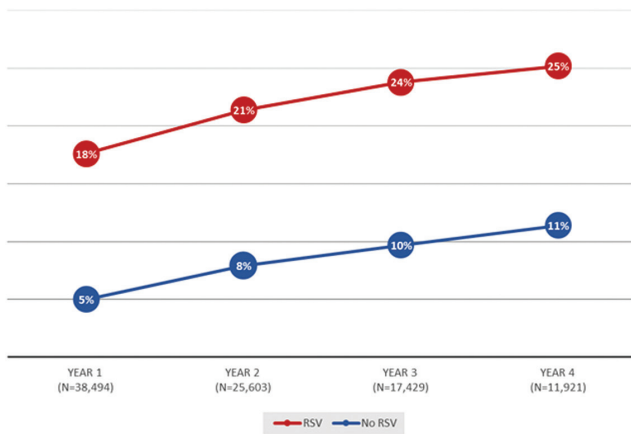


2000–December 31, 2016) to identify full-term infants with and without a RSV diagnosis in the first year of life (RSV and non-RSV cohorts respectively). Infants were excluded if they had any of the following: prematurity (<37 weeks' gestation), low birth weight, small for gestational age, congenital heart or chronic lung disease, asthma or wheezing; or had received palivizumab. At least 2 years' continuous follow-up post birth was required throughout the ≤5-year follow-up period. RSV/non-RSV infants were 1:1 matched for gender, region and health plan type. Cumulative incidence of recurrent wheezing or asthma was identified by ICD-9/10 codes, through 1, 2, 3 and 4 years (Y) post-index (1 year after birth) follow-up, and analyzed using conditional logistic regression.

Results. Matched RSV/non-RSV pairs totaled 38,494 (Y1), 25,603 (Y2), 17,429 (Y3), and 11,921 (Y4) for the years' follow-up. Demographic characteristics, birth year and month were evenly represented between cohorts. Other infections during the perinatal period were more common in the RSV vs. the non-RSV cohort (5.4% vs. 3.2%; $P < 0.0001$), as were other respiratory conditions (5.8% vs. 2.6%; $P < 0.0001$), and antibiotic use (76.7% vs. 44.7%; $P < 0.0001$). Rates of influenza and pneumococcal vaccinations were comparable between cohorts. Cumulative incidence of recurrent wheezing or asthma in the RSV cohort was more than two-fold higher compared with the non-RSV cohort for each follow-up period ($P < 0.001$) (Figure 1).

Conclusion. Healthy, full-term, commercially insured children infected with RSV during the first year of life had from 2.2- to 3.6-fold increased risk of developing recurrent wheezing or asthma in the next 1–4 years. This reveals an important medical need for interventions targeting RSV infection in infants.

Figure 1.



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2353. Respiratory Syncytial Virus (RSV) in Preterm Infants: Epidemiology, Clinical Pattern, and Risk Factors in a Pediatric Hospital in Argentina

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Background. RSV is the main agent that causes Acute Lower Respiratory Tract Infection (ALRI) in children. Preterm infants (PT) have a higher risk of hospitalization and complications associated with RSV infection. The aim of this study was to describe epidemiology, clinical pattern and risk factors associated to RSV infection in PT infants.

Methods. Prospective, Cross-sectional study of patients admitted for ALRI, 2000–2017. Virological diagnosis was made by fluorescent antibody assay of nasopharyngeal aspirates or RT-PCR. We compared epidemiological and clinical features, complications and lethality between full term (FT) and PT infants. Logistic regression was performed to establish lethality risk factors in PT.

Results. A total of 15,451 patients included, 13,033 were tested and 45% (5,831) had positive samples; RSV was predominant (81.3%, 4,738) all through the study period showing a seasonal epidemic pattern (May–July); 14% (655) were PT.

