSV if a respiratory specimen tested positive (cycle threshold [Ct] value was <40) for RSV by rRT-PCR. The unit of analysis was a hospitalization, so an individual child may be enrolled more than once. The surveillance period detailed in this report varied by site and occurred from November 2007 through July 2010 (33 months) in Santa Rosa, from February 2009 through July 2010 (18 months) in Quetzaltenango and from November 2009 through July 2010 (9 months) in Guatemala City.

Data Sources and Analysis

Demographic, epidemiological and clinical characteristics of the children were obtained by surveillance nurses through standardized interviews with caregivers, and some clinical data were also extracted from medical charts. Demographic and epidemiological data included sex, age, indicators of socioeconomic status and underlying health conditions, which were all provided through parental report. Clinical data included presenting signs and symptoms, a standardized pulmonary exam by a pediatrician, chest radiograph results determined by a hospital radiologist, pulse oximetry readings obtained by surveillance nurses, hospital course and discharge diagnosis. Case fatality ratios were calculated for children who died in the hospital. Ninety-five percent confidence intervals (CIs) were calculated for these ratios assuming a binomial distribution.

The seasonality of RSV was assessed at Santa Rosa and Quetzaltenango by the number of RSV hospitalizations and the proportion of all ARI hospitalizations that were RSV-

associated by month and year. Incidence rates were calculated at these locations over calendar years 2008 to 2009 for Santa Rosa and 2009 for Quetzaltenango because the proportion of residents who seek care at these locations could be estimated from a health utilization survey.[23]

For the rates, numerators were the number of RSV hospitalizations stratified by site and age category (0 through <6 months, ≥6 through <12 months, ≥12 months through <24 months and ≥24 months through <60 months). For the denominators, population census figures for 2008 and 2009 were provided by Instituto Nacional De Estadistica (the National Institute of Statistics) in Guatemala.[24] They reflect 2002 census counts that were adjusted for undercounting and population growth. Denominators for children <1 years old were evenly divided between children 0 through 6 months of age and ≥6 through <12 months of age.

In order to adjust for the proportion of the population that would seek care at the facilities conducting surveillance, a community health utilization survey was done before the start of surveillance.[23] Adult family members were asked where their family sought hospital care for a severe ARI-related complaint. Because 33% of Santa Rosa residents and 69% of Quetzaltenango residents reported seeking care at the hospitals under surveillance, crude incidence rates were divided by 0.33 and 0.69, respectively, to determine the adjusted incidence rate for each catchment area.

Proportions were used to describe the clinical characteristics and outcomes of children with RSV hospitalizations at all 3 sites. Comparisons were made between RSV-positive and RSV-negative cases. Comparisons were also made between children with severe RSV infection (as defined by death or need for ICU admission or mechanical ventilation) and those RSV-infected without severe infection. To test for statistical significance in bivariate analyses, chi-square and Fisher's exact tests were used for categorical variables and *t* tests or Wilcoxon rank sum were used for continuous variables at a significance level of 0.05. Multivariable logistic regression was used to determine independent factors associated with RSV infections and is reported as odds ratios (ORs) with 95% CIs. Covariates were included in the model if the *P* value was <0.10. Statistical analyses were performed in SPSS (version v. 15, IBM, Armonk, NY).

Ethical Considerations

Verbal consent was obtained from caregivers before screening children to determine eligibility. Once a child was determined to be eligible, written informed consent for enrollment and specimen collection were obtained from the caregivers. The protocol was approved by the institutional review boards of the Universidad del Valle de Guatemala and Centers for Disease Control and Prevention (Atlanta, GA) and approved by the Guatemalan Ministry of Public Health and Social Welfare.

RESULTS

Characteristics and Laboratory Results of Enrolled Children

Out of 2413 children who were eligible to participate, 2239 (93%) were enrolled in ARI surveillance across the 3 sites. Of these enrollees, 2193 (91% of all eligible) had respiratory specimens collected and tested by rRT-PCR and only these enrollees were included in all further analyses. Median age of the enrollees was 9.2 months and 36% were <6 months old (Table 1). Children enrolled at Santa Rosa and Quetzaltenango had similar age distributions ($P = 0.20$) but were younger than those at the Guatemala City site ($P < 0.001$). Eighty-six percent of enrollees had a monthly family income of <3000 Quetzals (approximately <375 US dollars) and 9% of families lacked electricity in their home. Twenty-five percent of children had an underlying medical condition reported by a caregiver—the most common of which was a history of prematurity (23%). There were significant differences in the proportion of children who were reported to have underlying medical conditions between the 3 sites, with the most (38%) reported in Guatemala City ($P < 0.001$ for all between site comparisons).

