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Clinical Studies
1. PREVALENCE OF HUMAN RESPIRATORY SYNCYTIAL VIRUS INFECTIONS AMONG SUSPECTED COVID-19 PERSONS

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Background: Respiratory tract infections are usually characterized by cold, cough, fever, and headaches. At the onset of the COVID-19 pandemic, emphasis on respiratory infections was shifted to it. Most persons however who showed signs of respiratory illnesses did not test positive for SARS-CoV-2. It is therefore important to perform differential diagnoses of other respiratory pathogens. Respiratory syncytial virus (RSV) is one of the major causes of respiratory infections. The prevalence of RSV and coinfections of RSV and SARS-CoV-2 has not been reported in Ghana.

Aim: This study aimed to determine the occurrence of RSV and coinfections of RSV and SARS-CoV-2 from COVID-19 suspected individuals.

Methodology: The study was a retrospective cross-sectional study. Stratified random sampling was used to select samples from the UHAS COVID-19 Testing Centre Biobank. Extracted RNA was used for a one-step PCR and the results were analyzed with SPSS.

Result: Out of 400 samples tested, 20.8% were positive for SARS-CoV-2 and 3 were positive for RSV. None of the samples was positive for both viruses. The samples were also screened for influenza A. None of the samples were positive for both influenza A and RSV.

Keywords: SARS-CoV-2, Coinfection, Differential diagnoses, Polymerase Chain Reaction, COVID-19

Conflict of Interest: None declared

2. INCREASE IN RSV DETECTION AMONG HOSPITALIZED ADULTS WITH ARI WITH SUPPLEMENTARY RSV SEROLOGY TESTING

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Background: Adding paired serological testing to nasal/nasopharyngeal swab PCR testing consistently increases RSV detection, but case yield by different serology tests has not been compared. We evaluated if a combination of protein-specific IgG antibody assays could identify RSV infections not detected by a lysate antibody assay.

Methods: We conducted prospective RSV surveillance at two Atlanta-area hospitals from Oct2018–March2020 for adults ≥50 years admitted with ARI and ≥18 years admitted with COPD/CHF exacerbations. NP/OP swabs were tested with FilmArray® respiratory panel. Acute and convalescent (21-60 days after enrollment) phase sera were originally tested with an RSV Lysate (A2 and B1) IgG enzyme immunoassay (EIA). Alternate total antibody Luminex immunoassays (antigens N, M, RSV A, and RSVB G-peptide) were performed on remnant sera from asymptomatic controls [subset], RSV PCR+ hospitalized ARI subjects [all available], and RSV PCR- hospitalized ARI patients without 4-fold rise on original serology [subset].

Results: Protein-specific IgG EIA s detected 1 additional >4-fold rise among both the 15 RSV PCR+ and 62 control subjects. Five additional >4-fold increases were identified among 63 PCR/lysate serology-negative subjects (7.9%), boosting the additional yield from adding serology to PCR testing from an 11% to 31% increase. M protein IgG detected most (4/5) of these.

Conclusions: Supplementary testing of paired serology specimens with protein-specific IgG EIA s identified RSV infections missed by lysate IgG EIA indicating a combination of assays may be needed to optimize detection of titer rises from RSV infection. Further research into the potential additive benefit of using multiple serologic tests is warranted.

Table. Counts of Subjects with a 4-fold Rise in Serology Titer between Acute and Convalescent Visits for Various RSV Serological Assays in Selected Study Populations

<table>
<thead>
<tr>
<th>Subject Type</th>
<th>Total Antibody Luminex IgG</th>
<th>Events newly Identified by IgG assay</th>
<th>Percent newly positive</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>V2/V1 Lysate</td>
<td>V2/V1 Viral Lysate Assay</td>
<td></td>
</tr>
<tr>
<td>Asymptomatic Controls</td>
<td>N</td>
<td>N-LXA</td>
<td></td>
</tr>
<tr>
<td></td>
<td>62</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Hospitalized ARI (PCR RSV+)</td>
<td>15</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Hospitalized ARI (PCR/Sero neg)</td>
<td>63</td>
<td>4</td>
<td>2</td>
</tr>
</tbody>
</table>

Keywords: RSV Diagnosis, Incidence, Serology, Immunology

Conflict of Interest: This study is an investigator-sponsored study funded by Pfizer. Evan Anderson: Consulted for Pfizer, Sanofi Pasteur, GSK, Janssen, Moderna, and Medscape, and his institution receives funds to conduct clinical research from MedImmune, Regeneron, PaxVax, Pfizer, GSK, Merck, Sanofi-Pasteur, Janssen, and Micron. He also serves on a safety monitoring board for Kentucky BioProcessing, Inc. and Sanofi Pasteur. He serves on a data adjudication board for WCG and ACI Clinical. Christina Rostad: Institution has received funds to conduct clinical research from BioFire Inc, GSK, MedImmune, Micron, Janssen, Merck, Moderna, Novavax, PaxVax, Pfizer, Regeneron, Sanofi-Pasteur. She is co-inventor of patented RSV vaccine technology which has been licensed to Meissa Vaccines, Inc. Nadine Rouphael: Institution has received funds from Merck, Pfizer, and Sanofi Pasteur. Robin Hubler, Elizabeth Begier, Qing Liu, Warren Kalina, Bradford Gessner: Pfizer employees and may own Pfizer stock.

3. TLR4 GENE POLYMORPHISMS INTERACTION WITH ASCARIS INFECTION IN SEVERE RSV BRONCHIOLITIS

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Introduction: The identification of gene-environment interactions allows the recognition of groups with higher risk of morbidity. This study evaluated the interaction between the presence of TLR4 gene polymorphisms and Ascaris infection with severe bronchiolitis in a tropical Colombian region.
Methods: We included all infants younger than 24 months hospitalized due to bronchiolitis in Hospital centers in the county of Rionegro, Colombia. To identify interaction between severe bronchiolitis and presence of RSV polymorphisms and Ascaris infection, we used log-binomial regression.

Results: 417 infants were hospitalized due to bronchiolitis, of which 115 (27%) had severe bronchiolitis. In infants with RSV acute infection and positive anti-Ascaris IgE, TLR4 Asp299Gly was associated to low risk of severe bronchiolitis (OR 0.09, CI 95% 0.01-0.48). Conversely, in infants RSV negative with negative anti-Ascaris IgE, TLR4 Asp299Gly was associated with an increased risk of severe bronchiolitis (OR 14.5, CI 95% 2.2-96).

Conclusion: In our population there is an interaction between the presence of severe bronchiolitis, TLR4 Asp299Gly and ile399Thr polymorphisms, neither Ascaris IgE levels and RSV. This association should be evaluated in other populations to elucidate its role in the pathogenesis of severe bronchiolitis.

Keywords: severe bronchiolitis, polymorphism, respiratory syncytial virus, Ascaris.

Conflict of Interest: None declared

### Table 2. OR for severe bronchiolitis: association with TLR4 mutation against anti-Ascaris IgE Levels and RSV

<table>
<thead>
<tr>
<th>Envirnoment</th>
<th>SNP</th>
<th>a-N(%)</th>
<th>Crude*</th>
<th>Adjusted*</th>
<th>P</th>
<th>P**</th>
</tr>
</thead>
<tbody>
<tr>
<td>RSV positive</td>
<td>Asp299Gly</td>
<td>Yes</td>
<td>2/128 (1.5%)</td>
<td>0.00 (0.01-0.50)</td>
<td>0.09 (0.01-0.50)</td>
<td>0.005</td>
</tr>
<tr>
<td>Negative anti-Ascaris IgE levels</td>
<td>No</td>
<td>126/128 (98.5%)</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>RSV negative</td>
<td>Asp299Gly</td>
<td>Yes</td>
<td>2/102 (2%)</td>
<td>0.00 (0.01-0.46)</td>
<td>0.04 (0.05-0.48)</td>
<td>0.005</td>
</tr>
<tr>
<td>Negative anti-Ascaris IgE levels</td>
<td>No</td>
<td>100/102 (99%)</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
</tbody>
</table>

*Logistic regression model, adjusted for age, smoking at home, exclusive maternal breastfeeding for at least six months.

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4. **INCREASED LEVEL OF IL-8 AND IL-35 IN NONSYPHARYNGEAL SWABS IN INFANTS WITH LOWER RESPIRATORY TRACT INFECTION CAUSED BY THE RESPIRATORY SYNCYTIAL VIRUS (RSV)**

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### Keywords
- Interleukin-33, Interleukin-8, lower respiratory tract infection, Respiratory Syncytial Virus, Biomarkers

### Conflict of Interest
- S.M.B acts as the Scientific Director of clinical trials PRO-tonCoV-2001 (ClinicalTrials.gov NCT05593042), PRO-QINF-3004 (Clinicaltrial.gov NCT05494047), PRO-nCoV-3001 (ClinicalTrials.gov NCT04992260), CoronaVac03CL (ClinicalTrials.govNCT04651790) funded by Sinovac Biotech to the institution.

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5. **SEVERE LOWER RESPIRATORY TRACT INFECTION DUE TO RSV ASSOCIATED TO RECURRENT WHEEZING AND ASTHMA IN ARGENTINA**

Mauricio T. Caballero (1,2)*, Damian Alvarez-Paggi (1,2), Ignacio Esteban (1), Florencia Nowogrodsky (1), Sofía Aranda (1), Emiliano Sosa (1), Alejandra Bianchi (1), Adrián Ferretti (1), Fernando P. Polack (1)

1. Fundacion INFANT, Argentina. 2 CONICET, Argentina

### Keywords
- Bronchitis, infant, respiratory syncytial virus, bronchiolitis, lower respiratory tract infection, recurrent asthma.

### Conflict of Interest
- Dr. Polack reports grants and personal fees from JANSEN, grants and personal fees from NOVAVAX, INC, personal fees from BAVARIAN NORDIC A/S, personal fees from Pfizer, personal fees from SANOFI, personal fees from REGENERON, personal fees from MERCK, outside the submitted work.
6. CONCORDANCE BETWEEN CHEST X RAY (CXR) AND POINT OF CARE ULTRASOUND (POCUS) FINDINGS IN CHILDREN DIAGNOSED WITH RSV INFECTION BY NASOPHARYNGEAL RT-PCR: THE ZAMBIA EXPERIENCE

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Background: Respiratory syncytial virus (RSV) pneumonia is a leading cause of infant mortality worldwide. RSV infection in resource-limited settings is diagnosed by CXR. POCUS is an alternative, non-radiating, imaging modality in these settings.

We compared CXR and POCUS imaging findings in children diagnosed with RSV using reverse transcriptase polymerase chain reaction (PCR) on nasopharyngeal (NP) samples.

Methods: 200 children ages 1-59 months with WHO-defined severe/very severe pneumonia were enrolled from the Emergency Department at University Teaching Hospital in Lusaka, Zambia. Demographic, clinical information, NP samples, a CXR and 12 lung POCUS images per patient were included.

All CXR and POCUS images were adjudicated by two radiologists independently. They were masked to the correspondence between CXR, POCUS images and PCR status.

Images were categorized as end point consolidation, no consolidation or normal on both, CXR and POCUS.

Results: 20% of cases tested RSV+ by PCR (44/200; 22%). The median age of the RSV+ participants was 7 months (IQR: 2-12). 32/44 (73%) patients had abnormal findings on POCUS on the left side while only 26/44 (59%) demonstrated abnormal findings on CXR on the same side. On the right side, 42/44 (95%) patients had abnormal findings while only 31/44 (71%) showed abnormal findings on CXR.

Conclusions: POCUS proved to be a reliable imaging alternative compared to CXR to diagnose RSV in limited resource settings. Abnormal findings were more often seen on POCUS than on CXR for children diagnosed with RSV by RT-PCR. This raises doubt whether CXR is a valid gold standard.

Keywords: Point of Care Ultrasound (POCUS), Chest X ray (CXR), RSV, Nasopharyngeal RT-PCR

Conflict of Interest: None declared

Table 1. Summary of imaging findings by modality & laterality

<table>
<thead>
<tr>
<th>Modality &amp; Laterality</th>
<th>Right Side</th>
<th>End Point Consolidation</th>
<th>Non-consolidation (Interstitial &amp;/or effusion)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CXR N=44(%)</td>
<td>16/44 (32%)</td>
<td>36/44 (82%)</td>
<td></td>
</tr>
<tr>
<td>POCUS N=44(%)</td>
<td>15/44 (34%)</td>
<td>44/44 (100%)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Modality &amp; Laterality</th>
<th>Left Side</th>
<th>End Point Consolidation</th>
<th>Non-consolidation (Interstitial &amp;/or effusion)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CXR N=44(%)</td>
<td>11/44 (25%)</td>
<td>36/44 (82%)</td>
<td></td>
</tr>
<tr>
<td>POCUS N=44(%)</td>
<td>8/44 (18%)</td>
<td>44/44 (100%)</td>
<td></td>
</tr>
</tbody>
</table>

7. BRONCHIOLITIS AND ROLE OF VITAMIN D

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INTRODUCTION: Respiratory syncytial virus is responsible for more than half cases of bronchiolitis in younger than 1 year age group. RSV is mild infection but vitamin D deficiency was as high as 47.8% in infants with bronchiolitis. Infants with low vitamin D levels comprised a significantly developing countries have shown that vitamin D deficiency is associated with increased risk and severity of infant viral respiratory tract infections including bronchiolitis. Vitamin D is known to play a significant role as immune modulator and appears to influence host defences. We present our observation of vitamin D deficiency and bronchiolitis in otherwise healthy infant of patients with severe bronchiolitis.

METHODS: Total 7 infants of 8-13 months, who presented with bronchiolitis attending our clinic. All infants were well nourished, fully immunized and were from upper socioeconomic strata of community. There vitamin D level were checked during management and were followed up

RESULTS: Our result showed that infants were deficient in vitamin D, none of them were on vitamin D supplements, They all improved with general management and vitamin D supplementation of 2000 iu/day for six months.

CONCLUSIONS: Present study though small, shows vitamin D deficiency, even in well nourish, immunized, may be trigger factor in occurrence of bronchiolitis mostly associated with RSV infection as vitamin D is an important immunomodulation factor in infants which is a important for activation of T and B cells advocating supplementation to trigger immune system. Further studies may require for studies

Keywords: Vitamin D

Conflict of Interest: None declared

8. BURDEN OF NON-MEDICALLY ATTENDED RSV INFECTIONS DURING INFANCY – A EUROPEAN-WIDE PROSPECTIVE BIRTH COHORT STUDY (RESCEU)

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6 Department of Pediatrics, University of Turku and Turku University Hospital, Turku, Finland
7 Centre for Inflammation Research, University of Edinburgh, Edinburgh, United Kingdom
8 Glaxo Smith Kline, Wavre, Belgium
9 Translational Pediatrics and Infectious Diseases, Pediatrics Department, Hospital Clínico Universitario de Santiago de Compostela, Santiago de Compostela, Spain
10 Genetics, Vaccines and Infections Research Group (GENVIP), Instituto de Investigación Sanitaria de Santiago, University of Santiago de Compostela, Spain
11 Centro de Investigación Biomédica en Red de Enfermedades Respiratorias (CIBERES), Instituto de Salud Carlos III, Madrid, España
12 Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands
Introduction: Nearly half of infants with a symptomatic respiratory syncytial virus (RSV) infection do not seek medical attention. Current focus on medically-attended RSV infections therefore underrepresents the true burden of RSV on society. To capture the population burden of RSV, we assessed the clinical and societal burden of non-medically attended RSV infections in healthy term-born infants during the first year of life.

Methods: The RESCEU study is a prospective, observational birth cohort study that enrolled healthy term-born infants (n=9164) between 2017 and 2020 in five European countries. We performed active RSV surveillance in a nested cohort (n=993) until the age of one year. During an RSV episode, parents kept a diary of symptoms, medicine use, healthcare resource use, and family impact.

Results: A total of 102 infants with a non-medically attended RSV episode were included. Median duration of any respiratory symptoms and moderate-severe respiratory symptoms were 14 days (IQR 4) and 5 days (IQR 3.5) respectively. Cough was the most common respiratory symptom (97.1%) and persisted for a median of 11 days (IQR 6). Commonly reported non-respiratory symptoms were feeding difficulties (69.6%), vomiting (54.9%) and fever (51.0%). Medicine use was reported in 53.9% of episodes. More than half of parents noted impairment in usual daily activities (58.9%) for a median duration of 5 days (IQR 8), and nearly a quarter (24.5%) reported absenteeism from work.

Conclusion: Even when medical attendance is not required, RSV infection in infancy poses a significant burden to infants, families and society at large. These findings are important for policymakers when deciding on the implementation of RSV immunoprophylaxis or maternal vaccination in a national immunization program.

Funding: This study was funded by the Innovative Medicines Initiative 2 Joint Undertaking, with support from the EU’s Horizon 2020 research and innovation programme and European Federation of Pharmaceutical Industries and Associations.

9. STOP RSV: DESCRIBING VIRAL CO-INFECTION WITHIN CHILDREN INFECTED WITH RESPIRATORY SYNCTIAL VIRUS (RSV) IN THE UK

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3. Liverpool University Hospitals NHS Foundation Trust, Liverpool

Background: Respiratory tract infections (RTI) are one of the leading causes of morbidity and mortality in children and adults. 3-5 million deaths occur/annum, with a significant impact on health and society. RSV is a common ‘seasonal’* RNA virus which can lead to severe RTI including bronchiolitis and pneumonia (*pre-COVID). Across Europe ~40% of hospital admissions are due to acute RTIs caused by RSV in children <2 years. Pre-COVID data showed RSV-human metapneumovirus (hMPV) co-infection is associated with a higher risk of admission into paediatric intensive care. This study aims to describe other viral pathogens that have been detected within RSV-infected children with RTI.

Objectives: To describe viral co-infection within children <3 years presenting with RTI that have laboratory-confirmed RSV (within the STOP-RSV Study to date ISRCTN:41075797).

Method: Nasal swabs were collected from n=1,140 children <3 years old from December 2021 – November 2022 and tested on a respiratory viral panel using Biofire and Panther analysers. Children are recruited from primary and hospital healthcare settings in Cheshire, Merseyside and Bristol, UK.