	PT	FT	OR	IC 95%	Two-tailed P
Gender	58.47%	56.19%	1.1	0.9, 1.3	0.274
Age (median)	7 (4–13)	7 (3–12)			0.001
Bronchiolitis	60.15%	61.39%	0.9	0.8, 1.1	0.548
Comorbidities	56.34%	38.75%	2.0	1.7, 2.4	0.000
Perinatal respiratory history	46.56%	5.46%	15.1	12.3, 18.5	0.000
Cardiopathy	8.09%	5.60%	1.5	1.1, 2.0	0.012
Malnourishment	10.09%	3.74%	2.9	2.1, 3.9	0.000
Chronic respiratory disease	41.37%	28.96%	1.7	1.5, 2.1	0.000
Bronchopulmonary dysplasia	5.95%	0.05%	128.8	31.0, 534.9	0.000
Immunosuppression	1.07%	1.97%	0.5	0.2, 1.2	0.114
Previous hospitalization (ALRI)	41.74%	23.94%	2.3	1.9, 2.7	0.000
Chronic neurological disease	7.48%	3.66%	2.1	1.5, 3.0	0.000
Re-admission	4.74%	3.00%	1.6	1.1, 2.4	0.020
Length of stay (median)	7 (5–10)	8 (5–11)			0.000
ICU requirement	10.84%	7.55%	1.5	1.1, 2.0	0.004
Nosocomial infection	7.86%	6.01%	1.3	1.0, 1.8	0.074
Lethality	3.09%	1.54%	2.0	1.2, 3.4	0.005

Congenital cardiopathy OR = 3.41(1.12–10.3), $P = 0.003$ and perinatal respiratory history OR = 3.1(1.6–6.1), $P < 0.001$ were the independent predictors for VSR lethality in PT.

Conclusion. RSV showed an epidemic pattern (May–July) and affected PT with certain comorbidities, with more severe disease, more complications during hospitalization and higher lethality than FT. RSV lethality in PT was more associated with congenital cardiopathy and perinatal respiratory history.

Disclosures. A. Gentile, Sanofi Pasteur: Consultant, Speaker honorarium.

2354. Performance of Novel Clinical Case Definitions for Respiratory Syncytial Virus Infections in Young Infants: A Latent Class Analysis

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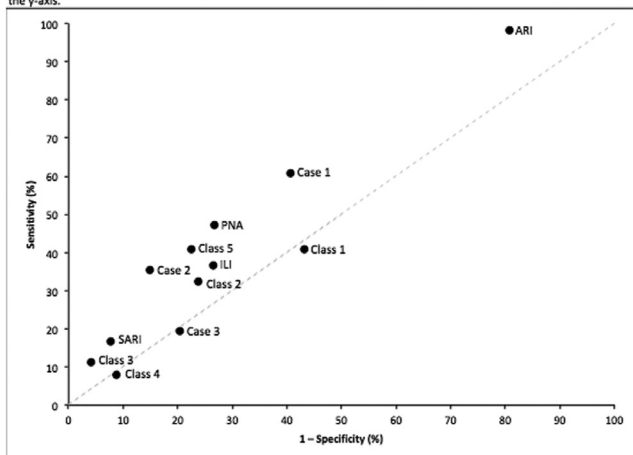
Background. Respiratory syncytial virus (RSV) is a major cause of pediatric morbidity and mortality worldwide. Appropriate case definitions are needed to accurately assess disease burden and evaluate novel RSV therapeutics and vaccines. Limited data exist on performance of RSV case definitions among young infants or in high-resource settings.

Methods. We used data collected on infants <6 months of age tested for RSV as part of routine clinical care at Children's Healthcare of Atlanta between January 2010 and December 2015. We evaluated sensitivity, specificity, positive (PPV), and negative predictive values (NPV) of clinical features, existing case definitions used by the World Health Organization (WHO), and alternative definitions we constructed using latent class analyses (LCA) to detect laboratory-confirmed RSV infection.