RSV was detected in 549 (25%) enrollees, and it was the virus most frequently identified of those tested over the surveillance period. Human metapneumovirus was detected in 16% of enrollees, parainfluenza virus types 1–3 in 13%, adenovirus in 13% and influenza virus in 6%. Coinfections (≥1 additional infection type) were detected in 105 (19%) of RSV-infected children: 54 (10%) had adenovirus, 27 (5%) had a parainfluenza virus, 19 (4%) had human metapneumovirus and 15 (3%) had influenza virus.

Incidence and Seasonality of RSV Infections

RSV hospitalizations generally started in June or July, peaked in August through September and declined from October through December (Fig. 1). Overall, annual rates of RSV hospitalizations ranged from 5.9 to 45.9 and 2.0 to 13.7 per 1000 children <1 year old and <5 years old, respectively, but varied by location and calendar year (Table 2). In Santa Rosa, rates were almost 7 times higher in 2009 compared with 2008 for children <5 years old. In 2009, the rate of RSV hospitalizations was more than 4 times higher in Santa Rosa compared with Quetzaltenango. The youngest age groups generally had the highest risk. Children <6 months old had rates that were from 9 to 30 times higher compared with the lowest rates in older age groups for each site and year (Table 2). The rate in children >12 months old ranged from 0.7 to 5.5 per 1000 per year.

Comparisons Between RSV-infected and RSV-uninfected Children

Demographic and clinical characteristics between RSV-infected and RSV-uninfected children were compared (Table 3). Children with RSV infections were younger than those who tested negative for RSV—49% compared with 31%, respectively, were <6 months old ($P < 0.001$). RSV-infected were less likely than RSV-uninfected children to have an underlying health condition reported (22% versus 26%, respectively; $P = 0.04$). RSV-positive children were more likely to have a reported fever ($P = 0.02$), cough ($P < 0.001$), feeding or drinking problems ($P < 0.001$), difficulty breathing ($P < 0.001$) and signs of respiratory distress (tachypnea, $P = 0.08$ or observed distress, $P < 0.001$) compared with

children who were RSV-negative, although large majorities in each group reported these symptoms. There was no significant difference between the 2 groups in the proportion who had oxygen saturation levels below 90% (30% in RSV-positive children and 26% in RSV-negative children, $P = 0.13$). Among children who had an interpreted chest radiography, 66% of children with RSV infections had an abnormal chest radiography, which was similar to the proportion among RSV-negative cases (63%). Pneumonia was the most common finding in both groups, but hyperaeration was more prevalent in RSV-positive children compared with RSV-negative children (33% versus 24%, respectively; $P = 0.003$). After controlling for surveillance site and other factors that were significantly associated with RSV infection on univariate analysis, age <6 months (adjusted OR [aOR]: 1.6; 95% CI: 1.2–2.5), cough (aOR: 3.6; 95% CI: 2.1–6.0), unable to drink or breastfeed (aOR: 1.3; 95% CI: 1.1–1.7), difficulty breathing (aOR: 1.6; 95% CI: 1.2–2.3) and signs of respiratory distress (aOR: 2.4; 95% CI: 1.8–3.1) remained significantly associated with having an RSV infection.

Hospital course and outcomes were similar among RSV-infected and RSV-uninfected children (Table 3). The median length of stay (5 days) and requirements for mechanical ventilation (7–8%) were similar between the 2 groups. Although children with RSV infections (25%) were more likely to be admitted to the ICU compared with RSV-negative children (19%), this difference did not reach statistical significance after controlling for age ($P = 0.06$). A similar proportion of children infected and uninfected with RSV died (3–4%).

Comparison Between Children With Severe RSV Infection and Nonsevere RSV Infection

As defined by death or the need for ICU admission or mechanical ventilation, age <3 months was the only factor identified as being associated with severe RSV disease (Table 4). Having an underlying health condition, including prematurity, was not associated with having severe disease. Being coinfected with any of the other viruses tested for was not associated with having severe disease (16% of severe cases were coinfected versus 20% of non-severe cases). Likewise, there was no association between being coinfected with any other individual virus type and severe RSV infection.

Deaths Among RSV-infected Children

Nineteen children with RSV infections (3.5%, 95% CI: 2.0–5.0%) died during their hospitalization, although the proximate cause of death was not obtained. By site, the case fatality ratio was 4.4% in Santa Rosa, 3.1% in Quetzaltenango and 0% in Guatemala City. Case fatality ratios did not differ by surveillance year. By age group, 5 (26%) deaths occurred in children <3 months old, 6 (32%) in 6 to <12 months olds, 7 (37%) in 12 to <24 months olds and 1 (5%) in 24 to <60 months olds. Among the RSV-infected children, having an underlying medical condition was not significantly associated ($P = 0.55$) with dying—1 (5%) child with an underlying condition died compared with 18 (3%) who did not have an underlying condition. Likewise, having an oxygen saturation below 90% was not associated with death (occurred in 31% of RSV-infected children who died compared with 30% of RSV-infected who did not die, $P = 0.90$).