Results: See Table

Conclusion: Overall 34% of our samples show RSV viral co-infection. Our hospital data suggests that Rhinovirus is commonly seen with RSV across all seasons. Although primary care data is currently limited - hMPV in Autumn 2022 is the leading RSV viral co-infection in primary care. Primary care patients are more difficult to recruit. We plan to present data on RSV co-infection’s relationship with disease severity and RSV:bacterial co-infection after STOP RSV study completion (n=2000) end March 2023.

Keywords: RSV, Viral co-infection, STOP-RSV Study, Primary care, hMPV

Conflict of Interest: AMC, DF awarded collaborative grant from Sanofi to conduct STOP RSV Study. AMC has worked as a paid consultant for Sanofi on influenza.

10. RISK FACTORS FOR SEVERE DISEASE IN INFANTS WITH RESPIRATORY SYNCTIAL VIRUS BRONCHIOLITIS

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(2) Department of Pediatrics
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Objective: To evaluate risk factors for severe disease in infants hospitalized with Respiratory Syncytial Virus (RSV) bronchiolitis.

Study design: We retrospectively identified all infants hospitalized with RSV bronchiolitis during two periods: pre-pandemic COVID19 period (2018 -2019) and pandemic period (2020-2021).

Results: 527 infants (276 in the pre-pandemic period and 251 in the pandemic period) were admitted to hospital, 26.7% (141/527) of which required admission to the PICU.

The frequency of comorbidities was similar in patients admitted (14.9%, 21/141) and not admitted (14.7%, 57/386) in the PICU. Seventy-five per cent (106/141) of infants admitted versus 44% (171/386) of those not admitted in PICU were under 3 months of age (OR 3.80 [CI 95% 2.47-5.86], p < 0.0001). The frequency of gestational age < 37 weeks was similar in infants admitted and not admitted to PICU (20.5% vs 15%), OR 1.46 (CI 95% 0.89-2.40).

During the pandemic period 17.5% (44/251) of infants were admitted to the PICU versus 35% (97/276) in the pre-pandemic period (0.45 [CI 95% 0.30-0.68], p < 0.0001). Age in infants admitted in the pandemic period was 6.1 ± 6.8 months versus 3.3 ± 4.1 in the pandemic period, p < 0.001.

Conclusion: Most children with RSV bronchiolitis admitted to PICU are healthy infants. Age < 3 months is the main risk factor for severe disease. Admission to the PICU was less frequent in children hospitalized during the pandemic period.

Keywords: Respiratory Syncytial Virus, bronchiolitis, risk factors for severe bronchiolitis

Conflict of Interest: Ruiz-Conterras J, has received grants/research support from Pfizer, Sanofi, GSK and Merck. No conflict of Interest for the remaining authors.
11. RISK ANALYSIS FOR EXPERIMENTAL RSV INFECTION IN THE OUTPATIENT SETTING – A LITERATURE REVIEW

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Background: Controlled Human Infection Models (CHIMs) emerged as a promising tool to limit costs and time for Respiratory Syncytial Virus (RSV) immunisation development. Quarantine facilities however, could be reduced by performing CHIMs in the outpatient setting. Because of COVID-19, the acceptance of self-quarantine and facemasks has increased, enhancing the opportunity for outpatient CHIMs.

Objectives: We aim to analyse the risk of outpatient CHIM on respiratory pathogens and to assess practical and ethical considerations in order to provide a framework for an RSV-CHIM in the outpatient setting.

Methods: A systematic literature review on outpatient CHIMs with respiratory pathogens was performed using Embase and PubMed-database, according to Cochrane handbook. Screening was performed by two independent researchers. Data on pathogens, inoculation dose and safety were extracted. Due to limited information on ethical and logistical considerations, authors were contacted for supplemental data.

Results: Our search identified 31 outpatient CHIMs. These CHIMs enrolled 1591 individuals, using rhinovirus (dose ranging 10-10,000 TCID₅₀, N=1004); Streptococcus pneumoniae (18,000-626,000 CFU, N=387); Bacille Calmette-Guérin (10² -2.4 x10⁵ CFU, N=151); and RSV-A2 (3.7-4.7 log₁₀ TCID₅₀, N=49). No serious adverse events (SAE’s) were reported. Only one article assessed and reported transmission to household members, with a rhinovirus transmission rate of 2.4%. The most important safety, ethical and logistical considerations for setting up outpatient CHIMs on respiratory pathogens were (1) safety precautions to minimize third-party transmission and exclusion of participants with vulnerable household members, (2) reduced burden to study participants, and (3) reduced study costs.

Conclusions: Thirty-one outpatient CHIMs enrolling almost 1600 participants were identified. Using adequate precautions to limit third-party transmission, CHIMs with respiratory pathogens could be performed in the outpatient setting allowing for rapid affordable vaccine development for RSV.

Keywords: Respiratory Syncytial Virus, RSV, Controlled Human Infection Model, CHIM, outpatient, respiratory pathogens, systematic review, vaccine development

Conflict of Interest: None declared

12. RESPIRATORY SYNCYTIAL VIRUS CONTROLLED HUMAN INFECTION MODELS (CHIM) AS A TOOL FOR ACCELERATED VACCINE DEVELOPMENT

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Background: Globally respiratory syncytial virus (RSV) is the second cause of death in infants. Thirty-three RSV prevention candidates are in development with an extended half-life monoclonal antibody within reach for high-income countries. Urgent next steps include ensuring access and affordability to RSV interventions of an RSV vaccine globally. RSV Controlled Human Infection Models (CHIM) limit costs and time of vaccine development and potentially prevent large and costly late-stage failures in clinical trials.

Objectives: The aim was to set up an RSV CHIM in the Netherlands. The primary outcome was at least one productive infection. Secondary outcomes included viral load and self-reported upper respiratory tract (URT) symptom scores over time.

Methods: Six healthy adults were inoculated with 0.5ml of 104PFU RSV-A Memphis 37. Nasal lavages were performed daily. URT symptoms (maximum score 24) and temperature were self-reported from baseline (day 0) through 10 days post-inoculation (DPI). We measured RSV viral load by RT-qPCR and viral titration by TCID50 on nasal washes. A productive infection was defined as two positive PCR tests on two consecutive days after 2 DPI.

Results: 83.3% (5/6) participants were infected with RSV. One RSV+ participant was asymptomatic. Symptoms started at median 2 DPI (range 0-3) with main complaints of sneezing and a runny nose. No participants developed a fever. The total URT symptom scores of infected participants peaked on 5 DPI (median score 4, range 1-4), which coincided with the peak in viral load on 4 DPI (median 5.32x10⁹ RSV copies/mL, range 4.88x10⁶ -1.52x10¹⁰).

Conclusion: We performed a successful proof-of-concept of RSV CHIM in the Netherlands with an infection rate of 83.3%. Next steps include use of RSV CHIM in the Netherlands as a tool for rapid vaccine development.
15. ACUTE VIRAL BRONCHIOLITIS IN HOSPITAL MONKOLE, 2020-2022, D.R. CONGO

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Introduction: Bronchiolitis is a respiratory infection and may be diagnosed also on the basis of clinical signs and symptoms. In low income countries, biological diagnosis is limited.

Objective: to evaluate the prevalence and the evolution of bronchiolitis in the hospitalized patients.

Method: Review study of severe acute respiratory distress in hospitalized preschool Congolese children with respiratory signs during the period from January 2020 to September 2022.

Results: 206 children were hospitalized, 111 (53%) were female, 95(47%) male, the average age was 7.3 months, 113(54%) children were under 6 months old. The symptoms which had motivated the consultation were 45% dyspnea and tachypnea, 31% were cough and 28% fever. 114 (55%) patients were admitted to intensive care, 133 (65%) had received oxygen and 169 (82%) patients had received antibiotic therapy. 3 children had died among those under 6 months old.

Conclusion: Despite the limited number of our patients. Our results reflect the presence of bronchiolitis taking into account the age of our patients.

14. BURDEN OF SEVERE ACUTE RESPIRATORY INFECTION IN CHILDREN YOUNGER THAN 2 YEARS IN THE GAMBIA

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Background: Severe acute respiratory infections (SARI), particularly respiratory syncytial virus (RSV), are an important cause of hospitalization and death in young children globally. Although burden of disease is highest in low- and lower-middle income countries, specific burden data are scarce. The aim of this study was to assess feasibility of estimating burden of SARI-related hospitalizations in children <2 years within the catchment area of the Edward Francis Small Teaching Hospital (EFSTH) in Banjul, The Gambia.

Methods: We used hospital admission charts to include all children <2 years who were admitted to the pediatric special care unit (PSCU) or neonatal intensive care unit (NICU) of EFSTH meeting the WHO SARI case definition between January 2020 – September 2021. Based on residence locations, the catchment area of the hospital was determined according to the WHO Manual for Estimating Disease Burden Associated With Seasonal Influenza. The incidence and mortality rates of SARI-related hospitalizations within the catchment area were calculated combining admission data and census data from the Gambia Bureau of Statistics.

Results: Between January 2020 – September 2021, in total 514 SARI-related admissions occurred (PSCU; n=258, NICU; n=256). In 2020 and 2021 the incidence rates of SARI-related hospitalization were 244.6 and 214.3 per 100,000 children respectively. Mortality rates were 58.0 and 40.2 per 100,000 children.

Conclusion: It is possible to estimate the burden of SARI-related hospitalizations for the catchment area of the EFSTH in The Gambia using retrospective data. We expect that a more accurate estimation can be made prospectively, also for RSV.

Keywords: Children, Severe Acute Respiratory Infection, Respiratory Syncytial Virus, mortality, incidence

Conflict of Interest: Louis Bont has regular interaction with pharmaceutical and other industrial partners. He has not received personal fees or other personal benefits. UMCU has received major funding (>€100,000 per industrial partner) for investigator-initiated studies from AbbVie, MedImmune, Janssen, the Bill and Melinda Gates Foundation, Nutricia (Danone) and MedMed Diagnostics. UMCU has received major funding or in kind funding as part of the public private partnership IMI-funded RESCEU project from GSK, Novavax, Janssen, AstraZeneca, Pfizer and Sanofi. UMCU has received major funding by Julius Clinical for participating in the INFORM study sponsored by MedImmune. UMCU has received minor funding for participation in trials by Regeneron and Janssen from 2015-2017 (total annual estimate less than €20,000). UMCU received minor funding for consultation and invited lectures by AbbVie, MedImmune, Ablynx, Bavaria Nordic, MAbXience, Novavax, Pfizer, Janssen (total annual estimate less than €20,000). LJB is the founding chairman of the ReSViNET Foundation.

15. PULMONARY SEQUELAE IN CHILDREN TWO YEARS AFTER HOSPITALISATION FOR RESPIRATORY SYNCYTIAL VIRUS LOWER RESPIRATORY TRACT INFECTION DURING INFANCY: AN OBSERVATIONAL STUDY.

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Respiratory Syncytial Virus (RSV) is the commonest cause of hospitalization for lower respiratory tract infection (LRTI) in children. RSV LRTI during early childhood may increase susceptibility to recurrent wheezing and asthma. The aim of this study was to describe the pulmonary sequelae at one and two years of age following RSV LRTI hospitalization in term infants during infancy. A longitudinal case-control study was undertaken in Johannesburg from April 2016 to December 2019. Cases constituted children hospitalized with PCR-confirmed RSV LRTI during infancy and controls were children not previously hospitalized with LRTI. A questionnaire detailing environmental and medical history, as well as a modified ISAAC questionnaire, was administered, and pulmonary function testing, including oscillometry, tidal breath flow-volume loops, and multiple breath wash-out, was performed, at one and two years of age. One (n=308) and two-year-old (n=214) cases were more likely than one (n=292) and two-year-old (n=209) controls to have experienced clinical pulmonary symptoms, including wheezing, received treatment for wheezing, and had any admissions for wheezing or any chest infection, after the initial RSV hospitalization. RSV LRTI during infancy led to an increase in airway resistance by two years, along with a decrease in compliance at both one and two years. There was an increased work of breathing at one year, but this was no longer present at two years. Children hospitalized with RSV LRTI during infancy had more clinical and pulmonary function sequelae through to two years of age when compared to healthy controls.

Keywords: RSV, pulmonary function testing, LRTI, sequelae

Conflict of Interest: None declared
16. DIFFERENCES IN BRONCHIOLITIS SEVERITY BETWEEN RSV-A AND RSV-B IN CHILDREN ADMITTED TO A REFERENCE CENTER IN CATALONIA (SPAIN) BETWEEN 2014 AND 2018

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Background: Respiratory syncytial virus (RSV)-related bronchiolitis is one of the main causes of hospitalization in children. Few studies have correlated RSV genotype (A or B) and bronchiolitis severity, observing discordant results. Our objective is to evaluate the differences in demographic and clinical characteristics between RSV-A and RSV-B bronchiolitis.

Methods: Patients aged ≤ 24 months with RSV-related bronchiolitis admitted in a tertiary hospital in Spain between 2014-2015 and 2016-2018 seasons were included. The effect of RSV genotype on severity variables was assessed by the relative risk or the median difference and the 95% confidence interval. Additionally, a multivariate analysis was performed.

Results: A total of 687 RSV-related bronchiolitis cases were included (322 RSV-A and 365 RSV-B), median age 86 days (interquartile range 39-215), 379 (55.2%) were males. No differences in age, sex, prematurity or comorbidities were observed between RSV-A and RSV-B infections. Compared to RSV-B, patients with RSV-A bronchiolitis were admitted with a higher severity score (RR=1.12). Hospital length of stay was one day longer for RSV-A (p-value<0.01). A higher proportion of RSV-A bronchiolitis required intensive care unit admission (RR 1.43), and stays tended to be longer than 7 days (RR=1.72). Additionally, in RSV-A bronchiolitis, respiratory support was one day longer (p-value<0.01) and the proportion of patients requiring invasive mechanical ventilation was higher (RR=2.46). These results were confirmed in the multivariate analysis.

Conclusions: According to our results, hospitalized patients with RSV-A bronchiolitis present higher severity at admission, longer hospital length of stay and more intensive care and respiratory support requirements.

Keywords: Respiratory syncytial virus; bronchiolitis; bronchiolitis severity; respiratory infections; RSV-A

Conflict of Interest: All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this work.
Evolution & Epidemiology
17. PREDICTORS OF POOR OUTCOMES OF RSV ACUTE LOWER RESPIRATORY INFECTIONS IN CHILDREN UNDER 5 YEARS OF AGE IN A MIDDLE-INCOME TROPICAL COUNTRY

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Objectives: The aim of the present study is to gain insight into the identification of region-specific factors associated with poor outcomes in children under 5 years of age with confirmed respiratory syncytial virus acute lower respiratory infection (RSV-ALRI) living in Colombia, a middle-income country, based on the National Public Health Surveillance System of the country.

Methods: An analytical cross-sectional study was conducted using epidemiological data from the records of morbidity and mortality of respiratory infections as registered in the surveillance system report of the National Institute of Health of Colombia 2018, including children under 5 years of age with confirmed RSV-ALRI. Predictor variables included demographic and clinical variables, as well as variables measured after hospital attendance. Outcome variables analyzed were respiratory failure, the need for pediatric intensive care unit admission, and mortality.

Results: Of a total of 8470 patients with a diagnosis of ALRI, we selected 1215 (14.3%) that were under 5 years of age and were positive for RSV. After controlling for potential confounders, it was found that age, gender, socioeconomic stratum, incomplete pneumococcal conjugate vaccine 13 immunization for age, cardiac disease, and malnutrition as comorbidities, chest X-ray findings, and development of sepsis independently predicted poor outcomes among the patients analyzed. Conclusions: The identified predictors for poor outcomes in RSVaffected children may be helpful for guiding efficient and targeted national and/or regional programs and public policies to assist in achieving Goal 3 of the Sustainable Development Goals adopted by the United Nations in 2015.

Keywords: acute respiratory infections, low to middle income countries, poor outcomes, respiratory syncytial virus

Conflict of Interest: None declared

18. ASSESSMENT OF IMMUNIZATION SERVICE DELIVERY AND MEASURES TAKEN FOR IMPROVEMENT IN SODDO TOWN, WOLAITA ZONE, ETHIOPIA

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Improving routine immunization in the urban population is an essential element to address immunization coverage and equity. The coverage of immunization services in urban areas is generally better than the rural areas.

The objective of the study is to identify barriers affecting vaccination access for children and disparities among communities in Sodo town in Wolaita zone, SNNPR region and to diverse strategies to improve the coverage, quality and equity of the vaccination.

Methods: An analytical cross-sectional study was conducted using epidemiological data from the records of morbidity and mortality of respiratory infections as registered in the surveillance system report of the National Institute of Health of Colombia 2018, including children under 5 years of age with confirmed RSV-ALRI. Predictor variables included demographic and clinical variables, as well as variables measured after hospital attendance. Outcome variables analyzed were respiratory failure, the need for pediatric intensive care unit admission, and mortality.

Results: Of a total of 8470 patients with a diagnosis of ALRI, we selected 1215 (14.3%) that were under 5 years of age and were positive for RSV. After controlling for potential confounders, it was found that age, gender, socioeconomic stratum, incomplete pneumococcal conjugate vaccine 13 immunization for age, cardiac disease, and malnutrition as comorbidities, chest X-ray findings, and development of sepsis independently predicted poor outcomes among the patients analyzed. Conclusions: The identified predictors for poor outcomes in RSVaffected children may be helpful for guiding efficient and targeted national and/or regional programs and public policies to assist in achieving Goal 3 of the Sustainable Development Goals adopted by the United Nations in 2015.

Keywords: acute respiratory infections, low to middle income countries, poor outcomes, respiratory syncytial virus

Conflict of Interest: None declared

19. RSV CO-DETECTION WITH OTHER RESPIRATORY VIRUSES AND ODDS OF HOSPITALIZATION AMONG CHILDREN <2 YEARS OLD, NEW VACCINE SURVEILLANCE NETWORK (2016–2020)

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Background: Risk factors for severe respiratory syncytial virus (RSV) illness include infancy, preterm birth, and underlying conditions, but the role of viral co-detection is unclear. We compared the odds of hospitalization of children with isolated RSV detection and those with RSV co-detection.