Results. Among 565 infants tested for RSV, 161 (28.5%) had laboratory-confirmed RSV infection. Among all case definitions evaluated, WHO-acute respiratory infection (ARI) ("cough or sore throat or shortness of breath or coryza, and a clinician's judgment that illness is due to infection") was the most sensitive [98.1%, 95% confidence interval (CI), 96.1–100.0, NPV 96.3%, 95% CI 92.2–100.0. The definition developed through LCA (cough and shortness of breath and coryza and wheeze and poor feeding and chest in-drawing) was the most specific (95.8%, 95% CI 93.8–97.8; PPV 51.4%, 95% CI 34.9–68.0).

Conclusion. The WHO ARI definition was the most sensitive for detecting laboratory-confirmed RSV infections among infants aged <6 months. However, alternative case definitions can confer higher specificity. Appropriate case definitions will vary depending on the content and setting in which they are utilized.

Figure 1. Receiver operator characteristic curve for RSV case definitions with 1-specificity on the x-axis and sensitivity on the y-axis.



Class 1: fever; **Class 2:** cough and fever and coryza; **Class 3:** cough and shortness of breath and coryza and wheeze and poor feeding and chest retractions; **Class 4:** apnea and shortness of breath; **Class 5:** cough and nasal discharge and poor feeding.

Case 1: wheeze or apnea or cyanosis; **Case 2:** chest in-drawing AND cough or tachypnea; **Case 3:** fever and any IMCI danger sign (lethargy or poor feeding confirmed by poor sucking/vomiting or seizure). **ARI** (acute respiratory infection): cough or sore throat or shortness of breath or coryza and a clinician's judgment that illness is due to infection; **IU** (influenza-like illness): acute respiratory illness with onset during last 7 days with temperature $\geq 38.0^{\circ}\text{C}$ and cough; **PNA** (pneumonia): fast breathing or chest in-drawing; **SARI** (severe ARI): acute respiratory illness with onset during previous 7 days requiring overnight hospitalization that includes history of fever or measured fever of $\geq 38.0^{\circ}\text{C}$ and cough and shortness of breath or difficulty breathing.

Disclosures. All authors: No reported disclosures.

2355. Clinically vs. Serologically Identified Varicella: A Hidden Infection Burden.

Lessons of 10-Year Follow-up in Varicella Endemic Countries

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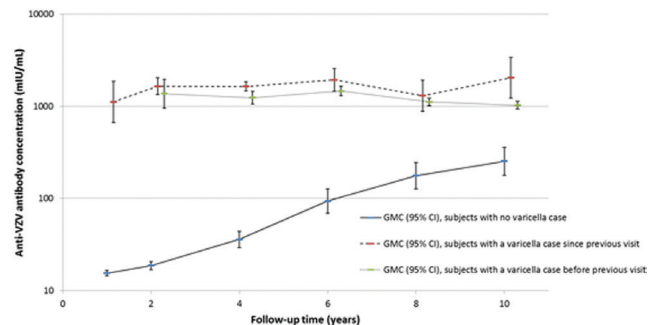
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Background. A randomized, controlled, long-term varicella vaccine efficacy study (NCT00226499) was conducted in several European countries with no universal varicella vaccination. The control group allows studying the immunological response profiles to natural varicella exposure and disease in children from 1 year of age onwards.

Methods. Of 5,803 subjects enrolled in the study, 744 were vaccinated with 2 doses of measles-mumps-rubella vaccine as active control. Follow-up lasted for up to 10 years. Varicella case ascertainment was done by combining PCR testing of skin lesions, epidemiological context and blinded clinical case adjudication by independent experts. A confirmed case required a positive PCR result or a positive epidemiological context with a positive case adjudication.

Results. In the control group, a total of 352 confirmed varicella episodes were captured; of which, 339 had an available serum sample taken before and after the episode at any of the year 1 or bi-yearly visits scheduled per protocol. All subjects were seronegative for anti-VZV antibodies before vaccination. The immunological profile showed that 96% of subjects with varicella episodes experienced an 8-fold increase of the anti-VZV titers when comparing the sample available after the episode vs. the one before the episode. The data indicate that the GMC levels were similar to that induced by 2-dose immunization with varicella vaccines, and persisted over many years after the varicella episode without indication of waning (figure). In subjects without any reported varicella episode, 8-fold increases of the anti-VZV titers between 2 successive blood samples were measured in up to 34% of consecutive pairs of serum samples.