DISCUSSION

RSV was the most commonly detected virus among Guatemalan children <5 years old who were hospitalized for ARI during the surveillance period. There was a distinct seasonality of RSV-associated hospitalizations, with most (86%) occurring between July and November. There was great variation by location and season, with overall rates ranging from 2.0 to 13.7 per 1000 children for children <5 years old. RSV infections and severe RSV disease mostly occurred in early infancy, but there was still significant disease burden in children >12 months old. Most RSV-infected children and most of those who died did not have an underlying health condition reported. The large burden and severity of RSV infections in young Guatemalan children suggests that this population could greatly benefit from prevention strategies, including vaccines against RSV that are currently under development.

We found a distinct RSV season in the areas under surveillance with most cases occurring during the rainy season that runs from May through December. This is consistent with findings from other tropical and subtropical climates that have a distinct rainy season.[25] The virus may be more stable in higher humidity conditions or social patterns may change during the rainy season, allowing for more efficient transmission.[25,26] In some geographic locations, RSV outbreaks have demonstrated a biennial pattern with severe outbreaks 1 year alternating with less severe ones, which was apparently observed in Santa Rosa.[27,28] However, more years of data are needed to confirm a biennial pattern at the locations under surveillance. It is also unclear the impact that 2009 influenza A pandemic (H1N1) may have had on rates of RSV because its peak coincided with the RSV peak (June through December of 2009) in the areas under surveillance.[20]

Worldwide, rates of RSV-associated hospitalizations for severe ALRI (defined by acute cough or difficulty breathing with chest wall indrawing) were reported to be similar among young children in developing and industrialized countries.[2] Annual rates in industrialized countries range from 2 to 6 per 1000 children <5 years old.[2,3,8,10,29,30] In developing countries, annual rates range from 3 to 18 per 1000 children <5 years old.[2,7,31,32] In children under 1 year old, a wide range of rates were found (10–166 per 1000 per year) in both developing and industrialized countries.[2] Data on the incidence of RSV hospitalizations in young children from Central America are limited. The estimated incidence of RSV-associated severe ALRI from a trial designed to measure the effects of indoor air pollution on ARI occurrence (RESPIRE) was 18 per 1000 per year in children <5 years old in 1 rural Guatemalan community over a 2-year period.[2,13] Despite using a rRT -PCR–based test that is likely more sensitive than the antigen-based testing[33] used in RESPIRE, we found lower rates of RSV hospitalizations. Likewise, we used a more sensitive case definition than used in RESPIRE because we did not limit cases to those with signs of respiratory distress. Consistent with our finding lower rates would be that the RESPIRE study employed active, community-based surveillance to identify cases. This method is thought to produce better case ascertainment compared with hospital-based systems in developing countries.[34] There may also be true differences in rates across the studies, years and sites due seasonal variations in the severity of outbreaks.

Rates of infection were up to 30 times higher in children <6 months old compared with older age groups, and early infancy was associated with more severe RSV disease. Both these findings are consistent with studies from developing and industrialized countries.[2,7,8,10,30,32] Unlike reports from industrialized countries,[4,35–37] the presence of underlying health conditions including prematurity, pulmonary disease and heart disease was not associated with a higher risk of severe RSV disease. This may represent an under-reporting of conditions because it was based on parental reporting[20] or because of lower neonatal survival rates among children born prematurely or with congenital heart disease in developing countries.[38,39] Other underlying conditions that contribute to disease severity, such as malnutrition, may go unrecognized and confound the relationship between other underlying conditions and disease severity. Regardless, the finding that most children with severe RSV disease do not have underlying health conditions is consistent with other studies.[10,40,41]

The case fatality ratio that we found (4%) for children <5 years old hospitalized for RSV was elevated compared with worldwide estimates. In a recently published meta-analysis, the case fatality ratio for RSV-associated ALRI was 2.1% (95% CI: 1.3–3.4%) in developing countries and 0.3% (95% CI: 0.2–0.4%) in industrialized countries.[2] Reasons for the higher ratio at the surveillance sites are unclear. Although the deaths occurred during the RSV hospitalizations, it is possible that other factors that were not captured contributed to or were the direct cause of death. Because the population under surveillance was relatively small, small variations may have a large impact on estimates, as reflected by the wide CIs. Host factors that were not measured, such as nutritional status, may have an impact on the severity of ARI disease in general[42] and RSV-associated disease, specifically.[43] In 2008, an estimated 50% of Guatemalan children had signs of chronic malnutrition.[44] Although we likely captured deaths among children hospitalized with RSV, a large number of RSV-associated deaths are believed to occur in children who do not have access to hospital care in resource poor settings, so we may have underestimated the impact of RSV on childhood mortality in Guatemala.[45] Likewise, reasons for variations in case fatality rates across sites are unclear. All sites have ICUs and are considered referral centers but may have different levels of experience in caring for severe patients. Small numbers precluded making comparisons between the severity of the disease and other patient characteristics that may explain differences in outcomes across sites.