Methods: We conducted active surveillance for cases of fever and/or respiratory symptoms (12/01/2016–04/01/2020) at seven U.S. medical centers that comprise CDC’s New Vaccine Surveillance Network. Demographic and clinical data were collected through parent/guardian interviews and chart abstractions. Nasal and/or throat swabs were collected and tested for RSV, rhinovirus or enterovirus (RV/EV), adenovirus (AdV), human coronaviruses (CoV) 229E, HKU1,
CYCLE THRESHOLD VALUE OF RESPIRATORY SYNCYTIAL VIRUS VARIES BY VIRAL CO-DETECTION

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Background: The cycle threshold (Ct) value from real-time polymerase chain reaction is a semi-quantitative measure inversely correlated with viral load. In children with respiratory syncytial virus (RSV)-associated acute respiratory illness, lower Ct values may be associated with worse clinical outcomes. We sought to compare the Ct value of RSV in children with single viral detection and those with multiple viral detections.

Methods: We conducted a prospective viral surveillance study and enrolled children <2 years old admitted to a large public hospital in Amman, Jordan (3/2010–3/2013). Demographic and clinical data were collected by parental interviews and chart abstractions. Nasal and/or throat swabs were collected and tested for RSV, rhinovirus (RV), adenovirus (AdV), human metapneumovirus (hMPV), parainfluenza viruses (PIV)1–3, and influenza (Flu). In 2020, we performed additional testing for PIV-4 and the common cold coronaviruses (CoV). We compared the Ct value of RSV in children with single viral detection and those with multiple viral detections.

Results: We enrolled 3,168 children, of whom 2,641 (83.4%) were virus-positive. RSV, the most frequently detected virus, was singly detected in 690 samples (49.4%). The most common viral combination was RSV/RV (n=354/707; 50.1%). The median RSV Ct value in 21 combinations was higher for RSV/CoV in children aged <2 years.

Conclusion: Co-detection of RSV with other respiratory viruses was not associated with increased hospitalization in children aged <2 years.
21. SURVEILLANCE OF COMMON RESPIRATORY VIRUSES, INCLUDING RSV AND SARS-COV-2 DURING THE COVID-19 PANDEMIC IN THE CENTRAL PROVINCE OF SRI LANKA

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Background: Respiratory Syncytial Virus (RSV) is a major respiratory pathogen, associated with significant morbidity. During the Covid-19 pandemic, aetiological diagnosis has been focused on detecting SARS-CoV-2. Thus knowing the circulation of other respiratory viruses is necessary to improve the management plans during the pandemic in Covid-19 suspected patients.

Methods: A total of 422 respiratory samples from Covid-19 suspected patients received to the National Hospital, Kandy, Sri Lanka were simultaneously tested using the real time RT-PCR for SARS-CoV-2 and PCR melting curve analysis for other respiratory pathogens from 1st of January to 31st of December 2021. The demographic data were acquired from medical records.

Results: Of the 422 Covid-19 suspected patients’ samples tested, 8% patients had SARS-CoV-2 infection. Overall detection rate of other respiratory pathogens were 45%. Of these, RSV was detected in 18% patients. Human rhino / enterovirus, human para influenza viruses, influenza viruses, human adenovirus, human CoV-C229E, human CoV-NL63 and human bocavirus were identified in 23%, 13%, 7%, 7%, 9%, 4% patients, respectively. Mixed infection with one or more viruses was observed in 11% patients.

Of the patients infected with RSV, RSV A and RSV B mono-infections were noted in 43% and 6%, respectively. Co-infection with RSV A and B was present in 51% patients. All the RSV infected patients had fever and cough. Seven RSV co-infections with other respiratory viruses were noted including one with SARS-CoV-2.

Conclusion: The current findings highlight the importance of diagnosing the other respiratory viruses including RSV during Covid-19 pandemic.

Keywords: RSV, Covid-19, Respiratory viruses, Central Province, Sri Lanka

Conflict of Interest: None declared

22. SEROPREVALENCE AND EPIDEMIOLOGICAL CHARACTERISTICS OF RESPIRATORY SYNCYTIAL VIRUS AMONG CHILDREN IN THE SUEZ CANAL AREA, EGYPT

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Respiratory syncytial virus (RSV) is the main cause of lower respiratory infection (LRTI) in children. This study aimed to determine the seroprevalence of RSV in Suez Canal University hospital and University Specialized hospital, Ismailia, Egypt from 2019 to 2020. The link of RSV with other factors like gender, sex, clinical presentations, and environmental conditions were also investigated. Real-time (rt)-PCR was used to test 150 nasopharyngeal aspirates from children who had acute respiratory illnesses believed to be RSV. A serological investigation was conducted on the serum samples to identify anti-HRSV IgG, anti-HRSV IgM utilizing enzyme-linked immunosorbent assay (ELISA) kits in accordance with the manufacturer instructions. Using rt-PCR, 37 (24.7%) of the 150 samples tested were positive for RSV. In 27/37 (72.9%) samples, RSV A was found, while in 10/37 (27.1%) samples, RSV B was identified. IgM and IgG seroprevalence for HRSV were 8.2% and 71%, respectively. Cough was the main clinical sign seen in RSV positive patients (30/37, 81.1%), followed by rhinorrhea (27/37, 72.9%), and nasal congestion (25/37, 67.6%). There were a 2:1 male to female ratio among the examined children. Twelve (23.4%) out of the 37 positive patients were less than 5 years old. RSV levels were at their peak in the winter, particularly from December to February. Our study found that RSV infections were more common than RSVB infections in the Ismailia Province of Egypt, particularly in males during the winter and children under the age of five. Further studies are required to molecularly characterize the RSV circulating genotype.

Keywords: Occurrence, Respiratory Syncytial Virus, RSV, Seroprevalence, Serological investigation.

Conflict of Interest: None declared

23. GENETIC ANALYSIS OF RESPIRATORY SYNCYTIAL VIRUS ASSOCIATED PNEUMONIA IN CHILDREN AGED < 5 IN PAKISTAN

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BACKGROUND: RSV is the most important viral cause of severe acute respiratory tract infections (ARI) in children worldwide. The aim of the current study was to genetically characterize the RSV strains in children aged less than 5 years admitted to a tertiary care hospital in Karachi, Pakistan.

METHODS: A total of 1,121 children admitted with respiratory illness such as bronchiolitis and pneumonia were recruited in this study. To genetically characterize the RSV, M gene of RSV from real- time PCR positive samples was amplified and sequenced. The sequences were subsequently aligned with RSV genotype A and B reference sequences. Phylogenetic relationship of RSV M gene and its epidemic dynamics was analyzed through a Maximum Likelihood tree.

RESULTS: Out of the 1,121 samples, 226 (20%) were found positive for RSV using real- time PCR, while M gene was amplified only from 30/226 samples. All the samples clustered with genotype B reference sequences indicating genotype B to be the prevalent strain in the infected children. Majority of the sequence formed a monophyletic cluster, indicating that majority of the infection was carried out by a ‘founder virus’ sharing similar genetic characteristics.

CONCLUSION: The study data show the high burden of RSV in children in Pakistan. Genetic analysis indicated that the RSV infection is carried out by phylogenetically similar genotype B strains evolving from a common founder virus. This information can further be explored to understand the epidemic dynamics of RSV in children.

Keywords: Respiratory syncytial virus, M protein, acute respiratory infections, molecular phylogeny

Conflict of Interest: None declared
24. ADDING SALIVA SPECIMENS INCREASES PCR DETECTION OF RESPIRATORY SYNCYTIAL VIRUS AMONG HOSPITALIZED ADULTS OVER NASOPHARYNGEAL/NASAL SWABS ALONE

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Background: Nasopharyngeal (NP)/nasal swabs are the most common samples obtained for RSV PCR testing, and nearly all published RSV incidence estimates in adults are based on such testing. However, saliva has been successfully used for viral respiratory pathogen detection and been recently shown to increase RSV detection when added to NP swab RT-PCR. We sought to compare RSV detection by PCR testing of NP/nasal swab alone versus NP swab plus saliva.

Methods: This ongoing, prospective cohort study enrolls patients aged ≥18 years hospitalized for acute lower respiratory tract disease (aLRTD) in 2 hospitals in Bristol, UK. We present results from 2022. NP/nasal swabs and saliva samples were obtained at hospital admission/enrollment and tested with VIASURE Viral Multiplex PCR from CerTest. NP swab was the preferred approach, but if declined, an alternative respiratory specimen such as midturbinate nasal swab was collected.

Results: Among 1,379 patients with paired NP/nasal swab and saliva specimen results, 2 were positive by NP/nasal swab, 2 by both NP/nasal swab and saliva, and 7 by saliva only (Figure). RSV prevalence by NP swab alone was 0.29% and 0.80% using both saliva and NP/nasal swab, consistent with a 2.75-fold increase in RSV prevalence with addition of saliva testing (95% CI: 1.26–6.01).

Conclusion: These preliminary UK data suggest addition of saliva to NP/nasal sampling may substantially increase RSV detection in adult aLRTD patients, consistent with previous US data. Additional specimen collection including adding sputum is in process to expand on these results.

Keywords: Saliva, nasopharyngeal swab, RSV, polymerase chain reaction, epidemiology, disease burden, disease diagnosis

Conflict of Interest: Authors with Pfizer affiliations are employees of Pfizer and may own Pfizer stock. CH is Principal Investigator of the AvonCAP Study which is an investigator-led University of Bristol study funded by Pfizer and has previously received support from the NIHR in an Academic Clinical Fellowship. JO is a Co-Investigator on the AvonCAP Study. AF is a member of the Joint Committee on Vaccination and Immunization (JCVI) and chair of the World Health Organization European Technical Advisory Group of Experts on Immunization (ETAGE) committee. In addition to receiving funding from Pfizer as Chief Investigator of this study, he leads another project investigating transmission of respiratory bacteria in families jointly funded by Pfizer and the Gates Foundation. The AvonCAP study is a University of Bristol–sponsored study which is investigator-led, funded by Pfizer Inc., and conducted as a collaboration between Pfizer and University of Bristol.

25. DETECTION OF RESPIRATORY SYNCYTIAL VIRUS SUBSTANTIALLY INCREASES WHEN ADDING SPUTUM, SALIVA, AND SEROLOGY TESTING TO NASOPHARYNGEAL SWAB RT-PCR

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BACKGROUND. Nearly all RSV incidence estimates are based on nasal/nasopharyngeal (NP) swab RT-PCR testing. Adding additional specimen types increases RSV detection. Prior studies only made pairwise comparisons and did not investigate synergistic effect of adding multiple specimen types. We compared RSV detection by NP swab RT-PCR alone versus NP swab plus saliva, sputum, and serology.

METHODS. In this US-based prospective cohort study over two seasons (27Dec2021–01Apr2022; 22Aug2022–11Nov2022) of patients aged ≥40 years hospitalized for acute respiratory illness (ARI), NP swab, saliva, and sputum were collected at enrollment and PCR tested (luminex ARIES platform). Serology specimens were obtained (enrollment and 30–60-day visit). We calculated RSV detection rate for NP swab alone and NP swab plus any other specimen type/test.

RESULTS. Among 1772 patients, 100% had NP swab, 99% saliva, 34% sputum, and 13% paired serology specimens tested. RSV was detected in 57 (3.2%) patients by NP swab alone and 103 (5.8%) patients by NP swab plus additional specimens, corresponding to a 1.81 times higher detection rate (95%CI:1.52–2.15). Limiting to the 99 subjects with all specimen types (ie, NP swab, saliva, sputum, and serology), there was a 3.50-fold increase in detection (95%CI:1.08–11.29) compared to NP swab alone (2.0% versus 7.1%).

CONCLUSIONS. RSV detection was several-fold higher when additional specimen types were added to NP swab even with a relatively low percentage of subjects with sputum and serology results. Hospitalized RSV ARI burden estimates in adults based solely on NP swab RT-PCR should be adjusted for underestimation.

Keywords: Respiratory Syncytial Virus, Acute Respiratory Illness, Polymerase Chain Reaction, Disease Diagnosis, Serology, Epidemiology, Disease Burden

Conflict of Interest: Authors with Pfizer affiliations are employees of Pfizer and may own Pfizer stock. This study funded by Pfizer and was conducted as a collaboration between Norton Infectious Diseases Institute, Norton Healthcare, and Pfizer. Norton Infectious Diseases Institute, Norton Healthcare, is the study sponsor.
26. INCIDENCE AND MORTALITY RATE OF SEVERE ACUTE RESPIRATORY INFECTION IN CHILDREN <2 YEARS ADMITTED TO THE EMERGENCY DEPARTMENT IN CAMEROON

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INTRODUCTION: Severe acute respiratory infection (SARI) is a leading cause of hospital admission and death in young children, especially in low- and middle-income countries (LMICs). A vaccine against respiratory syncytial virus (RSV), a main underlying pathogen of SARI, is expected to become available. Data on the burden of severe SARI and/or RSV disease in LMICs, like Cameroon, is important for future vaccine implementation programmes, but currently lacking.

METHODS: Children <2 years admitted with SARI to the 22-bed emergency department (ED) between September 2020 and September 2021 were included. Data were collected retrospectively through admission books present at the ED. SARI incidence and mortality rates were calculated using local census data based on the WHO Manuel for Estimating Disease Burden Associated with Seasonal Influenza.

RESULTS: A total of 196 emergency SARI admissions +2 years with a median age of 172.0 (IQR 82.0-336.5) days were identified. 46 (23.5%) cases died during admission. At least other hospitals with access to in total 54 pediatric ED beds are situated in the Douala region. Demographic census showed a total catchment population of 47 214 children under 2. We calculated an annual incidence and mortality by all-cause SARI of 415.1 and 97.4 per 100 000 children respectively.

CONCLUSION: The WHO Manual for Estimating Disease Burden Associated with Seasonal Influenza is a feasible method for obtaining data on SARI burden in LMICs. We will use the model in our prospective GOLD ICU studies in which we determine the presence of RSV infection in 10 GAVI-eligible countries.

Keywords: disease burden, Cameroon, severe acute respiratory infection, Respiratory Syncytial Virus, children

Conflict of Interest: None declared

27. WITHIN-SEASON CHANGES IN THE AGE DISTRIBUTION OF RSV CASES: ANALYSIS OF AGE-SPECIFIC SURVEILLANCE DATA FROM THE NETHERLANDS, PORTUGAL, SINGAPORE, SOUTH AFRICA, AND NEW ZEALAND

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8. Sanofi Pasteur, Lyon, France.

Background: Understanding changes in the age distribution of RSV cases is important to assess the population impact of RSV. We studied whether the age of RSV cases varies within a season, moving towards younger or older age groups as time passes. Methods: We used surveillance data (2008-2018) from the Global Epidemiology of RSV (GERi) project for the Netherlands and Singapore (primary care surveillance), and Portugal, South Africa, and New Zealand (secondary care surveillance). Separately in each country, each season (Jul-Jun in the Northern hemisphere, calendar year elsewhere) was divided into “quarters”, (i.e. periods when the first, second, third, and fourth 25% of RSV cases in the season occurred). We fitted multilevel logistic regression models with season as a higher-level variable to study whether the odds of being aged above vs. below a pre-set cut-off (varying across countries depending on the age distribution of RSV cases) changed within a season. Results: Over time within a season, RSV cases became increasingly likely to be aged ≥6 years in the Netherlands (4th vs. 1st quartile: OR 2.53, 95% CI 1.74-3.85) and ≥5 years in Portugal (2.86, 2.35-3.47), and <1 year in South Africa (1.72, 1.45-2.04) and New Zealand (1.64, 1.33-2.00). No trend was observed in Singapore. Results were robust to a range of sensitivity analyses. Conclusions: Our findings suggest that the age profile of RSV cases shifts within a season. The variability among countries may reflect differences in household size, social structuring, and health-seeking and testing behaviours, but remains to be fully understood.

Keywords: RSV; epidemiology; surveillance; age distribution.

Conflict of Interest: Conflict of interests: JP declares that Nivel has received unrestricted research grants from IMI, Sanofi and the Foundation for Influenza Epidemiology outside the submitted work. MB and RK are employees of Sanofi and may hold shares and/or stock options in the company.

Funding: Sanofi and AstraZeneca.

28. CO-CIRCULATION OF RESPIRATORY SYNCYTIAL VIRUS IN CASES OF SARI DURING THE SARS-COV-2 PANDEMIC PERIOD IN BRAZIL (2020 TO 2022).

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Epidemiological analyses were performed with SARI cases by RSV (WE 01/2020 to 46/2022) notified to the System of the Surveillance of the Influenza and other respiratory viruses in Brazil. January 2020 to November 2022, 30,933 SARI cases by RSV were recorded and 768 were deceased cases. 45% in 2021 and 50% in 2022 (EW46). 82% of cases were detectable by RT-PCR. RSV were present mainly in children less than 2 y.o. (85%), and children between 3 to 6 y.o. (6%). Regarding SARI deaths caused by RSV, mainly children less than 2 y.o. (34%) and older adults more than 60 y.o. (46%) were affected. 64.5% to deaths had one or more risk factors, heart disease represented 48% of deceased cases. January to March 2020, Southeast and South (34%) were the Brazilian regions that reported more SARI cases by RSV. October to December, the Southeast (52%) and North (35%) presented a higher number of cases. January to March 2021, the cases were protagonists in Southeast (64%), Midwest (12%). April to September 2021, cases predominated in South (46%, peak EW46). At the end of the year, Southeast reported again an increase of cases (65%, peak EW46). Up to the EW46/2022 Southeast reported 52% of SARI cases by RSV (January to March). Midwest e Northeast had high RSV circulation between January and June in all analyzed years. RSV co-circulation was observed during the COVID-19 pandemic, and were observed more reports of SARI cases by RSV in children less than 2 y.o in all Brazilian states.

Presenting Author*, Co-Authors and Affiliations

Keywords: SARI; SARS-COV-2; RSV; CO-CIRCULATION; DESCRIPTIVE EPIDEMIOLOGY; BRAZIL

Conflict of Interest: I declare that I have no conflict of interest
28. BURDEN OF RESPIRATORY SYNCYTIAL VIRUS (RSV) DISEASE IN LATIN AMERICA: A SYSTEMATIC REVIEW AND META-ANALYSIS

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5. Vaccine Medical, Pfizer SAS, Bogota, Colombia.
6. Pfizer Inc, New York, New York, USA.