Conclusion. To our knowledge, this is the first long-term analysis of the immunological history of anti-varicella immunological profile in young children exposed to a high varicella force of infection. About one-third of subjects not vaccinated against varicella developed an anti-VZV immune response although no varicella disease was

reported. Sub-clinical varicella may occur more frequently than anticipated. The total incidence of varicella infections might be under-estimated by syndromic surveys only.

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2356. Neurological Disorders and Radiological Findings. How Are They Related in Congenital Zika Syndrome?

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Background. Although Zika virus (ZIKV) infection causes a broad-spectrum of congenital neurological disorders, radiographic correlates of clinical outcome are lacking. During 2015–2016 ZIKV outbreak we faced a high incidence of microcephaly (MCP) in Rio Grande do Norte State (RN), located in northeast of Brazil. Among all regions, the northeast was the most affected by ZIKV. We aimed to identify distinct CT brain scan findings associated with congenital ZIKV infection and correlate them with neuro-clinical disorders in babies with MCP. Their mothers had exanthematous diseases (ED) compatible with ZIKV infection during their pregnancy.

Methods. Medical evaluation was performed on 38 babies with MCP, up to 17 months old, followed at a center for child rehabilitation in RN. All subjects underwent CT brain scan. Cohort enrollment occurred with subjects born between January 2015 and May 2016.

Results. 38 babies with MCP underwent head CT. 68.5% were male, 31.5% were female. The main clinical presentations were spasticity, irritability and seizure. On CT, all subjects had brain volume reduction. Intracranial calcification (IC) was observed in all of the subjects who presented with irritability and seizures ($n = 27$) and in 83.3% of subjects with spasticity. Lissencephaly was seen in 80% of subjects with irritability, 75% of subjects with seizures and 50% with spasticity. Ventricular dilatation was seen in 19 subjects, all of whom had spasticity, 60% who presented with irritability and 50% who presented with seizures.

Conclusion. These new data from a relatively large study, demonstrate that neuro-radiographical findings are associated with clinical syndromes in affected neonates. IC was the most prevalent CT scan finding (after reduction in the brain volume). It seems to be the most common radiological finding related to neuro-clinical disorders in ZIKV infection. This study may be used to better describe the congenital Zika syndrome, its clinical/radiological outcomes and natural history.

Disclosures. All authors: No reported disclosures.

2357. Radiological Findings in Microcephaly Cases During 2015–2016 Zika Outbreak: A Descriptive Study

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Background. Studies have demonstrated radiological findings in microcephaly (MCP) related to Zika virus (ZIKV). The 2015–2016 ZIKV epidemic led to an increase in the prevalence of MCP in the northeast region of Brazil. Rio Grande do Norte State (RN), a Brazilian northeast state, was highly impacted by this outbreak. This study aimed to evaluate CT scan findings in living babies whose mothers had exanthematous diseases (ED) compatible with ZIKV infection during their pregnancy.

Methods. We evaluated the CT brain scan images of 38 subjects up to 17 months whose mothers had ED during pregnancy. All these MCP cases were followed at a reference center for children rehabilitation in RN. Cohort enrollment occurred within babies born between January 2015 and May 2016.

Results. All subjects had brain volume reduction, followed by intracranial calcification ($N = 27$). Lissencephaly and ventricular dilatation were found in 19 cases. Pachygyria was observed in 11 subjects (28.9%) and cerebellar atrophy was observed in 8 subjects (21%). All subjects reported with pachygyria had lissencephaly. In addition, all subjects observed with intracranial calcifications had pachygyria.

Conclusion. It is a large and well detailed case series of CT brain scan performed in living babies with MCP related to ZIKV. These findings observed are supportive evidence to prove the severity of brain damages caused by ZIKV due to its neurotropism. This pattern of CT scan images should be compared with CT brain images observed