There are other limitations to interpreting these findings. Some of the key risk factors of interest, such as underlying conditions, were based on caregiver self-report and their accuracy may be low. Because RSV rates commonly vary from year-to-year, the rates for the years under surveillance may not be reflect the average disease burden of RSV, particularly for the 1 year of surveillance conducted at the Quetzaltenango site. Descriptions of clinical and epidemiological features of RSV hospitalizations likely represent the 3 sites under surveillance but may not be representative of the country nor of all of Central America. All surveillance hospitals provide intensive care services, so the acuity and outcomes may differ from other hospital settings. Additionally, an unknown number of children who would qualify for hospital admission may not have had access to the facilities and either recovered or died in the community. Finally, there may have been either under- or overreporting

of utilization of the hospitals under surveillance, which may have resulted in over- or underestimation of incidence rates, respectively.

This analysis demonstrates the significant burden of severe RSV infections in young children in Guatemala. Currently, there are no effective treatments for RSV, other than providing supportive care.[46] Current prevention strategies include isolation in healthcare settings and hand hygiene measures. Providing RSV immunoprophylaxis with a monoclonal antibody given as monthly injections during the RSV season has been shown to reduce the risk of hospitalizations in children born prematurely with or without chronic lung disease or congenital heart disease.[47,48] Some facilities in Guatemala have started providing immunoprophylaxis to premature infants (personal communication, attending physician in Guatemala City), but costs prohibit its widespread use, even among high-risk populations in industrialized countries.[49,50] Also, most children hospitalized with RSV do not have an underlying health condition for which its use would be recommended. The best preventive strategy would be a safe and effective vaccine for young infants, although a substantial burden also occurs among older children. Development of vaccines for young infants has been difficult because of safety concerns and inability of vaccines to induce protective immunity in this age group.[51] Genetically engineered live attenuated RSV strains are in the early stages of development as candidate vaccines for young infants with other vaccine technologies being employed for older children and adults.[19] Until a vaccine is developed, more studies are needed to assess the impact of this disease on local and global communities so that appropriate resources may be allocated toward prevention and therapeutic efforts against RSV.

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REFERENCES

1. Black RE, Cousens S, Johnson HL, et al. ; Child Health Epidemiology Reference Group of WHO and UNICEF. Global, regional, and national causes of child mortality in 2008: a systematic analysis. Lancet. 2010;375:1969–1987. [PubMed: 20466419]
2. Nair H, Nokes DJ, Gessner BD, et al. Global burden of acute lower respiratory infections due to respiratory syncytial virus in young children: a systematic review and meta-analysis. Lancet. 2010;375:1545–1555. [PubMed: 20399493]
3. Vicente D, Montes M, Cilla G, et al. Hospitalization for respiratory syncytial virus in the paediatric population in Spain. Epidemiol Infect. 2003;131:867–872. [PubMed: 14596527]
4. Deshpande SA, Northern V. The clinical and health economic burden of respiratory syncytial virus disease among children under 2 years of age in a defined geographical area. Arch Dis Child. 2003;88:1065–1069. [PubMed: 14670770]