Background: Previous systematic reviews highlighted the evidence gaps about the burden of RSV in Latin America and the Caribbean (LAC).

Objectives: To determine the incidence and prevalence, severity, and associated direct/indirect costs of RSV in LAC by country, age, risk groups, co-infections, RSV subtype A and B; discriminating seasonality and RSV outbreaks. To describe results over time, focusing pre/post-Covid-19 pandemic periods.

Methods: We are carrying out a systematic review following Cochrane methods, the PRISMA/MOOSE statements (PROSPERO registration in process).

Inclusion criteria. Types of studies: observational/surveillance, experimental/quasi-experimental, economic analyses, and clinical guidelines published since 01/01/2012. Types of participants: population of any age from LAC. Outcomes: epidemiological (incidence, prevalence, case fatality rate, specific mortality, hospitalization rates, complications), costs (direct/indirect in international dollars), and immunoprophylaxis recommendations.

Search strategy (from 01/01/2012–): PubMed, Lilacs, Embase, CINAHL, Cochrane Library, Web of Science, Tufts Economic Database, EconLit, reference lists of included articles, conference proceedings, relevant websites.

Table 1. Proportion countries and publication year (N=405)

<table>
<thead>
<tr>
<th>Countries (%)</th>
<th>Publication year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brazil (22%)</td>
<td>2012 (1)</td>
</tr>
<tr>
<td>Colombia (12%)</td>
<td>2013 (7)</td>
</tr>
<tr>
<td>Argentina (10%)</td>
<td>2014 (7)</td>
</tr>
<tr>
<td>Mexico (8%)</td>
<td>2015 (5)</td>
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<tr>
<td>Chile (7%)</td>
<td>2017 (11)</td>
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<tr>
<td>Peru (4%)</td>
<td>2017 (12)</td>
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<tr>
<td>Puerto Rico (3%)</td>
<td>2018 (9)</td>
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<tr>
<td>Uruguay (2%)</td>
<td>2019 (13)</td>
</tr>
<tr>
<td>Cuba (2%)</td>
<td>2020 (12)</td>
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<tr>
<td>El Salvador (2%)</td>
<td>2021 (14)</td>
</tr>
<tr>
<td>&gt;LAC countries (2%)</td>
<td>2022 (11)</td>
</tr>
</tbody>
</table>

Independent selection, data extraction, and risk of bias assessment (RoB) through COVIDENCE®.

RoB: US NHLBI Institute checklist for observational studies, Cochrane tools for quasi-experimental designs, and CHEERS checklist and CiCERO tool for economic analyses.

Statistical analysis: proportion meta-analysis applying an arc-sine transformation by seasonality and RoB. Subgroup analysis according to objectives.

Preliminary results: 405/1732 screened studies included for full-text assessment (87% children, 13% adults), including 29 economic studies. The most represented countries were Brazil (22%), Colombia (12%), and Argentina (10%); 2012-2022 publication rate ranged from 1 to 14% (Table 1). Results will be presented at the conference.

Keywords: Respiratory Syncytial Virus, RSV, Disease Burden, Latin America, Systematic review, Meta-analysis.

Conflict of Interest: Study supported by Pfizer Argentina. Authors have no conflict of interest to declare.

50. EPIDEMIOLOGY OF HUMAN RESPIRATORY SYNCYTIAL VIRUS AMONG CHILDREN AGED 0-5 YEARS OLD WITH ACUTE RESPIRATORY TRACT INFECTION IN NGAOUNDRÈ (CAMEROON)

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Background: Human Respiratory Syncytial Virus (HRSV) is a major cause of acute respiratory infections (ARI) among children. The mapping of the distribution of the HRSV in the Adamawa region is needed for a better understanding of the burden of HRSV Cameroon. This study aimed to determine the factors associated with HRSV among children aged between 0-5 years old with ARI using point-of-care-testing kits in Ngaoundéré.

Methods: Nasopharyngeal swabs were collected from 100 children aged from 0-5 years old presenting respiratory symptoms (wheezing, cough, and runny nose) at the National Influenza Regional Hospital between July 27th and October 10th 2019. Collected samples were subjected to a point-of-care testing to detect HRSV antigens. Demographics and clinical symptoms were collected using a questionnaire and analyzed using Chi-square test or Fisher’s exact test.

Results: The total HRSV-associated ARI prevalence was 24%. HRSV was most prevalent among children between 0-2 years of age (83.3%, 20/24). Apnea was more frequently present in HRSV positive than negative patients (54.2%, 13/24; vs. 30.3%, 23/76; p=0.05). Underlying conditions (congenital heart disease and sickle cell, p=0.05) were more frequent among HRSV positive patients. Hospitalization rate was higher among HRSV positive than negative patients (50.0%, 12/24; vs. 14.5 %, 11/76; p<0.01).

Conclusion: HRSV was associated with respiratory symptoms and hospitalization of under 5 children in Ngaoundéré. This study complements other HRV studies in Cameroon where the disease burden may have been underestimated and points out the need to conduct surveillance of HRV and design effective primary preventive measures against ARI in Cameroon.

Keywords: Human Respiratory Syncytial Virus, Acute Respiratory Infections, Infants, Apnea, Point-of-care testing

Conflict of Interest: None declared

31. UNDERSTANDING THE AGE SPECTRUM OF RESPIRATORY SYNCYTIAL VIRUS ASSOCIATED HOSPITALISATION AND MORTALITY BURDEN BASED ON MODELLING METHODS: A SYSTEMATIC ANALYSIS

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† Correspondent author

Background: Modelling studies based on excess morbidity and mortality are important for understanding RSV disease burden for age groups that are less frequently tested for RSV. We aimed to understand the full age spectrum of RSV morbidity and mortality burden based on modelling studies, and the value of modelling studies in RSV disease burden estimation.
Methods We conducted a systematic review of modelling studies reporting excess RSV hospitalisation or mortality rates. Reported rates were synthesised by age group, clinical diagnosis, and country income group.

Results We included 26 and 6 studies from high-income countries and upper-middle-income countries, respectively. RSV-associated hospitalisation and mortality both showed a U-shape age pattern with higher rates observed at the extremes of age (Figure). Upper-middle-income countries had consistently higher RSV mortality rates than high-income countries across all ages. RSV mortality rate was highest in infants for upper-middle-income countries while highest in adults aged ≥75 years for high-income countries. Over 70% of RSV hospitalisations in children <5 years could be captured in laboratory records whereas less than 10% of RSV hospitalisations could be captured beyond 5 years. Pneumonia and influenza mortality could capture half of all RSV mortality in older adults but only 10–30% of RSV mortality in children.

Conclusions Our study provides insights into the age spectrum of RSV hospitalisation and mortality. RSV disease burden using laboratory records alone could be substantially severely underreported for age groups ≥25 years. Our findings confirm infants and older adults should be prioritised for RSV immunisation programmes.

Keywords: Respiratory syncytial virus; model; hospitalisation; mortality; burden of disease; systematic reviews.

Conflict of Interest: YL reported grants from the World Health Organization and Wellcome Trust, outside the submitted work. HN reports grants from the Innovative Medicines Initiative outside the submitted work; consulting fees from the Gates Foundation, Pfizer, and Sanofi; honoraria from AbbVie; support from Sanofi for attending meetings; and participation on advisory boards from Sanofi, Janssen, Novavax, Revival, Resvinet, and WHO outside the submitted work. All other authors declared that they have no competing interests.

53. RSV SUBGROUPS A AND B EPIDEMIOLOGY AND DIFFERENCES IN CLINICAL SEVERITY

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Introduction: Understanding differences between RSV-A and RSV-B circulating strains provides insights for the development of prevention strategies and public health interventions. We aimed to describe the global distribution of RSV-A and RSV-B subgroups and compare their clinical severity.

Methods: A literature review from PubMed and Google Scholar (1986–2022) was performed and extended using snowballing from references in captured publications.

Results: Among 120 references identified, 56 were included in this analysis. As observed in 14 publications reporting distribution of RSV-A and RSV-B, both strains generally co-circulate within a season, with predominance varying over seasons and countries. Among 137 RSV seasons analyzed in 29 countries (covering both hemispheres) between 1990 and 2021, RSV-A was predominant in 75 seasons (54.7%), RSV-B was predominant in 49 seasons (35.8%), and 13 seasons (9.5%) had no clear predominance. In both northern and southern hemispheres, genotype diversity decreased over the study period. Since 2015, ON1 and BA9 became the sole genotypes for RSV-A and RSV-B, respectively, in the 14 countries with available data from 10 publications.

Of 42 studies reporting RSV subgroup impact on clinical severity, 26 reported no significant differences in severity between subgroups A and B while 14 versus 2 studies reported that RSV-A or RSV-B infection resulted in more severe outcomes, respectively.

Conclusions: RSV-A and RSV-B both contribute substantially to the global RSV burden, with a tendency for higher disease severity due to RSV-A. However, firm conclusions are hampered due to high study heterogeneity.

Keywords: RSV-A, RSV-B, subgroups, epidemiology, clinical severity

Conflict of Interest: DC, ChN, BG and EB are Pfizer employees

53. MODELING THE CLINICAL AND ECONOMIC BURDEN OF RESPIRATORY SYNCYTIAL VIRUS (RSV) AMONG ADULTS ≥60 YEARS OF AGE IN THE UNITED STATES

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Background: Each year, 3–7% of older adults in the United States (US) experience respiratory syncytial virus (RSV) infection. The objective of this study was to estimate the annual burden of RSV among US older adults.

Methods: A Markov model was developed to estimate the annual clinical and economic burden of symptomatic RSV among adults aged ≥60 years in the US (n=81,001,651). RSV epidemiology, health care resource use and cost inputs (2022 US dollars) were obtained from published literature and standard US sources. A unit costing approach was used to estimate RSV direct medical costs and the model included both market and nonmarket productivity losses of RSV cases.

Figure 1. Annual RSV-related symptomatic ARI, URTD, LRTD and medical attendance among US adults aged ≥60 years
Results: In the base-case analysis, the model estimates 3,031,750 symptomatic RSV cases annually among adults aged ≥60 years, including 1,094,349 medically-attended cases (Figure 1). Of the 1,276,526 lower respiratory tract infections, 171,415 are hospitalized and 13,919 result in death. The annual economic burden of RSV is estimated at nearly $2.8 billion in direct costs and almost $4.7 billion in indirect costs, for a total of over $7.4 billion from the societal perspective. Although 60–64-year-olds have lower hospitalization and mortality rates vs. ≥65-year-olds, they still experience considerable RSV-related burden (e.g., 802,602 annual symptomatic RSV cases resulting in over $1.1 billion in productivity losses). RSV burden remained high across sensitivity analyses.

Conclusions: RSV has a high burden in US adults aged ≥60 years. Additional analyses are needed to estimate the impact of RSV vaccination on reducing the disease burden.

Funding: GlaxoSmithKline Biologicals SA (VEO-000319)

Keywords: RSV, burden of disease, economic model, older adults

Conflict of Interest: Daniel Molnar, Elizabeth La, Frederik Verelst, Desmond Curran, and Sara Poston are employed by GSK and hold shares in GSK. Jonathan Graham is employed by RTI Health Solutions, a not-for-profit organization, which received funding from GSK for the conduct of this study. The authors declare no other financial and non-financial relationships and activities.

34. RSV BURDEN IN INFANTS ATTENDING HOSPITAL EMERGENCY DEPARTMENTS IN IBERIA. THE RHEDI STUDY

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7. CUF Descobertas Lisboa
8. Hospital de Santa Maria Lisboa
9. Hospital Pediátrico Coimbra

BACKGROUND: The full extent RSV disease burden on infant’s population in the emergency departments (ED) is unknown.

OBJECTIVES: To describe the epidemiology of acute respiratory infections (ARI) and to estimate the clinical and economic burden of RSV through prospective ARI surveillance in ED visits of children ≤2 years of age, including possible complications, for 2 consecutive seasons. Additionally, co-circulating viral pathogens causing ARI will be analyzed.

METHODS: Prospective, hospital-based surveillance in ED in eight pediatric hospitals in Spain and Portugal covering six metropolitan areas in Iberia. At least 2,000 children ≤2 years with ARI or otitis media attending ED will be recruited using a sampling frame to maximize representation of populations attending each hospital ED, recruiting 8 subjects/week/site, at least 50% with LRTI. A line list of all LRTI cases attending ED in each site will be collected. Medical services, direct costs and clinical outcomes before, during and 14 days after ED visit will be captured. A nasopharyngeal swab will be collected in all subjects during ED visit and centrally analyzed. Information on any additional healthcare utilization (medically-attended) and out-of-pocket costs before and after the ED visit will be collected from the parents by questionnaire.

RESULTS: RHEDI surveillance started in Jan-2022. Due to the epidemiological impact of the pandemic was paused in Apr-2022 and resumed in Sep-2022.

CONCLUSIONS: The REDHI design seems adequate to capture RSV burden in infants attending ED.

Keywords: RSV, Emergency room, Urgent care, RSV burden

Conflict of Interest: FM-T reports honoraria from GSK group, Pfizer, Sanofi Pasteur, MSD, Seqirus, Biofabri, and Janssen for taking part in advisory boards and expert meetings and for acting as a speaker in congresses, outside the submitted work; and principal investigator-role in randomised controlled trials for GSK, Pfizer, Sanofi Pasteur, MSD, Seqirus, Biofabri, Janssen, Ablynx, Gilead, Regeneron, Roche, Abbott, Novavax, and MedImmune, with honoraria paid to his institution.

35. SAFETY AND EFFICACY OF NISREVMAB FOR PREVENTION OF MEDICALLY ATTENDED RSV LOWER RESPIRATORY TRACT INFECTION IN ALL INFANTS ENROLLED IN THE PHASE 3 MELODY TRIAL

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7. Hospital Pediátrico Coimbra
8. Hospital Regional Universitario de Málaga. Andalucía
9. CUF Descobertas Lisboa
10. Hospital de Santa Maria Lisboa
11. Hospital Pediátrico Coimbra

BACKGROUND: Nirsevimab, a monoclonal antibody with extended half-life, was developed to protect infants against lower respiratory tract infection (LRTI) due to respiratory syncytial virus (RSV). The Phase 3 MELODY study (NCT03979313) aimed to assess nirsevimab efficacy in late pre-term and term infants (≥35 weeks gestational age); however, the coronavirus disease 2019 pandemic interrupted enrollment. Based on the 1490 infants randomized prior to the pause, the primary endpoint was met: nirsevimab demonstrated an efficacy of 74.5% (95% confidence interval [CI]: 49.6, 87.1) against medically attended (MA) RSV LRTI. However, the analysis was underpowered to determine efficacy against hospitalization-associated RSV LRTI. Here we report efficacy in the full enrolment cohort.

Methods: Infants were randomized 2:1 to one intramuscular injection of nirsevimab (<5 kg, 50 mg; ≥5 kg 100 mg) or placebo before their first RSV season. Efficacy was evaluated over 150 days post-dose using predefined disease severity criteria. Adverse events (AEs) were monitored up to 360 days post-dose.

Keywords: RSV, Safety, Efficacy, MELODY, Infant, nirsevimab, prophylaxis, LRTI, AEs

Conflict of Interest: Daniel Molnar, Elizabeth La, Frederik Verelst, Desmond Curran, and Sara Poston are employed by GSK and hold shares in GSK. Jonathan Graham is employed by RTI Health Solutions, a not-for-profit organization, which received funding from GSK for the conduct of this study. The authors declare no other financial and non-financial relationships and activities.
Results: Overall, 3012 infants were randomized (dosed: 1998 nirsevimab, 996 placebo). Efficacy against hospitalization-associated RSV LRTI was 76.8% (95% CI: 49.4, 89.4) and 78.6% (95% CI: 48.8, 91.0) against very severe MA RSV LRTI through an RSV season. Efficacy against MA RSV LRTI was consistent (76.4%; 95% CI: 62.3, 85.2). Treatment-related AE incidence was similar across treatment groups (nirsevimab, 1.3%; placebo, 1.5%).

Conclusion: A single dose of nirsevimab was well tolerated and provided a consistent level of protection to late pre-term and term infants against hospitalization-associated RSV LRTI and very severe MA RSV LRTI.

Keywords: nirsevimab, respiratory syncytial virus, infants

Conflict of Interest: WI Muller has received grant/research support from Ansun, Astellas, AstraZeneca, Eli Lilly, Enanta Pharmaceuticals, Gilead, Janssen, Karius, Melinta, Merck, Moderna, Nabria, Paratek, Pfizer, Roche, Tetrathapase; and consulting fees from Adagio Therapeutics, Finley Law Firm, P.C., PreventionBio, Seqirus. R Dagan has received grant/research support from AstraZeneca/MedImmune, MSD, Pfizer; consulting fees from MSD, Pfizer; and speaker bureau for GlaxoSmithKline, MSD, Pfizer, Sanofi. LL Hammitt has received grant/research support from AstraZeneca, Merck, NIH, Pfizer. X Sáez Llorens has received grant/research/support from AstraZeneca. B Seoane Nuñez, A Grenham, EJ Kelly, VS Mankad, T Takas, A Leach, and T Villafana are employees and shareholders of AstraZeneca. S Madhi, M Baca Cots, M Bosheva, CI Llapur, and JM Novoa Pizarro have no conflicts of interest to disclose.

Clinical events and healthcare resource utilization during the index inpatient stay and during the post-discharge period

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Background: Respiratory syncytial virus (RSV) causes acute respiratory illness (ARI) and hospitalization among adults. We conducted a prospective, population-based surveillance study to estimate the incidence of RSV-associated hospitalizations in adults before the COVID-19 pandemic to allow for monitoring of changes in RSV burden over time and following the potential introduction of RSV vaccines.

Methods: Hospitalized adults aged ≥18 years meeting criteria for ARI were enrolled during the 2016-2017 and 2017-2018 RSV seasons at 3 U.S. medical centers: Baylor Scott and White (Temple, TX), Vanderbilt University (Nashville, TN), and University of Pittsburgh (Pittsburgh, PA). Nasal and throat swabs were collected and tested for RSV using real-time reverse transcription polymerase chain reaction. We estimated the incidence of RSV-associated hospitalizations for 100,000 population for each season by site and age group, using U.S. census and hospital market share data.