5. Eriksson M, Bennet R, Rotzén-Ostlund M, et al. Population-based rates of severe respiratory syncytial virus infection in children with and without risk factors, and outcome in a tertiary care setting. Acta Paediatr. 2002;91:593–598. [PubMed: 12113331]
6. Nokes DJ, Okiro EA, Ngama M, et al. Respiratory syncytial virus epidemiology in a birth cohort from Kilifi district, Kenya: infection during the first year of life. J Infect Dis. 2004;190:1828–1832. [PubMed: 15499540]
7. Robertson SE, Roca A, Alonso P, et al. Respiratory syncytial virus infection: denominator-based studies in Indonesia, Mozambique, Nigeria and South Africa. Bull World Health Organ. 2004;82:914–922. [PubMed: 15654405]
8. Iwane MK, Edwards KM, Szilagyi PG, et al. ; New Vaccine Surveillance Network. Population-based surveillance for hospitalizations associated with respiratory syncytial virus, influenza virus, and parainfluenza viruses among young children. Pediatrics. 2004;113:1758–1764. [PubMed: 15173503]
9. Singleton RJ, Bruden D, Bulkow LR. Respiratory syncytial virus season and hospitalizations in the Alaskan Yukon-Kuskokwim Delta. Pediatr Infect Dis J. 2007;26(suppl 11):S46–S50. [PubMed: 18090200]
10. Hall CB, Weinberg GA, Iwane MK, et al. The burden of respiratory syncytial virus infection in young children. N Engl J Med. 2009;360:588–598. [PubMed: 19196675]
11. Resch B, Gusenleitner W, Müller W. The impact of respiratory syncytial virus infection: a prospective study in hospitalized infants younger than 2 years. Infection. 2002;30:193–197. [PubMed: 12236559]
12. Weber MW, Milligan P, Sanneh M, et al. An epidemiological study of RSV infection in the Gambia. Bull World Health Organ. 2002;80:562–568. [PubMed: 12163920]
13. Bruce N, Weber M, Arana B, et al. Pneumonia case-finding in the RESPIRE Guatemala indoor air pollution trial: standardizing methods for resource-poor settings. Bull World Health Organ. 2007;85:535–544. [PubMed: 17768502]
14. Laguna-Torres VA, Sánchez-Largaespada JF, Lorenzana I, et al. Influenza and other respiratory viruses in three Central American countries. Influenza Other Respi Viruses. 2011;5:123–134.
15. The World Bank. Available at: http://data.worldbank.org/country/guatemala. Accessed December 27, 2010.
16. Department of State, United States. Available at: http://www.state.gov/r/pa/ei/bgn/2045.htm. Accessed December 27, 2010.
17. WHO, UNICEF. Countdown to 2015 Decade report (2000–2010): Taking Stock of Maternal, Newborn and Child Survival. Geneva, Switzerland: World Health Organization; 2010.
18. UNICEF. ChildInfo. Monitoring the situation of children and women 2010;Country profile: Guatemala. Available at: http://www.childinfo.org/files/Countdown2015_Guatemala.pdf. Accessed April 9, 2013.
19. Murata Y Respiratory syncytial virus vaccine development. Clin Lab Med. 2009;29:725–739. [PubMed: 19892231]
20. Reyes L, Arvelo W, Estevez A, et al. Population-based surveillance for 2009 pandemic influenza A (H1N1) virus in Guatemala, 2009. Influenza Other Respi Viruses. 2010;4:129–140.
21. Lindblade KA, Arvelo W, Gray J, et al. A comparison of the epidemiology and clinical presentation of seasonal influenza A and 2009 pandemic influenza A (H1N1) in Guatemala. PLoS ONE. 2010;5:e15826. [PubMed: 21209850]
22. Fry AM, Chittaganpitch M, Baggett HC, et al. The burden of hospitalized lower respiratory tract infection due to respiratory syncytial virus in rural Thailand. PLoS ONE. 2010;5:e15098. [PubMed: 21152047]
23. Lindblade KA, Johnson AJ, Arvelo W, et al. Low usage of government healthcare facilities for acute respiratory infections in guatemala: implications for influenza surveillance. BMC Public Health. 2011;11:885. [PubMed: 22111590]
24. Census Estimates: Guatemala. Available at: https://dl.dropbox.com/u/5120563/Proyecciones%20INE%20Censo%202002.pdf. Accessed January 18, 2013.
25. Weber MW, Mulholland EK, Greenwood BM. Respiratory syncytial virus infection in tropical and developing countries. Trop Med Int Health. 1998;3:268–280. [PubMed: 9623927]

26. Yusuf S, Piedimonte G, Auais A, et al. The relationship of meteorological conditions to the epidemic activity of respiratory syncytial virus. Epidemiol Infect. 2007;135:1077–1090. [PubMed: 17346359]
27. Duppenthaler A, Gorgievski-Hrisoho M, Frey U, et al. Two-year periodicity of respiratory syncytial virus epidemics in Switzerland. Infection. 2003;31:75–80. [PubMed: 12682811]
28. Lyon JL, Stoddard G, Ferguson D, et al. An every other year cyclic epidemic of infants hospitalized with respiratory syncytial virus. Pediatrics. 1996;97:152–153. [PubMed: 8545218]
29. Henrickson KJ, Hoover S, Kehl KS, et al. National disease burden of respiratory viruses detected in children by polymerase chain reaction. Pediatr Infect Dis J. 2004;23(suppl 1):S11–S18. [PubMed: 14730265]
30. Yorita KL, Holman RC, Steiner CA, et al. Severe bronchiolitis and respiratory syncytial virus among young children in Hawaii. Pediatr Infect Dis J. 2007;26:1081–1088. [PubMed: 18043442]
31. Olsen SJ, Thamthitiwat S, Chantra S, et al. Incidence of respiratory pathogens in persons hospitalized with pneumonia in two provinces in Thailand. Epidemiol Infect. 2010;138:1811–1822. [PubMed: 20353622]
32. Sutmöller F, Ferro ZP, Asensi MD, et al. Etiology of acute respiratory tract infections among children in a combined community and hospital study in Rio de Janeiro. Clin Infect Dis. 1995;20:854–860. [PubMed: 7795085]
33. Henrickson KJ, Hall CB. Diagnostic assays for respiratory syncytial virus disease. Pediatr Infect Dis J. 2007;26(suppl 11):S36–S40. [PubMed: 18090198]
34. Nokes DJ, Ngama M, Bett A, et al. Incidence and severity of respiratory syncytial virus pneumonia in rural Kenyan children identified through hospital surveillance. Clin Infect Dis. 2009;49:1341–1349. [PubMed: 19788358]
35. Boyce TG, Mellen BG, Mitchel EF Jr, et al. Rates of hospitalization for respiratory syncytial virus infection among children in medicaid. J Pediatr. 2000;137:865–870. [PubMed: 11113845]
36. Buckingham SC, Quasney MW, Bush AJ, et al. Respiratory syncytial virus infections in the pediatric intensive care unit: clinical characteristics and risk factors for adverse outcomes. Pediatr Crit Care Med. 2001;2: 318–323. [PubMed: 12793934]
37. Willson DF, Landrigan CP, Horn SD, et al. Complications in infants hospitalized for bronchiolitis or respiratory syncytial virus pneumonia. J Pediatr. 2003;143(suppl 5):S142–S149. [PubMed: 14615713]
38. Lawn JE, Kerber K, Enweronu-Laryea C, et al. Newborn survival in low resource settings–are we delivering? BJOG. 2009;116(suppl 1): 49–59. [PubMed: 19740173]
39. Trucco SM, Barnoya J, Larrazabal LA, et al. Detection rates of congenital heart disease in Guatemala. Cardiol Young. 2010;21:153–160. [PubMed: 21138614]
40. Shay DK, Holman RC, Newman RD, et al. Bronchiolitis-associated hospitalizations among US children, 1980–1996. Jama. 1999;282:1440–1446. [PubMed: 10535434]
41. Shay DK, Holman RC, Roosevelt GE, et al. Bronchiolitis-associated mortality and estimates of respiratory syncytial virus-associated deaths among US children, 1979–1997. J Infect Dis. 2001;183:16–22. [PubMed: 11076709]
42. Tupasi TE, Mangubat NV, Sunico ME, et al. Malnutrition and acute respiratory tract infections in Filipino children. Rev Infect Dis. 1990;12(suppl 8):S1047–S1054. [PubMed: 2270404]
43. Okiro EA, Ngama M, Bett A, et al. Factors associated with increased risk of progression to respiratory syncytial virus-associated pneumonia in young Kenyan children. Trop Med Int Health. 2008;13:914–926. [PubMed: 18482199]
44. Loewenberg S Guatemala's malnutrition crisis. Lancet. 2009;374:187–189. [PubMed: 19623681]
45. Sutanto A, Gessner BD, Djlantik I, et al. Acute respiratory illness incidence and death among children under two years of age on Lombok Island, Indonesia. Am J Trop Med Hyg. 2002;66:175–179. [PubMed: 12135290]
46. American Academy of Pediatrics Subcommittee on Diagnosis and Management of Bronchiolitis. Diagnosis and management of bronchiolitis. Pediatrics. 2006;118:1774–1793. [PubMed: 17015575]
47. Feltes TF, Cabalka AK, Meissner HC, et al. ; Cardiac Synagis Study Group. Palivizumab prophylaxis reduces hospitalization due to respiratory syncytial virus in young children with

hemodynamically significant congenital heart disease. J Pediatr. 2003;143:532–540. [PubMed: 14571236]

48. IMpact. The IMpact-RSV Study Group. Palivizumab, a humanized respiratory syncytial virus monoclonal antibody, reduces hospitalization from respiratory syncytial virus infection in high-risk infants. Pediatrics. 1998;102:531–537.
49. American Academy Of Pediatrics. Policy Statement—Modified recommendations for use of Palivizumab for prevention of respiratory syncytial virus infections. Pediatrics. 2009;124:1694–1701. [PubMed: 19736258]
50. Samson L Prevention of respiratory syncytial virus infection. Paediatr Child Health. 2009;14:521–532. [PubMed: 20885804]
51. van Drunen Littel-van den Hurk S, Mapletoft JW, Arsic N, et al. Immuno-pathology of RSV infection: prospects for developing vaccines without this complication. Rev Med Virol. 2007;17:5–34. [PubMed: 17004293]

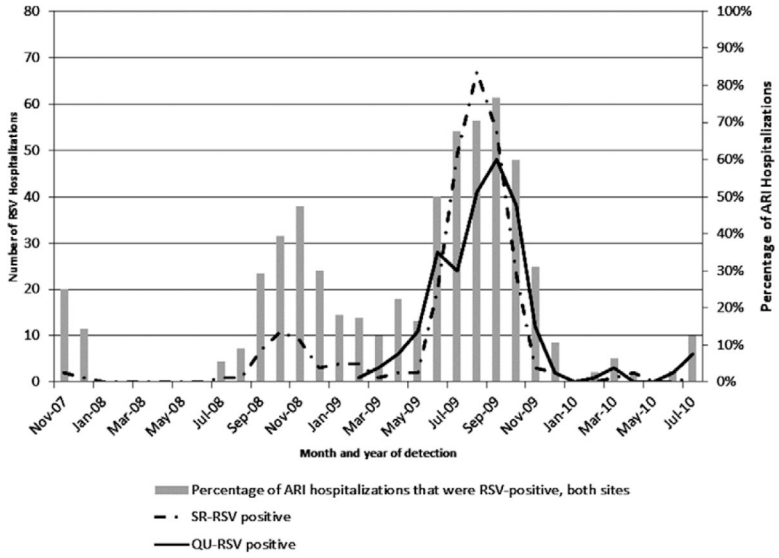

FIGURE 1.