Results: Among 3,478 patients enrolled, 233 (6.7%) tested positive for RSV. Annual incidence of RSV-associated hospitalizations among adults across the three sites ranged from 85 to 135 per 100,000 during the 2016-2017 season, and from 85 to 89 per 100,000 during the 2017-2018 season. Age-group specific incidence over both seasons ranged from 46 to 94 hospitalizations per 100,000 adults aged 18-64 years, and from 239 to 356 per 100,000 adults aged ≥65 years.

Conclusions: We found a high burden of RSV-associated hospitalizations among adults before the COVID-19 pandemic, particularly among those aged ≥65 years. These findings underscore the potential need for safe and effective RSV vaccines to prevent hospitalizations among older adults.

Keywords: RSV, respiratory syncytial virus, RSV-associated hospitalizations, RSV burden, adults

Conflict of Interest: Fernanda Silveira – Research grant from Ansun Biopharma; Richard Zimmerman – Research funding from CDC, NIH, Sanofi Pasteur, H. Keipp Talbot – Research funding from CDC; Emily Martin - Research funding from Merck
Background: Relative to influenza, there is a lack of awareness about respiratory syncytial virus (RSV) and its impact on outcomes in older adults.

Objective: To evaluate clinical events and healthcare resource utilization among older adults hospitalized for RSV versus influenza in the US.

Methods: Patients ≥60 years old hospitalized for RSV or influenza in the Optum Clinformatics Extended De-Identified DataMart database (07/01/2015-02/29/2020) were matched 1:2 using propensity score matching. Outcomes included patients developing new cardiorespiratory conditions during the index hospitalization or the up-to-12-month post-discharge period and patients discharged to or having long-term care (LTC)/home care services post-discharge (evaluated among patients with no LTC/home care services during the baseline period).

Results: A total of 4,204 patients hospitalized for RSV (mean age: 78.7 years, 62.6% female) were matched to 8,408 patients hospitalized for influenza (mean age: 78.6 years, 62.2% female). During the index hospitalization, more patients with RSV than influenza developed a respiratory condition (92.5% versus 77.8%; P < 0.001; post-discharge: 25.3% versus 25.5%; P = 0.936) or a cardiovascular condition (29.5% versus 27.7%; P = 0.048; post-discharge: 16.2% versus 16.7%; P = 0.456; see table below). Among patients without baseline LTC services, more patients with RSV than influenza (40.0% versus 37.4%; P = 0.004) were discharged to or had LTC services post-discharge (home care services: 43.9% versus 39.4%; P < 0.001).

Conclusions: Older adults hospitalized for RSV had worse reported cardiorespiratory outcomes and utilized LTC/home care services more frequently post-discharge (thus not returning to full health) than those hospitalized for influenza, highlighting the need for prophylactic strategies such as RSV vaccination.

Keywords: clinical events, healthcare resource utilization, respiratory syncytial virus, influenza, cardiorespiratory diseases, inpatient, post-discharge, long-term care, home care, comparison, older adults

Conflict of Interest: JKD and GK are employees of Janssen Scientific Affairs, LLC and stockholders of Johnson & Johnson. BE, AH, SS, PL and MHL are employees of Analysis Group, Inc., which has provided paid consulting services to Janssen Scientific Affairs, LLC.
Methods: The 2016-2019 National Inpatient Sample databases were used to identify hospitalizations coded for RSV and RSV-attributable conditions (i.e., pneumonia, chronic obstructive pulmonary disease [COPD], congestive heart failure [CHF], asthma, acute respiratory infections [ARI], and influenza) among patients ≥60 years. Literature-derived proportions for each condition were used to estimate RSV-attributable hospitalizations for RSV season (i.e., October-April) by race/ethnicity (i.e., non-Hispanic Blacks, Hispanics, non-Hispanic Whites, non-Hispanic others). Rates per 100,000 US population (≥60 years) were computed.

Results: The annual rate of RSV-coded hospitalizations was 36.5 per 100,000 US population (non-Hispanic Blacks, 35.6; Hispanics, 35.4; non-Hispanic Whites, 36.7; non-Hispanic others, 36.6). Including RSV-attributable hospitalizations, the annual rate of RSV hospitalizations ranged from 373 to 533 hospitalizations per 100,000 US population. By race/ethnicity, the highest hospitalization rate per 100,000 US population was reported for non-Hispanic Black (452-634), followed by non-Hispanic White (377-544), non-Hispanic other (302-413), and Hispanic (298-407) (Figure).

Conclusions: Rates for RSV-coded hospitalizations were similar by race/ethnicity; however, considerable differences were observed when RSV-attributable hospitalizations were included. Rates for RSV-attributable COPD and CHF hospitalizations were higher for non-Hispanic Blacks. Overall, RSV is associated with a substantial number of hospitalizations among adults ≥60 years in the US.

Keywords: RSV-attributable conditions, hospitalization rate, racial disparity

Conflict of Interest: RCP, AH, FB, and JM are salaried employees of RTI Health Solutions, which received research funding from Janssen to perform this study. RTI Health Solutions, LLC, and Johnson & Johnson stock/stock options. ML reports personal fees from Merck, Pfizer, Seqirus, and Curevo; grants from Johnson & Johnson; and Moderna; and grants, personal fees from Merck, outside the submitted work.

Table. Characteristics, Length of Stay, and Costs for RSV and Influenza Hospitalizations Among Older Adults in the United States.

<table>
<thead>
<tr>
<th>Condition</th>
<th>RSV Hospitalizations (n, %)</th>
<th>Influenza Hospitalizations (n, %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of hospitalizations</td>
<td>100 (100)</td>
<td>100 (100)</td>
</tr>
<tr>
<td>Age (years), mean (SD)</td>
<td>75.5 (9.3)</td>
<td>76.1 (9.3)</td>
</tr>
<tr>
<td>Primary diagnosis*</td>
<td>22,250 (20.6%)</td>
<td>31,475 (28.4%)</td>
</tr>
<tr>
<td>Co-morbidities</td>
<td>190,475 (96.2%)</td>
<td>456,625 (73.9%)</td>
</tr>
<tr>
<td>Metabolic conditions*</td>
<td>68,195 (39.5%)</td>
<td>415,975 (64.2%)</td>
</tr>
<tr>
<td>Cardiac conditions*</td>
<td>66,325 (55.0%)</td>
<td>322,745 (48.6%)</td>
</tr>
<tr>
<td>Chronic kidney disease*</td>
<td>56,489 (46.7%)</td>
<td>24,845 (44.3%)</td>
</tr>
<tr>
<td>Severe*</td>
<td>23,490 (21.6%)</td>
<td>188,250 (26.3%)</td>
</tr>
<tr>
<td>Mechanical ventilator use*</td>
<td>2,975 (2.7%)</td>
<td>62,545 (9.4%)</td>
</tr>
<tr>
<td>Died in hospital*</td>
<td>4,995 (4.6%)</td>
<td>25,600 (3.5%)</td>
</tr>
<tr>
<td>Length of stay (days)</td>
<td>6 (5-16)</td>
<td>5.5 (5-15)</td>
</tr>
<tr>
<td>Median (SD)</td>
<td>5.0</td>
<td>4.0</td>
</tr>
<tr>
<td>Total cost (2019 US dollars)</td>
<td>128,260 (100.0%)</td>
<td>660,980 (100.0%)</td>
</tr>
<tr>
<td>Median (SD)</td>
<td>$16,250 ($12,930)</td>
<td>$44,265 ($32,503)</td>
</tr>
</tbody>
</table>

*Statistically significantly different at significance level of 0.05 (p, p-value ≤ 0.05)
Conclusions: RSV hospitalizations tended to be longer, more expensive, and associated more with other pulmonary conditions than influenza hospitalizations among adults ≥60 years. Mechanical ventilator utilization and death were reported marginally more for RSV hospitalizations. Future RSV prevention strategies, including vaccination, should be considered given RSV’s burden of illness.

Keywords: RSV hospitalization, influenza hospitalization, burden of illness

Conflict of Interest: RCP, AH, FB, and JM are salaried employees of RTI Health Solutions, which received research funding from Janssen to perform this study. JKD and GKH are employees of Janssen Scientific Affairs, LLC and hold Johnson & Johnson stock/stock options. ML reports personal fees from Merck & Co, Pfizer, Seqirus, and Curevac; grants from Johnson & Johnson, Novavax, and Moderna; and grants, personal fees from GSK, outside the submitted work.

41. IMPACT OF SUBTYPE DISTRIBUTION ON SEASONALITY OF RESPIRATORY SYNCYTIAL VIRUS INFECTION: A GLOBAL SYSTEMATIC ANALYSIS

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Background: Previous studies reported inconsistent findings regarding the association between respiratory syncytial virus (RSV) subtype distribution and timing of RSV seasonal epidemics, likely due to not accounting for confounders such as meteorological factors. We aimed to improve the understanding of the association through a global-level systematic analysis that accounted for these potential confounders.

Method: We included published data on RSV seasonality from a systematic review and unpublished data shared from collaborators. The RSV season onset and offset were defined based on annual cumulative proportion. Linear regression models with study-level clustered standard errors were conducted to analyse the association of proportion of RSV-A in an RSV season with RSV onset and offset separately, while accounting for meteorological factors.

Results: We included 36 studies from 20 countries, which cumulatively provided data for 179 study-years in 1995–2019. RSV subtype distribution was not statistically significantly associated with RSV onset or offset globally; the only exception was for RSV offset in the tropics in one model, with a 4-day delay in offset per 10% increase in RSV-A proportion (Figure). Models that included both RSV subtype distribution and meteorological factors only jointly explained 2–4% of the variations in RSV onset and offset.

Conclusion: Globally, RSV subtype distribution had negligible impact on RSV onset and offset. RSV subtype distribution and meteorological factors jointly could only explain limited variations in RSV onset and offset. The role of population susceptibility, mobility, viral interference, and non-pharmaceutical interventions should be investigated in future studies.

Keywords: RSV, seasonality, subtype, meteorological, impact

Conflict of Interest: None declared

42. RISK FACTORS FOR RESPIRATORY SYNCYTIAL VIRUS-ASSOCIATED ACUTE LOWER RESPIRATORY INFECTION IN CHILDREN UNDER FIVE YEARS: AN UPDATED SYSTEMATIC REVIEW AND META-ANALYSIS

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8. Centre for G

Background: Respiratory syncytial virus (RSV) is the most common pathogen in acute lower respiratory infections (ALRI) and poses a substantial pediatric disease burden worldwide. In 2015, we published a systematic review on risk factors for RSV-ALRI. Several new studies have been published over the past 7 years; therefore, we aimed to update this review.

Methods: We conducted an updated literature search among three English databases (from August 2015 to September 2021) and additionally searched three Chinese databases (from January 1995 to September 2021) to identify studies reporting the association between individual-level risk factors and RSV-ALRI. We performed random effects meta-analyses to estimate pooled odds ratios (ORs) for each individual risk factor.

Results: A total of 43 studies were included among which 22 studies were from the updated search. Results showed that male sex (OR: 1.23; 95% CI: 1.19–1.28), maternal smoking (1.40; 1.32–1.48), low birth weight (1.77; 1.09–2.85), prematurity (1.85; 1.74–1.97), one sibling (1.67; 1.23–2.25), three or more siblings (1.70; 1.12–2.57), hemodynamically significant congenital heart disease (2.59; 1.07–6.26), HIV-infected (3.74; 2.65–5.27), bronchopulmonary dysplasia (1.19; 1.02–1.40) and Down syndrome (3.10; 2.73–3.53) were significantly associated with RSV-ALRI in children under five years. Multiple births, rural residency and passive smoking were found not to be statistically significantly associated with RSV-ALRI.

Conclusion: We identify multiple risk factors that are associated with higher risks of RSV-ALRI in young children. The findings can be used to identify sub-group(s) of young children with higher risks of RSV-ALRI for planning of future prevention and intervention strategies.

Keywords: RSV, ALRI, risk factor, systematic review, meta-analysis

Conflict of Interest: None declared

Meta-analysis results of risk factors for RSV-ALRI based on studies applying multivariate analyses
43. IMPACT AND COST-EFFECTIVENESS OF STRATEGIES TO PREVENT RESPIRATORY SYNCYTIAL VIRUS (RSV) DISEASE IN VIETNAM – A MODELING STUDY

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Background: New prevention strategies for RSV are emerging, but it is not clear if they will be cost-effective in low-middle income countries. We evaluated the potential impact and cost-effectiveness of a single dose of maternal vaccine (RSVpreF, Pfizer) and of monoclonal antibody (mAb) for newborns (Nirsevimab™, Sanofi, Astra Zeneca) in Vietnam.

Methods: A new RSV module of the UNIVAC decision-support model was used to calculate RSV burden in children <5 years, with and without RSV prevention strategies (maternal vaccination and infant mAb) over the period 2025-2034 in Vietnam. The primary outcome measure was the cost (2021 US$) per Disability Adjusted Life Year (DALY) averted, from a societal perspective. Each strategy was compared to no RSV intervention, and to each other. Hospital surveillance data was combined with data from a recent cost-of-illness study and other inputs from the scientific literature. We ran probabilistic uncertainty analyses and assessed the sensitivity of our cost-effectiveness results to changes in the dose price, duration of protection and other key inputs.

Results: From our preliminary analysis, RSVpreF vaccine ($3.50/dose, 81.8% efficacy, 6 months protection) could be cost-saving and Nirsevimab™ ($3.50/dose, 78.4%, 5 months protection) could cost less than 0.01 times the Vietnam national GDP per capita (2021) to avert each DALY. Our results were very sensitive to the dose price, efficacy and duration of protection of each strategy.

Conclusions: RSVpreF vaccine and Nirsevimab™ may be cost-effective in Vietnam if appropriately priced. The new RSV module provides evidence-data to inform forthcoming national decisions on RSV prevention strategies.

Keywords: RSV, Low-middle income countries, maternal vaccine, monoclonal antibody, economic evaluation

Conflict of Interest: None declare

44. ESTIMATING THE ECONOMIC BURDEN OF RESPIRATORY SYNCYTIAL VIRUS (RSV) INFECTIONS IN INFANTS IN VIETNAM: A COHORT STUDY

Lien Anh Ha Do (1,2)*, Elisabeth Vodicka (3), An Nguyen (4), Lê Thị Ngọc Kim (5), Nguyễn Thị Thanh Hải (5), Nguyễn Thu Ngọc (6), Thái Quang Tùng (5), Kim Muhiolland (1,2,7), Cao Minh Thang (6), Le Nguyen Thanh Nhan (5), Tran Anh Tuan (5), Clinton Pecenka (3)
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7. London School of Hygiene and Tropical Medicine, London, United Kingdom

Background: RSV is the leading cause of acute lower respiratory tract infections (LRTIs) in children under 2 years of age. No information is available on the costs of RSV in Vietnam.

Methods: A prospective cohort study evaluated household and societal costs associated with LRTIs stratified by RSV status and severity among children <2 years of age at a major pediatric referral hospital in southern Vietnam, during Sep 2019 – Dec 2021. Direct medical, non-medical, and indirect costs were collected from billing records and from questionnaires. All costs are reported in 2022 US dollars.

Results: Among 536 children enrolled in the study, 210 (39.2%) children from the outpatient department, 318 children (59.3%) from the respiratory department, and 8 children (1.5%) from the intensive care unit (ICU). There were 19.6% (105/536) RSV positive cases: 3.9% from the outpatient department, 15.7% from the respiratory department, and none from the ICU. The median total cost associated with LRTI per patient was US$52 (IQR 32-85) for outpatients and US$184 (IQR 109-287) for inpatients. For RSV-associated LRTIs, the median total cost per infection episode per patient was US$52 (IQR 32-85) for outpatients and US$165 (IQR 95-249) for inpatients. The total out-of-pocket cost of one non-ICU admission of RSV-associated LRTI ranged from 55 to 105 percent of the monthly minimum wage per person in Ho Chi Minh City.

Conclusion: These are the first data reporting the substantial economic burden of RSV-associated illness in Vietnam and highlighting the urgency of RSV disease prevention.

Keywords: Respiratory syncytial virus, lower respiratory tract infections, direct cost, indirect cost

Conflict of Interest: None declared

45. ROLE OF RSV INFECTION AND FACTORS ASSOCIATED WITH APNEA DURING ACUTE RESPIRATORY TRACT INFECTIONS

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1. Fundación INFANT, Buenos Aires, Argentina.
2. Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET).

BACKGROUND: Apnea is one of the most severe complications of acute respiratory tract infections (ARI) in infants. Its mechanisms and risk factors are poorly understood and the role of immune mediators in apnea inception remains unclear.

METHODS: Cross-sectional, multicenter study conducted in Buenos Aires, that included infants hospitalized due to ARI. Predictors in patients with apnea were compared to those with ARI and no apnea. Nasal aspirates were obtained from all hospitalized children and tested for viruses by RT-PCR and also for biomarkers previously hypothesized to influence the development of apnea (IL1ß, TNFα, IFNy, IL4).

RESULTS: We enrolled 5008 infants younger than 2 years. 77 infants presented apnea on admission or during hospitalization (estimated population incidence of 1.47 per 1,000 infants). RSV was detected in 32 infants with apnea. Increased odds for developing apnea during ARI were associated with prematurity, age, birth weight, malnutrition, chronic underlying disease, and severe crowding. Severe crowding (OR 1.02-4.97), age ≥1.5 months (OR 3.91-15.49), prematurity (OR 2.34-10.16), and weight $ score < -2 (OR 3.52-14.93) were independently associated with an increasing odds ratio for apnea in multivariable hierarchical analyses. The presence of RSV did not significantly alter the odds of disease. Viral loads of RSV and levels of biomarkers did not differ between groups.

CONCLUSIONS: Apnea during ARI was associated with prematurity, age and weight during illness, and it is not confined to infants with RSV infection. We found no association between apnea and biomarkers evaluated. Further investigation is needed to elucidate immune determinants of apnea.