Number of RSV hospitalizations by site and proportion of ARI hospitalizations that were RSV-positive, by month and year: Santa Rosa (SR) and Quetzaltenango (QU), Guatemala (November 2007 through July 2010).

TABLE 1.

Demographic Characteristics and Medical Conditions of Children Enrolled in Acute Respiratory Infection Surveillance, by Site: Guatemala (November 2007 to July 2010)

	Santa Rosa	Quetzaltenango	Guatemala City	All Sites
	N = 849	N = 667	N = 677	N = 2193
Characteristics	**n (%)**	**n (%)**	**n (%)**	**n (%)**
Male sex	498 (59)	392 (59)	407 (60)	1297 (59)
Median (mean) age in mo	9.1 (13.0)	7.8 (11.7)	11.1 (16.0)	9.2 (13.5)
Age groups				
0 through <3 mo	191 (23)	155 (23)	127 (19)	473 (22)
3 through <6 mo	119 (14)	110 (17)	84 (12)	313 (14)
6 through <12 mo	214 (25)	180 (27)	149 (22)	543 (25)
12 through <24 mo	181 (21)	130 (20)	146 (22)	457 (21)
24 through <60 mo	144 (17)	92 (14)	171 (25)	407 (19)
Monthly income of family				
≤Q1000 (approximately <125 USD)	583 (69)	339 (51)	90 (13)	1012 (46)
Q10001–3000 (approximately 126–375 USD)	262 (31)	168 (25)	455 (67)	885 (40)
>Q3001 (approximately >376 USD)	0 (0)	20 (3)	101 (15)	121 (6)
Data missing	4 (1)	140 (21)	31 (5)	175 (8)
Electricity in home				
Present	746 (88)	595 (89)	659 (97)	2000 (91)
Any underlying medical conditions [*]	113 (13)	186 (28)	254 (38)	553 (25)
Prematurity [†]	92/699 (13)	149/551 (27)	167/496 (34)	408/1746 (23)
Pulmonary disease [‡]	21 (2)	22 (3)	71 (10)	114 (5)
Heart disease	1 (0.1)	21 (3)	53 (8)	75 (3)
Immunodeficiency [§]	1 (0.1)	2 (0.3)	0 (0)	3 (0.1)
Other condition	0 (0)	5 (0.7)	15 (2)	20 (0.9)

Column percentages may not add to 100% because of rounding.

[*] The presence of an underlying condition was determined by asking parents whether these conditions had been diagnosed by a physician. Children may have more than 1 underlying medical condition.

[†] Prematurity was defined as being born before 9 months gestational age. Data on prematurity were only collected for children <24 months old at admission.

‡Pulmonary disease includes asthma and other pulmonary conditions.

§Indicates a history of HIV/AIDS or other immunodeficiencies.

Q indicates Quetzals (the currency of Guatemala); USD, US dollars.

TABLE 2.

Annual Crude and Adjusted Rates of RSV Hospitalizations per 1000 Children, by Site, Year and Age Group: Santa Rosa and Quetzaltenango, Guatemala

	Population	No. of Cases	Crude Rate per 1000	Adjusted Rate per 1000
Santa Rosa 2008				
0 through <6 months	3830	11	2.9	8.7
6 through <12 months	3830	4	1.0	3.2
<12 months	7660	15	2.0	5.9
12 through <24 months	7506	3	0.4	1.2
24 through <60 months	21,820	7	0.3	1.0
0 through <60 months	36,986	25	0.7	2.0
Santa Rosa 2009				
0 through <6 months	3860	83	21.5	65.2
6 through <12 months	3860	34	8.8	26.7
<12 months	7119	117	15.2	45.9
12 through <24 months	7573	12	1.6	4.8
24 through <60 months	22,090	40	1.8	5.5
0 through <60 months	37,382	169	4.5	13.7
Quetzaltenango 2009				
0 through <6 months	5675	74	13.0	18.9
6 through <12 months	5675	20	3.5	5.1
<12 months	11,350	94	8.3	12.0
12 through <24 months	11,140	5	0.4	0.7
24 through <60 months	32,479	27	0.8	1.2
0 through <60 months	54,969	126	2.3	3.3

Rates were adjusted for the proportion stating that they sought care at the Santa Rosa (33%) or Quetzaltenango (69%) surveillance facilities at the time of the health utilization survey.

TABLE 3.

Demographics, Clinical Characteristics, Hospital Course and Outcomes of Children Hospitalized With RSV-positive Infections Compared With Children Who Were RSV-negative for All 3 Sites: Guatemala (November 2007 to July 2010)

	RSV-infected	RSV-uninfected	
	N = 549	N = 1644	
Characteristics	**n (%)**	**n (%)**	***P***
Male sex	317 (58)	980 (60)	0.44
Median (mean) age in mo	6.0 (9.3)	10.6 (14.9)	<0.001
Age groups			
0 through <3 mo	171 (31)	302 (18)	<0.001
3 through <6 mo	100 (18)	213 (13)	0.002
6 through <12 mo	139 (25)	404 (25)	0.73
12 through <24 mo	91 (17)	366 (22)	0.01
24 through <60 mo	48 (9)	359 (22)	<0.001
Any underlying medical condition [*]	120 (22)	433 (26)	0.04
Prematurity [†]	104/494 (21)	304/1252 (24)	0.15
Pulmonary disease [‡]	11 (2)	103 (6)	<0.001
Heart disease	7 (1)	68 (4)	0.001
Presenting signs and symptoms			
Reported fever	396 (72)	1267 (77)	0.02
Reported cough [‡‡]	532 (97)	1501 (91)	<0.001
Reported feeding or drinking problems [‡‡]	416 (76)	1070 (65)	<0.001
Reported difficulty breathing [‡‡]	500 (91)	1350 (82)	<0.001
Measured tachypnea [§]	223 (41)	599 (36)	0.08
Observed respiratory distress [¶ ‡‡]	433/503 (86)	887/1306 (68) (63)	<0.001
Measured oxygen saturation <90% [‖]	149/500 (30)	338/1288 (26)	0.13
Abnormal chest radiography [**]	200/302 (66)	386/612 (63)	0.35
Hyperaeration	101/302 (33)	147/612 (24)	0.003
Pneumonia	147/302 (49)	283/612 (46)	0.49
Median/mean/range in length of stay (days) [††]	5.0/6.5/1–47	5.0/7.55/1–384	0.66
Severe disease, excluding death			
Intensive care admission	138 (25)	318 (19)	0.001
Mechanical ventilation	43 (8)	116 (7)	0.54
Deaths	19 (4)	51 (3)	0.68

[*] The presence of an underlying condition was determined by asking parents whether these conditions had been diagnosed by a physician. Children may have more than 1 underlying medical condition.

[†] Prematurity was defined as being born before 9 months gestational age. Data on prematurity were only collected for children <24 months old at admission.

[‡] Includes asthma and other pulmonary conditions.

[§] Cutoffs for tachypnea, by age: ≥60 breaths/minute for age <2 months; ≥50 breaths/minute for age 2 through ≤12 months; and ≥40 breaths/minute for age 13 through <60 months.

[¶] Includes observed chest indrawing and/or nasal flaring. It was only reported for children <24 months of age.

[‖] Includes only hospitalizations where oxygen saturation level was measured.

[**] Includes only hospitalizations where chest radiography results were recorded. More than 1 finding may be described for each radiography.

[††] Includes only those hospitalizations for which length of stay was recorded (n = 542 for RSV-associated and n = 1593 for RSV-negative cases).

[‡‡] Indicates that factors were significant in multivariate analysis at a significance level of $P < 0.05$.

TABLE 4.

Demographic and Clinical Characteristics of Children With Severe* RSV Infections Compared With Children With Nonsevere RSV Infections for All Sites: Guatemala (November 2007 to July 2010)

	Severe RSV Infections	Nonsevere RSV Infections	
	N = 141	N = 408	
	n (%)	n (%)	*P*
Male sex	76 (54)	241 (59)	0.30
Median (mean) age in mo	3.7 (7.7)	6.4 (9.8)	0.03
Age groups			
0 through <3 mo	61 (43)	110 (27)	<0.001
3 through <6 mo	21 (15)	79 (19)	0.24
6 through <12 mo	29 (21)	110 (27)	0.13
12 through <24 mo	22 (16)	69 (17)	0.72
24 through <60 mo	8 (6)	40 (10)	0.13
Any underlying medical condition†	30 (21)	90 (22)	0.85
Prematurity‡	28/134 (21)	76/369 (21)	0.94
Pulmonary disease§	2 (1)	9 (2)	0.57
Heart disease	3 (2)	4 (1)	0.31
Virus codetected	22 (16)	83 (20)	0.22
Adenovirus	12 (9)	42 (10)	0.54
Parainfluenza	7 (5)	20 (5)	0.84
Human metapneumovirus	2 (1)	17 (4)	0.12
Influenza	3 (2)	12 (3)	0.61

*Severe RSV disease was defined by death or the need for ICU admission or mechanical ventilation.

†The presence of an underlying condition was determined by asking parents whether these conditions had been diagnosed by a physician. Children may have more than 1 underlying medical condition.

‡Prematurity was defined as being born before 9 months gestational age. Data on prematurity were only collected for children <24 months old at admission.

§Includes asthma and other pulmonary conditions.