Keywords: Acute respiratory tract infections, Apnea, Respiratory Syncytial Virus, Infants, Biomarkers, Epidemiology

Conflict of Interest: Dr. Polack reports grants and personal fees from JANSSEN, grants and personal fees from NOVAVAX, INC, personal fees from BAVARIAN NORDIC A/S, personal fees from PFIZER, personal fees from SANOFI, personal fees from REGENERON, personal fees from MERCK, outside the submitted work.
46. MOLECULAR CHARACTERIZATION OF RESPIRATORY SYNCYTIAL VIRUS GLYCOPROTEIN G GENE IN ISMAILIA PROVINCE, EGYPT 2020 AND 2021

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Limited data are available to date regarding respiratory syncytial virus (RSV) prevalence and genotypes circulating in Egypt, particularly Ismailia Province. Our study aimed to investigate the genetic variability of the glycoprotein G gene and the predominant RSV genotypes among children in University Hospital, General hospital, and Suez Canal Authority Hospital of Ismailia Province, Egypt in 2020-2021. A total of 564 nasopharyngeal aspirates were collected from children that showed respiratory manifestations suspected to be RSV. The samples were screened by real-time RT-PCR to detect and quantify the virus. Conventional RT-PCR was used to analyze the positive samples to amplify the hRSVA and hRSVB G region. The PCR amplicons were purified, sequenced, and phylogenetic trees were constructed. Of the 564 samples, 325 (57.62%) and 239 (42.38%) were male and female, respectively. Additionally, 166 (29.43%) were positive by real-time RT-PCR, but only 142 (25.18%) produced amplicons by conventional RT-PCR. Group A RSV predominates over group B RSV, with 61 strongly positive bands (57 hRSVA and 4 hRSVB) and 81 weakly positive (59 hRSVA and 19 hRSVB). On a phylogenetic tree, the majority of the characterized hRSVA strains (3/4; 75%) were grouped with the ON1 genotype, which was first emerged in Canada, 2010 while one strain (1/4; 25%) was clustered within strains related to the N1 genotype. In the sequenced strains, a nucleotide insertion that affects amino acid alignment has been demonstrated. Further studies may be necessary to understand the regional and worldwide molecular epidemiology and evolution of RSV and their inducers for greater host adaptation.

Keywords: Egypt, Molecular characterizations, RSV genotypes, hRSVA, and hRSVB

Conflict of Interest: None declared

47. DEVELOPMENT OF A NEW TILED AMPICLON APPROACH FOR RSV WHOLE GENOME SEQUENCING

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3. Child Life and Health, University of Edinburgh, UK

Background: Large scale immunisations against RSV are likely to be introduced in the near future. How these will disrupt viral transmission, and how viral genome variability will affect immunisation effectiveness, remains unknown. Current RSV sequencing approaches rely on a small number of relatively large amplicons which are not easily applicable to sub-optimal samples. We therefore designed a novel short amplicon approach for sequencing complete RSV genomes.

Methods: RSV primer scheme design was based on 6 recent RSV A and RSV B consensus sequences from varying locations and years (GISAID platform). Primal scheme (Quick et al., 2017) was used for multiplex primer design of a two tiling primer amplicron scheme. To allow the use of existing SARS-CoV-2 sequencing infrastructure, ~400bp amplicons were chosen resulting in 50 amplicons per subtype. For validation we selected NHS Lothian (Scotland) RSV samples from 2019 to 2022 and followed the ARTIC-iLocost-v3 nanopore library preparation method, with modifications. Data analysis was performed using an in-house version of the “fieldbioinformatics” pipeline.

Results: Both primer schemes successfully amplified clinical RSV samples with genome coverage up to 99%. We tested these in a subsection of our sample pool from 2022 with low Ct values and all results were within expected coverage for the majority of samples.

Conclusion: We have developed an effective, easy-to-use tiled amplicon approach, suitable for a range of samples which can be used with existing SARS-CoV-2 sequencing methodologies. It is likely to be of use to laboratories sequencing RSV globally, particularly those in low- and middle-income countries.

Keywords: Public Health, Surveillance, Next Generation Sequencing, Amplicon based sequencing method

Conflict of Interest: None declared

48. ECONOMIC AND HEALTH-RELATED QUALITY OF LIFE BURDEN IN ADULTS WITH RSV: A SYSTEMATIC LITERATURE REVIEW AND GAP ANALYSIS

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Background: Respiratory syncytial virus (RSV) is a major cause of severe respiratory disease in older adults aged ≥ 65 years and adults with underlying conditions such as chronic heart or lung disease and those with immunocompromising conditions.

Methods: A systematic literature review (SLR) of publications in the last 20 years was conducted on 18 May 2022 to understand the economic and health-related quality of life (HRQOL) burden of RSV infection in all adults, older adults, and high-risk adults globally. The databases searched were PubMed, Embase, Cochrane, PsycINFO, and EconLit, with no language limits. Population size for extraction of healthcare resource use (HCRU) outcomes was limited to ≥ 100 patients; there were no size limits for other outcomes.

Results: Sixty-five studies were included for RSV costs (n = 21), HCRU (n = 35), and HRQOL (n = 9). The SLR revealed major evidence gaps (Table), including limited data beyond the hospital setting; inconsistent age subgroups for cost; few HCRU outcomes stratified by age; lack of cost, HCRU, and HRQOL data by comorbidity; variation in types of cost outcomes reported; lack of information on indirect costs; lack of geographic diversity, with most cost and HCRU studies conducted in the United States; and lack of country-specific HRQOL data.

Conclusions: The evidence limitations and gaps identified the need to better characterize the economic and humanistic burden of RSV in adults. Addressing these gaps is important to allow for effective implementation and evaluation of preventative strategies, including anticipated RSV vaccines for older adults.
Keywords: economic burden; health-related quality of life burden; adults; older adults; older age; aged ≥ 65 years; underlying conditions; chronic heart disease; chronic lung disease; immunocompromising; comorbidities; costs; healthcare resource use; global; United States; multi-country; systematic literature review; evidence gaps; evidence limitations

Conflict of Interest: AC, MG, JC, and SW are full time employees of RTI Health Solutions. Their compensation is connected to the studies on which they work. PG and CP are employees of ModernaTX, Inc., and may hold shares and/or stock options in the company.

49. CHANGES IN RESPIRATORY SYNCYTIAL VIRUS SEASONALITY DURING THE COVID-19 PANDEMIC, UNITED STATES, 2017–2022

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National Center for Immunization and Respiratory Diseases, CDC

Background. The COVID-19 pandemic affected the epidemiology of many respiratory diseases. We described respiratory syncytial virus (RSV) seasonality in the United States during pre-pandemic and pandemic periods from July 2017 to October 2022.

Methods. We analyzed weekly RSV PCR detections and percent positivity reported to CDC’s National Respiratory and Enteric Virus Surveillance System. Laboratories reporting ≥36 weeks annually with an average of ≥10 weekly tests performed were included. RSV seasons were defined both nationally and regionally by consecutive weeks with RSV positivity ≥3% (seasonal epidemic threshold).

Results. Pre-pandemic RSV seasons (2017–2018, 2018–2019, 2019–2020) were typical whereas pandemic RSV seasons (2021–2022 and the ongoing 2022 season) were atypical. Nationally, the median RSV onset across three pre-pandemic seasons (2017–2020) occurred at week 41 (October), peaked at week 51 (December), and lasted 27 weeks before the offset at week 16 (April). RSV circulation during the 2020–21 surveillance season remained below the seasonal epidemic threshold. The 2021–22 season began 20 weeks earlier in week 21 (May), peaked at week 30 (July), and lasted 33 weeks until week 1 (January 2022). During 2022, RSV positivity surpassed the 3% seasonal epidemic threshold in week 24 (June) and had not peaked by October 22, 2022. During both pre-pandemic and pandemic periods, the RSV season began earliest in Florida and later in Northern and Western regions. Conclusions. RSV seasonality changed substantially during the COVID-19 pandemic. As RSV circulation might continue to exhibit atypical seasonality, timely RSV monitoring and reporting can inform prevention activities.

Keywords: RSV, respiratory syncytial virus, seasonality, COVID-19, United States

Conflict of Interest: None declared

50. INCIDENCE OF RESPIRATORY SYNCYTIAL VIRUS (RSV)-ASSOCIATED HOSPITALIZATION AMONG AMERICAN INDIAN AND ALASKA NATIVE CHILDREN ≤5 YEARS OF AGE DURING THREE CONSECUTIVE RSV SEASONS, 2019–2022

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4. Yukon-Kuskokwim Health Corporation, Yukon Kuskokwim Delta, USA
5. Division of Viral Diseases, Centers for Disease Control and Prevention, Atlanta, USA
6. Vanderbilt University Medical Center, Nashville, USA

Background: Historically and presently, American Indian/Alaska Native (AI/AN) persons endure health and socioeconomic inequities that result in disproportionate burden of disease. AI/AN children experience high rates of acute respiratory infection (ARI) hospitalization, up to half of which are due to respiratory syncytial virus (RSV).

Methods: We conducted active surveillance for ARI in hospitalized AI/AN children age ≤5 years in the US southwest (Navajo Nation and White Mountain Apache Tribal lands) and Alaska (Yukon Kuskokwim [YK] Delta and Anchorage) over three RSV seasons (November–March) of 2019–2020, 2020–21, and 2021–22. Cases were defined using a modified International Classification of Diseases, 10th Edition [ICD-10] code list including those with the International Classification of Diseases, 11th Edition [ICD-11] code list. Influenza and RSV cases were differentiated using data on age, seasonality, and geographic location.

Results: We enrolled 501 children: 324 in 2019–20; 21 in 2020–21; and 156 in 2021–22. RSV was the pathogen most commonly detected (53%) in 2019–20. RSV hospitalization seasonal incidence per 1,000 children was highest in the first year of life and ranged from 19.2 (Anchorage) to 112.2 (YK Delta; Table). RSV incidence declined during the SARS-CoV-2 pandemic. No RSV was detected among participants

Conflict of Interest: None declared

Table. Seasonal RSV-associated hospitalization incidence per 1,000 children (95% confidence interval)

Prevalence of PCR tests positive for respiratory syncytial virus (RSV) nationally, by U.S. Department of Health and Human Services (HHS) regions, and in the state of Florida, United States, July 2017–October 2022 Graphs show 3-week centered moving averages of RSV laboratory positivity nationally, by HHS Region (headquarters city), and in Florida during July 2017–October 2022. The black dotted line represents 3% laboratory positivity (seasonal epidemic threshold). In the National Respiratory and Enteric Virus Surveillance System, surveillance years begin in week 27 and end the following year in week 26. States in HHS Regions can be found at https://www.hhs.gov/about/regions/index.html.

Legend: The seasonal epidemic threshold is represented by the black dotted line. The red area represents seasonality above the seasonal epidemic threshold. The yellow area represents seasonality below the seasonal epidemic threshold.
in the 2020–21 season and incidence was lower in 2021–22 compared to 2019–20. The declines in incidence may also reflect reduced care seeking and reduced testing for RSV because of the pandemic.

**Funding:** United States Centers for Disease Control and Prevention (U01 IP001116-02-00).

**Keywords:** RSV; Indigenous; American Indian/Alaska Native; health disparity

**Conflict of Interest:** NH reports research funding to her institution from Sanofi and Quidell; she also reports receipt of an educational grant from Genetech, Inc. LLH reports research funding to her institution from Pfizer, Inc. and Merck & Co. CGS reports research funding to her institution from the Department of Defense and NIH. JEA is an employee of Pfizer Vaccines and may receive stock or stock options.

## 51. USING MULTIPLE METHODS TO ESTIMATE RESPIRATORY SYNCYTIAL VIRUS (RSV)-ASSOCIATED HOSPITALIZATION RATES IN CHILDREN AGED <5 YEARS — HAMILTON COUNTY, OHIO, 2009–2017

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**Background:** In the United States, RSV commonly causes hospitalization in young children and is the leading cause of hospitalizations in infants. Currently, there are several vaccines and monoclonal antibody products in development. As these products become available, burden estimates are critical to guide implementation recommendations and quantify impact.

**Methods:** We estimated RSV-associated hospitalization rates in children aged <5 years in Hamilton County Ohio from 2009-2017 using multiple methods including: passive surveillance (clinical testing), adjusted active surveillance (systematic testing of children with acute respiratory illness), capture-recapture analysis, and modeling of ICD discharge diagnosis codes.

**Results:** Passive surveillance rate estimates were the lowest every year, ranging from 0.8 (95% CI: 0.6, 1.1) to 2.4 (95% CI: 2.0, 2.8) per 1,000 children. Adjusted RSV-associated hospitalization rates from active surveillance ranged from 1.5 (95% CI: 0.8, 2.8) to 7.1 (95% CI: 4.7, 10.0); adjusted active rates were lower during the first three surveillance years when surveillance was conducted 2-3 days per week compared with rate estimates using capture-recapture (ranging from 3.6 (95% CI: 2.2, 6.9) to 5.8 (95% CI: 4.7, 7.6)) and ICD code modeling estimates (ranging from 2.7 (95% CI: 2.4, 3.1) to 5.8 (95% CI: 5.4, 6.4)). Rate estimates were greater in years where active surveillance increased to 4 or more days/week.

**Conclusion:** When active surveillance is conducted 4 or more days/week, estimates of RSV-associated hospitalizations increased into ranges consistent with values obtained from capture-recapture and ICD code modeling.

**Keywords:** RSV, Capture-Recapture, Hospitalization Rates

**Conflict of Interest:** None declared

## 52. LABORATORY-CONFIRMED RSV HOSPITALIZATION RATES AMONG ADULTS IN THE UNITED STATES, BY RACE AND ETHNICITY ACROSS FOUR SEASONS—RSVNET, 2018-2019 THROUGH 2021-2022 SEASONS


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13. University of Rochester School of Medicine and Dentistry, Rochester, New York, United States
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16. Vanderbilt University Medical Center, Nashville, Tennessee, United States
17. Salt Lake County Health Department, Salt Lake City, Utah, United States

**Background:** Respiratory syncytial virus (RSV) is a major cause of hospitalizations among older adults. However, racial and ethnic disparities in RSV-associated hospitalization rates have not been systematically investigated among adults in the United States.

**Methods:** RSV-NET is a population-based active surveillance system for RSV-associated hospitalizations in 12 states, covering ~9% of the U.S. population.

**Table 1. Comparison of RSV Hospitalization Rates in Children Aged <5 Years Using Multiple Methods, Hamilton County, OH, 2009–2017**

<table>
<thead>
<tr>
<th>Surveillance Year</th>
<th>Rate (95% CI)</th>
<th>Rate (95% CI)</th>
<th>Rate (95% CI)</th>
<th>Rate (95% CI)</th>
<th>ICD-10 Coding*</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009–10</td>
<td>1.6 (1.3, 2.3)</td>
<td>2.3 (1.2, 3.2)</td>
<td>1.6 (2.6, 5.5)</td>
<td>4.5 (4.1, 4.9)</td>
<td></td>
</tr>
<tr>
<td>2010–11</td>
<td>2.2 (1.8, 2.7)</td>
<td>3.8 (2.6, 5.2)</td>
<td>4.4 (3.6, 5.7)</td>
<td>4.9 (4.5, 5.4)</td>
<td></td>
</tr>
<tr>
<td>2011–12</td>
<td>1.4 (1.1, 1.7)</td>
<td>1.5 (0.9, 2.4)</td>
<td>4.0 (3.0, 5.4)</td>
<td>4.2 (3.8, 4.6)</td>
<td></td>
</tr>
<tr>
<td>2012–13</td>
<td>2.4 (2.0, 3.0)</td>
<td>3.6 (2.9, 5.2)</td>
<td>4.2 (3.7, 5.2)</td>
<td>5.8 (4.9, 6.8)</td>
<td></td>
</tr>
<tr>
<td>2013–14</td>
<td>1.6 (1.2, 2.3)</td>
<td>1.7 (1.5, 2.4)</td>
<td>5.5 (4.0, 8.3)</td>
<td>4.3 (3.9, 4.8)</td>
<td></td>
</tr>
<tr>
<td>2014–15</td>
<td>2.1 (1.8, 2.7)</td>
<td>3.8 (3.0, 5.1)</td>
<td>5.2 (4.6, 6.4)</td>
<td>4.6 (4.0, 5.2)</td>
<td></td>
</tr>
<tr>
<td>2015–16</td>
<td>1.6 (1.3, 2.0)</td>
<td>1.8 (1.4, 2.5)</td>
<td>3.6 (2.8, 4.5)</td>
<td>4.7 (3.7, 5.7)</td>
<td></td>
</tr>
<tr>
<td>2016–17</td>
<td>0.8 (0.6, 1.1)</td>
<td>0.7 (0.6, 0.9)</td>
<td>1.8 (1.4, 2.3)</td>
<td>1.8 (1.5, 2.2)</td>
<td></td>
</tr>
</tbody>
</table>

*Adjusted active surveillance includes children with acute respiratory illness or those who test positive for RSV or respiratory testing with adjustment for proportion of eligible enrollees and the number of days of active surveillance per year.

**Conflict of Interest:** None declared
RSV-NET cases are residents of a defined catchment area with a positive RSV test ordered by a healthcare professional 14 days prior to or during hospitalization. From October 2018 – September 2022, age-adjusted cumulative hospitalization rates per 100,000 population among adults ≥18 years were calculated by race and ethnicity using U.S. census catchment denominators.

Results: Among 8,911 hospitalizations, 8,607 (96.9%) had race/ethnicity information available. Among these, 5,399 (62.7%) were non-Hispanic White adults, followed by 1,844 non-Hispanic Black (21.4%), 844 Hispanic (9.8%), 451 non-Hispanic Asian/Pacific Islander (API) (5.2%), and 46 non-Hispanic American Indian or Alaska Native (AI/AN) (0.5%) adults. Rates were highest in Black, Hispanic, and AI/AN adults, although the group with the highest rate varied by season; rates were consistently lowest in White and API adults (Figure). In 2021-22, rates were 15.9 for Hispanic adults, followed by 15.0, 12.5, 10.3 and 7.2 for Black, AI/AN, White and API adults, respectively.

Conclusions: Across four seasons, RSV hospitalization rates differed by race and ethnicity, with the highest rates in Hispanic, Black and AI/AN adult populations. If vaccines or other preventive measures become available for adults, equitable access is needed to minimize racial and ethnic disparities in RSV hospitalizations.

Keywords: Race and ethnicity, Adult RSV, Hospitalizations, Epidemiology, Health equity

53. CO-DETECTION OF RESPIRATORY SYNCYTIAL VIRUS WITH OTHER RESPIRATORY VIRUSES BEFORE AND DURING THE COVID-19 PANDEMIC

Haya Hayek, Justin Z. Amarín, Asim Khanfar, Tess Stopczynski, Jonathan Schmitz, Natasha B. Halasa

Background: Co-detection of respiratory syncytial virus (RSV) with certain respiratory viruses is associated with increased illness severity. The seasonality of RSV and other respiratory viruses was disrupted during the COVID-19 pandemic. We aimed to explore RSV co-detection across age groups before and during the pandemic in Nashville, Tennessee.

Methods: We conducted a retrospective cohort study of patients who were tested using the BioFire® FilmArray Respiratory Pathogen Panel (RPP) 2.0 at Vanderbilt University Medical Center from April 2018 to August 2022. The RPP is a provider-ordered multiplex PCR assay that detects 21 common respiratory pathogens. We then retrieved the results of SARS-CoV-2 molecular testing for patients who were RSV-positive, stratified the cohort by age group, and analyzed the co-detection status of RSV.

Results: A total of 56,106 samples were tested, and 3,214 (5.7%) were RSV-positive. RSV was co-detected with at least one other virus in 39.4%, 30.2%, 15.2%, and 12.5% of those 0–4, 5–17, 18–64, and ≥65 years old, respectively. Co-detection of RSV with rhinovirus (RV) was the most common across all age groups before and during the pandemic. Before the pandemic, co-detection of RSV with common cold coronaviruses in adults ≥18 years old was as common as RSV/RV co-detection, but they were replaced with SARS-CoV-2 during the pandemic (Figure 1). The distribution of RSV single detection and co-detection was comparable before and during the pandemic (Figure 1 and Figure 2).

Conclusion: The frequency of RSV co-detection with other respiratory viruses varied by age group but did not appreciably vary before and during the pandemic.

Conflict of Interest: CDC funds the CT Emerging Infections Program which pays my, James Meek’s, salary. E.J.A has consulted for Pfizer, Sanofi Pasteur, GSK, Janssen, Moderna, and Medscape, and his institution receives funds to conduct clinical research unrelated to this manuscript from Medimmune, Regeneron, PaxVax, Pfizer, GSK, Merck, Sanofi-Pasteur, Janssen, and Micron. He serves on a safety monitoring board for Kentucky BioProcessing, Inc. and Sanofi Pasteur. He serves on a data adjudication board for WCG and ACI Clinical. His institution has also received funding from NIH to conduct clinical trials of COVID-19 vaccines. H. Keipp Talbot’s institution has received research funding from CDC.
54. MODELLING THE IMPACT OF COVID-19 AND THE ASSOCIATED NON-PHARMACEUTICAL INTERVENTIONS ON RSV SEASONALITY IN EUROPE

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3. Vaccine & Infectious Disease Institute, University of Antwerp, Belgium
4. Centre for Infectious Disease Control, National Institute for Public Health and the Environment, Bilthoven, The Netherlands
5. GSK, Rockville, Maryland, US

Background: The seasonality of RSV has been affected by the COVID-19 pandemic and the associated non-pharmaceutical interventions (NPIs) (e.g. school closures). Other factors may also have played a role (e.g. viral interference). We are currently building a model to evaluate the impact of these different factors to better understand the seasonality of RSV in Europe in the COVID-19 era.

Methods: We will construct a multi-level longitudinal regression model to investigate the potential contribution of different public health interventions and other relevant factors on the changes in RSV seasonality. Four analyses are anticipated: a model for the overall pattern of RSV seasonality and separate models for the start, duration and peak of the epidemic. Data sources considered will include: 1) RSV surveillance data from EU countries in the GERI project from 2005-2022 (Czech Republic, Netherlands, Portugal, Romania and Spain), 2) the ECDC-JRC Response Measures Database and the Oxford COVID-19 Government Response Tracker, which archive NPIs introduced in Europe, 3) SARS-CoV-2 data collected by WHO, and 4) climate data (e.g. temperature and humidity) available from NOAA. Importantly, the GERI data are age-specific.

Results: The modelling analyses are planned to be completed by mid-2023. However, by February 2023, we will be able to provide an update on the availability of all data and preliminary analyses.

Conclusions: Understanding changes in the seasonality of RSV in Europe since 2020 (COVID-19 era) is essential and will allow public health authorities to better align prevention and control measures (e.g. passive immunization programs) in the coming years.

Keywords: Respiratory Syncytial Virus; Europe; Surveillance; Epidemiology; Seasonality; COVID-19

Conflict of Interest: JP declares that Nivel has received unrestricted research grants from WHO, IMI, Sanofi and the Foundation for Influenza Epidemiology outside the submitted work. GDS and RAC are employees of GSK.

This collaborative study is funded by ‘Innovative Medicines Initiative 2 Joint Undertaking’ (PROMISE project).

55. ASSESSING PARENTS’ AWARENESS AND ATTITUDES TOWARDS PREVENTION OF RESPIRATORY SYNCYTIAL VIRUS IN INFANTS AND YOUNG CHILDREN IN AUSTRALIA

Charlie Holland (1)*, Amber Bates (2), Catherine Hughes (3), Megan Baker (1), Peter C Richmond (4, 5, 6, 7), Samantha Carlson (1, 8), Hannah C Moore (1, 9)

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4. Discipline of Paediatrics, School of Medicine, University of Western Australia
5. Vaccine Trials Group, Wesfarmers Centre of Vaccines & Infectious Diseases, Telethon Kids Institute
6. Perth Children’s Hospital, Child and Adolescent Health Service
7. Department of Immunology, Perth Children’s Hospital, Child and Adolescent Health Service
8. School of Social Sciences, The University of Western Australia, Perth, Western Australia, Australia
9. School of Population Health, Curtin University, Perth, Western Australia, Australia

Background: Prior to the implementation of respiratory syncytial virus (RSV) immunisation programs, there needs to be sufficient community disease awareness and acceptance of new immunisation strategies. We assessed this in the Australian community setting, focusing on future maternal vaccines and infant monoclonal antibodies.

Methods: We administered a nationwide cross-sectional survey online in 2022, targeting “future” (pregnant, or planning) and/or “current” parents of children aged 05 years aged 18-80 years. Questions, provided in English, centred on demographic characteristics, knowledge of RSV and associated conditions, and attitudes towards future passive RSV immunisation strategies.

Results: From 1,992 eligible participants, two non-mutually exclusive subgroups were formed; “future” parents (N=464) and “current” parents (N=1931; 403 of which were also pregnant/planning). Participants were from across Australia, predominately (86.6%) aged 25-39 years and 68.5% with university education. The majority (89.6% current; 78.7% future) had heard of RSV. Of those participants only 64.2% (current) and 50.0% (future) were aware that pneumonia is associated with RSV; 71.8% (current) and 52.1% (future) were aware that bronchiolitis is associated. In adjusted logistic regression analyses, current parents had a 12-fold increased likelihood of RSV awareness compared to future parents. There was a high level of acceptance for RSV maternal vaccines (79.3% future) and infant immunisation (81.7% of all participants).

Conclusions: While RSV awareness and immunisation acceptance was reasonably high, there was limited knowledge of associated conditions, especially in future parents with no prior children. Our findings provide contemporary insights into RSV community awareness to be used for future education and awareness campaigns.

Keywords: RSV, Awareness, Parents, Infants, Children, Acceptance, Immunisation

Conflict of Interest: None declared

56. ARE MOTHERS IN RURAL AREAS A CRITICAL INTERVENTION TOOL IN THE PREVENTION OF RSV-LIKE INFECTIONS? A CASE FOR EMPOWERMENT OF MOTHERS IN RESOURCE-POOR RURAL COMMUNITIES.

Chinedu Anthony Iwu (1)[2]*, Ebere Ibezim (1)[2], Ifeanyi Charles Nwagbara (1)[2], Ositadinma Mbereke Pius (3), Victor Chibiko (2), Mitchelle Adaobi Iwu (4)

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2. Imo State University Teaching Hospital Orlu, Nigeria
3. Rivers State University, Port Harcourt, Nigeria
4. University of Texas at Dallas

Introduction: Respiratory syncytial virus (RSV) has been documented to play a significant aetiological role in the development of fatal acute lower respiratory tract infections (ALRIs) in infants. In Nigeria, RSV antigen detection studies have reported prevalence rates as high as 54%, especially during the rainy season months (June-August).
57. SURVEILLANCE OF COMMON RESPIRATORY VIRUSES IN SENEGAL DURING THE COVID-19 PANDEMIC: FOCUS ON RESPIRATORY SYNCYTIAL VIRUS (RSV)

Mamadou Malado Jallow (1*), Marie Pedepa Mendy (1), Mamadou Aliou Barry (2), Sara Sy (1), Ndienké Koba Ndiaye (1), Déborah Goudiaby (1) and Ndongo Diá (1).

1. Virology department, Institute Pasteur, Dakar, Senegal
2. Epidemiology Unit, Institute Pasteur, Dakar, Senegal

Different public health measures have been implemented to counter the transmission of SARS-CoV-2. These measures, might have contributed to containing the circulation of other respiratory viruses, including RSV. So here, we investigated the epidemiology and seasonality of RSV infection during the COVID-19 pandemic. From January 2020 to December 2021, nasopharyngeal swabs are collected from patients with ILI or SARI presenting to healthcare sentinel sites across the country. For viral respiratory pathogens detection, including RSV, a multiplex RT-PCR was used. In total, 4160 samples were received of which 89.6 % ILI cases and 10.4 % SARI cases, and the most observed symptoms were cough (92.4%) and fever (68.9%). Children ≤ 5 years accounted for 35.6 % of all participants. RSV was detected in 224 (5.4 %) cases of the 4160 samples tested with 12.5 % found in co-infection with at least one another respiratory virus. The most common co-infecting viruses were with influenza viruses (11.6%), HRV (11.2%), AdV (4 %) and SARS-CoV-2 (3.6 %). RSV infection were more identified in SARI (10.6 %) compared to ILI (4.8 %) patients. Globally, we observed a shift in the seasonality of RSV during the Covid-19 pandemic (systematic increase in RSV infections between September-November each year), which usually circulates during the rainy season (June-September). Overall, results obtained in this study suggest that circulation of SARS-CoV2 has significantly affected the seasonality of RSV in Senegal, highlighting that the detection of other common respiratory pathogen(s) should not be ignored during the COVID-19 pandemic.

Keywords: RSV, Epidemiology, Seasonality, ILI, SARI, COVID-19, Senegal

Conflict of Interest: None declared

58. CIRCULATION OF RESPIRATORY VIRUSES, INCLUDING RSV, DURING THE COVID-19 PANDEMIC IN THE GAMBIA.

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2. Medical Research Council Unit The Gambia at London School of Hygiene & Tropical Medicine (MRCG@LSHTM), Department of Nutrition, Keneba, The Gambia
3. Medical Research Council Unit The Gambia at London School of Hygiene & Tropical Medicine (MRCG@LSHTM), Head of Clinical Services Department, Fajara, The Gambia
4. Medical Research Council Unit The Gambia at London School of Hygiene & Tropical Medicine (MRCG@LSHTM), Department of Data Management, Fajara, The Gambia

Introduction: In many countries, non-pharmaceutical interventions to limit SARS-CoV-2 transmission resulted in significant reductions in other respiratory viruses. However, similar data from Africa are limited. We explored the extent to which viruses such as influenza, RSV, and rhinovirus co-circulated with SARS-CoV-2 in The Gambia during the COVID-19 pandemic.

Methods: Between April 2020 and March 2022, respiratory viruses were detected using RT-PCR in nasopharyngeal swabs collected from 1397 participants with influenza-like illness.

Results: Overall virus positivity was 44.2%, with prevalence higher in children <5 years (80%) compared to children aged 5-17 years (53.1%), adults aged 18-50 (39.5%) and >50 years (39.9%), p<0.0001. RSV A was detected in 25 (1.8%) out of which 12 (48.0%) were under 5 years old. There were 10 RSV coinfection with SARS-CoV-2 (3.0%) and with rhinovirus (70%). Of the 41 hospitalized cases, 3 (7.3%) were associated with RSV A.

Conclusions: Common respiratory viruses, including RSV, continued to circulate during the COVID-19 pandemic in The Gambia. Though RSV was detected in low numbers, it is important to note that it was still detected during the Pandemic and a high number of that in under 5 years old.

Keywords: Respiratory virus, RSV, SARS-CoV-2, COVID-19 Pandemic

Conflict of Interest: None declared

59. AGE-SPECIFIC ESTIMATES OF RSV-ASSOCIATED HOSPITALIZATIONS IN 6 EUROPEAN COUNTRIES BASED ON ROUTINELY COLLECTED HEALTH CARE DATA: A TIME SERIES ANALYSIS

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8) Centre for Global Health, Usher Institute, University of Edinburgh
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10) Fondazione Penta ONUHS, Padova, Italy
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13) Department of Clinical Research, Nordsjellands University Hospital, Hilleroed, Denmark

Background: Burden estimates based on RSV-coding of hospital admissions are known to underestimate the burden of RSV, while coding practices at hospitals differentiates throughout Europe. With vaccines soon coming to market, robust, age-specific, burden estimates across Europe will be an important tool for intervention evaluation.

Methods: We conducted multi-season regression-analysis of weekly respiratory infection associated hospitalizations and weekly laboratory-confirmed cases of RSV and influenza, based on national health registers and laboratory databases across six European countries (OK, NL, ENG, SCO, NO, FIN). The burden of RSV-associated hospitalizations was estimated by age-group, clinical diagnosis, and presence of underlying medical conditions.

Results: Hospitalizations of children with respiratory infections were clearly associated with RSV. Proportions associated with RSV in countries ranged from 28% to 60% in children <3 months, with substantial proportions of admissions with respiratory infections associated with RSV in children <3 years and none in children 5-17 years. Associated proportions were highest among hospitalizations with ICD-10 codes of 'Bronchitis and bronchiolitis'. In all countries the annual incidence of RSV-associated hospitalizations was >40 per 1000 persons in age group 0-2 months. In children 1-2 years the incidence rate ranged from 1.3-10.5 hospitalizations per 1000.

Conclusion: Our findings highlight the substantial proportion of RSV-infections among hospital admissions across different ages and may help public health professionals and policy makers when planning prevention and control strategies. In addition to our findings, we are preparing a repeated analysis with data covering 2017-2022 and additional countries to estimate the new burden of RSV-associated hospitalizations in Europe.

Keywords: Respiratory syncytial virus, Viral hospitalizations, Burden of disease, RSV, Public Health, Time series analysis, Vaccination preparedness

Conflict of Interest: AM, AT, CK, HB, LS, LF, MVb, MW, TL, XW, have no conflicts to declare outside the submitted work. HC declared that funding for the submitted work was obtained from the KnIT platform (DBT-Government of India), Gates Venture; ST and MB are employees of Sanofi. TKF declared participating in research funded by Pfizer outside the submitted work. TH declared personal fees from Janssen outside the submitted work. YL reports grants from WHO and Wellcome Trust, outside the submitted work.

60. DISEASE BURDEN ESTIMATES OF ACUTE LOWER RESPIRATORY INFECTIONS DUE TO RESPIRATORY SYNCYTIAL VIRUS IN UNDER-FIVE CHILDREN IN INDIA: A SYSTEMATIC ANALYSIS

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2: Centre for Community Medicine, All India Institute of Medical Science, New Delhi
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Background: Assessment of respiratory syncytial virus’s (RSV) role in childhood acute lower respiratory infections (ALRIs) is available through limited cohort studies, with data gaps at national level. This systematic analysis aimed to estimate RSV-ALRI morbidity and mortality among under-five children in India for 2020.

Methods: RSV-ALRI, ALRI data obtained from review of papers (hospital-based & cohort studies) published between January 2000 and March 2021 from India; pooled estimates calculated for RSV positivity proportions in ALRI, ALRI incidence (episodes/1000 child-year), ALRI hospitalisation (hospitalisation episodes/1000 child-year), and ALRI in-hospital case fatality ratio using random-effects meta-analysis model. National RSV-ALRI burden estimates generated by applying RSV positivity meta-estimates to ALRI burden estimates for Indian population in 2020; overall death estimates generated using sample registration system data for proportional pneumonia deaths (2015-2017). Uncertainty intervals calculated using Monte-Carlo simulations.

Results: 27 studies included [ALRI data (13 studies), RSV positivity data (12 studies), and 2 studies reporting both; unpublished data (2 studies)]. Nationally, in children <5 years, 12.6 (uncertainty range [UR]:9.9-15.2) million episodes of RSV-ALRI hospitalisations, 33000 (UR:28300-38000) RSV-ALRI overall deaths of which 23600 (UR:18100-28800) were in-hospital deaths (Table 1) estimated for year 2020.

Conclusion: RSV associated respiratory infections impose a major burden of ill-health among under-five children in India, especially in infancy. With likelihood of effective maternal vaccine, monoclonal antibody, or pediatric vaccine availability in near future, disease burden estimates will be useful for policy decisions.

Acknowledgement: Funders – KnIT platform (DBT-Government of India), Gates Venture; Technical Advisory Group

Keywords: Respiratory syncytial virus; RSV; acute lower respiratory infection; RSV- ALRI; ALRI; morbidity and mortality; national disease burden; under-five children

Conflict of Interest: None declared

61. IMPACT OF THE COVID-19 PANDEMIC ON ACUTE LOWER RESPIRATORY INFECTIONS (ALRI) IN CHILDREN HOSPITALIZED IN A PEDIATRIC HOSPITAL IN BUENOS AIRES


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2. Virology, Children’s Hospital “Ricardo Gutierrez”
3. Commission of Investigations of the Province of Buenos Aires (CIC)

Introduction: Respiratory viruses are the main cause of ALRI in the pediatric population. In 2020, the pandemic (COVID-19) caused a high global impact with a dramatic reduction in hospitalizations for ALRI.

Objective: to describe the impact of the COVID-19 pandemic on hospitalizations for SARI in HNHRG and the pattern of viral circulation during and after the COVID-19 pandemic.

Methods: Prospective, cross-sectional, descriptive study of patients hospitalized for SARI, comparing the years 2019 and 2022. Virological diagnosis was made by IIF or RT-PCR of nasopharyngeal aspirates.
Results: For the intra-pandemic period, in 2020, the situation atypical, with an important reduction (-82%) in the number of ALRI cases compared to 2019. There were no cases of ALRI due to RSV or influenza. In 2021, 262 ALRI cases were hospitalized, with viral test positivity of 45% (n=117). RSV was predominant 74.3% (87/117), followed by COVID-19 11.9% (n=14), rhinovirus 7.7% (n=9) and adenoaviruses 1.7% (n=2) with no detection of Influenza virus.

During the first six months of 2022, a total of 252 cases of children hospitalized with ALRI with a positivity rate of 66.4%. In EW 6, early circulation of influenza began, and Metapneumovirus (MNV) was the predominant agent (30.24%) with a marked peak of cases in EW 19 and 20; RSV was the second agent (12.9%), followed by rhinovirus (11.29%), influenza (6.5%) and adenoaviruses (2.8%).

Conclusion: Active epidemiological surveillance is an important tool to assess changes in respiratory viruses epidemiological pattern, seasonality and the number of hospitalizations.

Keywords: RSV, respiratory infections, epidemiological surveillance

Conflict of Interest: None declared

62. GENOMIC EPIDEMIOLOGY OF RSV IN THE INFANT POPULATION OF GHANA

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2 Nuguchi Memorial Institute for Medical Research, University of Ghana
3 Dept of Medical Laboratory sciences, School of biomedical And Allied Health Sciences, University of Ghana
4 Fogarty International Center, National Institutes of Health, USA

Respiratory syncytial virus (RSV) is a major cause of lower respiratory tract infections in children below 5 years old. The C-terminal 3rd hypervariable region of the G gene in RSV subgroups A (RSV-A) and B (RSV-B) plays a major role in the disease pathogenicity and immune evasion.

In this project, we aimed to uncover the evolutionary history and transmission dynamics of the virus in the infant population of Accra, Ghana. To that end, we performed phylogenetic reconstructions and phylogeographic analysis of 12 samples (5 RSV-A and 7 RSV-B) collected from RSV-infected children in Accra between September 2015 to November 2016.

Our results indicated that the 2015-2016 season was dominated by RSV-B and that RSV-A was the dominant group circulating in the early 2016 season. Phylogenetic analysis revealed that most of the RSV-A belonged to the ON1 genotype, and RSV-B sequences were part of the Buenos Aires IX genotype. It appears that RSV-A and B in 2015 and 2016 strains in Ghana are distinct from the earlier ones that circulated during 2013 and 2014.

In addition, the Ghanaian strains were linked to RSV that circulated in Europe and parts of East Africa. These results demonstrate the connectivity on the RSV transmission network including Ghana and countries from other continents. This information will help inform more targeted implementation of control strategies, and shed light on the genetic diversity of the virus in the understudied country of Ghana, which will be valuable in the development of vaccines and therapeutics.

Keywords: Genomic, Phylogenetic, phylogeographic,
Conflict of Interest: None declared

63. PEDIATRIC AND ADULT RSV AND INFLUENZA HOSPITALIZATIONS IN BANDUNG, INDONESIA 2018-2019

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2. Center for Collaborative Research on Acute Respiratory Infection, Universitas Padjadjaran-Hasan Sadikin General Hospital, Bandung, Indonesia
3. University of Colorado School of Medicine & Children’s Hospital Colorado, Aurora, CO
4. Department of Public Health, Faculty of Medicine, Universitas Padjadjaran-Hasan Sadikin General Hospital, Bandung, Indonesia
5. Department of Microbiology and Parasitology Faculty of Medicine Universitas Padjadjaran, Bandung, West Java, Indonesia
6. Center for Global Health, Department of Epidemiology of Public Health, Aurora, CO

Background: Influenza and RSV are both significant sources of morbidity and mortality amongst under-fives, pregnant women, adults with COPD, the immunocompromised and older adults. Prevention of RSV will soon be a reality for some of these risk groups.

Methods: A 3-year study in 2 district and a tertiary care hospital in Bandung, West Java, (and 4 other states) was planned. All patients with acute lower respiratory tract infections (variously defined) in the inpatient wards and the ICU’s were the subjects of the study. A histo-

Results: For the intra-pandemic period, in 2020, the situation was atypical, with an important reduction (-82%) in the number of ALRI cases compared to 2019. There were no cases of ALRI due to RSV or influenza. In 2021, 262 ALRI cases were hospitalized, with viral test positivity of 45% (n=117). RSV was predominant 74.3% (87/117), followed by COVID-19 11.9% (n=14), rhinovirus 7.7% (n=9) and adenoaviruses 1.7% (n=2) with no detection of Influenza virus.

During the first six months of 2022, a total of 252 cases of children hospitalized with ALRI with a positivity rate of 66.4%. In EW 6, early circulation of influenza began, and Metapneumovirus (MNV) was the predominant agent (30.24%) with a marked peak of cases in EW 19 and 20; RSV was the second agent (12.9%), followed by rhinovirus (11.29%), influenza (6.5%) and adenoaviruses (2.8%).

Conclusion: Active epidemiological surveillance is an important tool to assess changes in respiratory viruses epidemiological pattern, seasonality and the number of hospitalizations.

Keywords: RSV, respiratory infections, epidemiological surveillance

Conflict of Interest: None declared

<table>
<thead>
<tr>
<th>Age at illness (days)</th>
<th>Tested for RSV</th>
<th>RSV A</th>
<th>RSV B</th>
<th>RSV Positivity</th>
<th>Tested for Flu</th>
<th>Flu A</th>
<th>Flu B</th>
<th>Flu C</th>
<th>Flu D</th>
<th>Flu E</th>
<th>Flu Positivity</th>
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<tr>
<td>0-20</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
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<td>31-60</td>
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<td>24</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>61-90</td>
<td>43</td>
<td>19</td>
<td>19</td>
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<td>47</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td>25</td>
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<td>40</td>
<td>3</td>
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<td>2</td>
<td></td>
<td></td>
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<td>18</td>
<td>18</td>
<td>42.9%</td>
<td>49</td>
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<td>1</td>
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<td>29</td>
<td>10</td>
<td>18</td>
<td>62.1%</td>
<td>31</td>
<td>3</td>
<td>1</td>
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<td>6</td>
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<td>19</td>
<td>35.8%</td>
<td>59</td>
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<td>4</td>
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<td>1</td>
<td>4.3%</td>
<td>24</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
<td>8.3%</td>
</tr>
<tr>
<td>45-69 years</td>
<td>45</td>
<td>7</td>
<td>7</td>
<td>15.6%</td>
<td>48</td>
<td>10</td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>6</td>
<td>4    2    20.0%</td>
</tr>
<tr>
<td>&gt;60 years</td>
<td>103</td>
<td>8</td>
<td>8</td>
<td>7.8%</td>
<td>107</td>
<td>16</td>
<td>10</td>
<td>3</td>
<td>6</td>
<td>6</td>
<td>4    2    15.0%</td>
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<tr>
<td>TOTAL</td>
<td>369</td>
<td>233</td>
<td>228</td>
<td>67.3%</td>
<td>747</td>
<td>81</td>
<td>56</td>
<td>17</td>
<td>21</td>
<td>35</td>
<td>14  8  2</td>
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RSV and Influenza Age Distribution

Conflict of Interest: All authors: Grant funding for this study was obtained from USAID. Eric AF Simões has received grants or contracts from AstraZeneca, Johnson and Johnson, Merck, Pfizer, and Roche; consulting fees from Adiago Therapeutics, Cidara Therapeutics, Merck, Nuance Pharmaceuticals, Pfizer and Sanofi; payment or honoraria from AstraZeneca and Pfizer; support for meeting attendance and/or travel from AstraZeneca; and has participated in Data Safety Monitoring Boards or advisory boards for Abbvie, Bill and Melinda Gates Foundation and GSK. All other authors declare no conflicts.
64. ESTIMATING RSV SEASONALITY FROM PANDEMIC DISRUPTIONS: A MODELLING STUDY

Fabienne Krauer (1)*, Tor Erlend Fjelde (2), Mihaly Koltai (1), David Hodgson (1), Marina Treskova-Schwarzbach (3), Christine Harvey (4), Mark Jit (1), Ole Wichmann (3), Thomas Harder (3), Stefan Flasche (1)

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3. Robert Koch Institut, Berlin, Germany
4. Health Protection NSW, NSW Ministry of Health, Australia

The seasonal pattern of RSV is determined by the duration of immunity, contact rates and pathogen viability. The magnitude of each of these parameters is not fully clear. The disruption of the regular seasonality of RSV during the COVID pandemic in 2020 due to control measures, and the delayed surge in RSV cases provides an opportunity to disentangle these factors and to understand the implication for vaccination strategies. We developed a mathematical model of RSV transmission, which simulates the sequential re-infection (SEIRRS4) and uses a flexible seasonal forcing function. Using MCMC we fit the model to laboratory confirmed RSV data from 2010-2022 from NSW while accounting for the reduced contact rates during the pandemic with Google mobility data. We estimated the baseline transmission rate, its amplitude and shape during RSV season as well as the duration of immunity. We then simulated the expected shifts in peak timing and amplitude under two vaccination strategies: continuous and seasonal vaccination. Our results show that RSV dynamics in NSW can be best explained by a high effective baseline transmission rate with a narrow seasonal peak with a maximum 13% increase compared to the baseline. We also estimate the duration of immunity to be 412 days (95% CI 391-434). The continuous vaccination strategy led to more extreme seasonal incidence with a delay in the peak timing and a higher amplitude whereas seasonal vaccination flattened the incidence curves.

Keywords: seasonality, covid, immunity, vaccination strategy

Conflict of Interest: This work was funded by the Innovation Fund of the Joint Federal Committee (Gemeinsamer Bundesausschuss). Additional funding: Fabienne Krauer received a grant from the Wellcome Trust (grant no. 221303/2/20/Z). Tor Erlend Fjelde received PhD funding from Huawei Technologies Research & Development (UK) Ltd. Mihaly Koltai received grants from the Epidemic Preparedness - Coronavirus research programme (grant no. 221303/2/20/Z) from Foreign, Commonwealth and Development Office / Wellcome Trust and the Bill & Melinda Gates Foundation INV-007610. David Hodgson received a National Institutes of Health grant (5R01AI141534-01A1). Mark Jit received RSV-related grants the Bill & Melinda Gates Foundation, the European Union's Horizon 2020 research and innovation programme SCI-PHE CORONAVIRUS-2020 - project EpIPose (No 101003688), the NIH HRPU in Modelling and Health Economics (grant code HPRU-2019-NIHRR200908) and the NIHR HPRU in Immunisation (grant code HPRU-2019-NIHRR200929). The author received support for attending meetings and involvement in consortia at the European Union. The authors have no other competing interests to declare.

65. BURDEN OF RSV INFECTION IN YOUNG CHILDREN IN EUROPEAN COUNTRIES (BRICE)

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2 Service de Pédiatrie, Centre Intercommunal de Créteil, Université Paris-Est, Créteil, France.
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4 Servicio de Pediatría y Enfermedades Infecciosas, Hospital Universitario La Paz, Madrid, Spain.
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6 Department of Health Sciences, Section of Pediatrics, Meyer Children’s Hospital and University of Florence, Florence, Italy.
7 Respiratory Unit, Department of Pediatric Medicine, Bambino Gesú Children Hospital, Rome, Italy.
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9 Paediatric Infectious Diseases Research Group, Institute for Infection and Immunity, St George’s, University of London, London, United Kingdom.
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12 Julius Clinical BV, Zest, the Netherlands.
13 Center for Observational and Real-World Evidence (CORE), Merck & Co. Inc., Rahway, NJ, USA.

Background: Respiratory syncytial virus (RSV) is the most common cause of hospitalisation in young children. COVID-19 has drastically changed the epidemiology of RSV. Therefore, policy makers need accurate and current information about the healthcare burden of RSV-associated disease in young children to make informed decisions about prevention recommendations.

Methods: We conducted the BRICE, a multicentre, prospective, study in five European countries (Spain, France, Germany, Italy, and the UK). The primary outcome was the population-based annual incidence rate of laboratory-confirmed RSV hospitalisation in children <2 years of age during three prospective (2020-2023) and one retropective (2018-2019) RSV seasons. Secondary outcomes included quality-of-life (QoL) impairment of children hospitalised.

Results: An interim analysis among 1,318 children in Spain, Germany, and the UK showed an annual incidence of hospitalisation per 1000 infant-years [95% CI] of 8.6 [7.9-9.3], 3.9 [3.4-4.4], and 5.9 [5.3-6.4] for the 2018-2019, 2020-2021, and 2021-2022 seasons, respectively. Across all RSV seasons, incidences were highest in children aged 0-6 months: 19.4 [17.4-21.5], 7.9 [6.7-9.3], and 14.4 [12.7-26.2] for the 2018-2019, 2020-2021, and 2021-2022 seasons, respectively. QoL impairment due to RSV hospitalisation most affected the respiratory system, motor functioning, and social functioning (mean differences between TNO-AZL Preschool Children’s QoL at discharge and hospitalisation: [95% CI] 37.6 [32.7-42.6], 25.4 [24.8-30.9], 24.4 [-2.5-51.2]).

Conclusion: Our interim analysis showed that RSV has caused substantial morbidity in young children in Europe before, during, and after the COVID-19 pandemic. New prevention strategies could have a big impact on the healthcare burden.

Funding: The BRICE study is sponsored by Merck Sharp & Dohme LLC, subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

66. HEALTHCARE UTILIZATION AND EXPENDITURES FOR RESPIRATORY SYNCTIVAL VIRUS AMONG US INFANTS BY AGE AT FIRST INFECTION

Derek Weycker (1) Amy Law (2)* Linnea Houde (1) Ahuva Averin (1) Mark Atwood (1) Kimberly Shea (2)

1. Policy Analysis Inc. (PAI)
2. Pfizer Inc.

Introduction: Respiratory syncytial virus (RSV) infection is common among young children. Existing literature suggests healthcare utilization and expenditures for RSV may differ among infants based on age at first infection, but evidence on the magnitude of such differences is limited.

Methods: We utilized data from the Merative MarketScan Commercial Claims and Encounters Database (2016–2019) to identify infants aged <12 months who had at least one episode of medically attended lower respiratory tract infection due to RSV (RSV-LRTI). All medical encounters for RSV-LRTI occurring within 30 days of first evidence were considered part of the same episode, and episodes were stratified by care setting. Healthcare utilization and expenditures (2020 USD) associated with the first RSV episode were tallied by age group.
Results: The study population included 47,458 infants: 47% (n=22,278) had their first RSV infection at <3 months, 23% (n=10,734) at 3-5 months, and 30% (n=14,466) at 6-11 months. RSV episodes among infants aged <3 months were more likely to require hospitalization (21%, vs. 13% [3-5 months] and 9% [6-11 months]), and had higher total healthcare expenditures ($5,373, vs. $2,532 and $1,708, respectively). Expressions for hospitalized episodes and ambulatory episodes were also higher among infants aged <3 months versus older infants.

Conclusion: Infants with their first RSV infection at <3 months of age incurred higher healthcare utilization and expenditures than infants aged 3-11 months. Strategies to prevent RSV infection among infants, especially the youngest, have the potential to yield substantive reductions in healthcare costs.

Keywords: healthcare utilization, healthcare expenditures, infants, respiratory syncytial virus, United States

Conflict of Interest: Funding for this study (including abstract preparation) was provided by Pfizer, Inc. to Policy Analysis Inc. (PAI). A Law and K Shea are employees of Pfizer, Inc. D Weycker, M Atwood, A Hanau, and L Houde are employees of PAI.

67. ANNUAL ECONOMIC BURDEN OF RESPIRATORY SYNCYTIAL VIRUS ILLNESS AMONG US INFANTS AGED <12 MONTHS

Linnea Houde (1) Ahuva Averin (1) Amy Law (2)* Derek Weycker (1) Kimberly Shea (2)

1. Policy Analysis Inc. (PAI)
2. Pfizer Inc.

Introduction. New preventives to protect infants from RSV illness during the first year of life are in development. The objective of this study was to estimate the total annual economic burden of RSV illness among US infants aged <12 months.

Methods. Total annual economic burden (2020 USD) was estimated by applying age-specific incidence rates of RSV among US infants obtained from published literature to the annual US birth cohort and multiplying the number of cases by the unit cost (direct and indirect) for RSV episodes. Direct costs were estimated by care setting using data from Merative MarketScan commercial and Medicaid databases (2016-2019); 63% of the population was assumed to have commercial insurance and 37% was assumed to have Medicaid, based on published estimates. Indirect costs were estimated as the number of assumed caregiver work loss days among employed caregivers multiplied by average daily wages.

Results. We estimated that among 3.7 million US infants aged <12 months, a total of 593,941 RSV episodes will occur each year, resulting in 48,357 hospitalizations, 144,985 emergency department visits, and 400,598 outpatient clinic visits. The total annual cost for treating RSV was estimated at $1.9 billion, comprising $1.5 billion for direct costs and $0.4 billion for indirect costs. Infants aged <3 months account for 45% of all RSV hospitalizations and 43% of overall total costs.

Conclusion. The total annual economic burden of RSV among US infants aged <12 months is considerable, especially among infants aged <3 months.

Keywords: Economic burden, total cost burden, infants, respiratory syncytial virus, United States

Conflict of Interest: Funding for this study (including abstract preparation) was provided by Pfizer, Inc. to Policy Analysis Inc. (PAI) A Law and K Shea are employees of Pfizer, Inc. D Weycker, A Hanau, and L Houde are employees of PAI.

68. COST-EFFECTIVENESS OF VACCINATION AGAINST RESPIRATORY SYNCYTIAL VIRUS (RSV) IN OLDER ADULTS: A LITERATURE REVIEW

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Introduction: Respiratory syncytial virus (RSV) causes a substantial burden in older adults. Multiple RSV vaccine candidates targeting older adults are undergoing clinical trials, and two succeeded phase 3 trials recently. This review aims to identify the influential parameters in published economic evaluations of RSV vaccination among older adults and to inform future evaluations.

Methods: A search was conducted in PubMed and ISPOR conference presentation database on 17th November 2022 without time/language restriction. Case reports, trials, reviews, cost-of-illness studies, and studies targeting only children or pregnant women were excluded.

Results: The searches yielded 691 citations, of which seven were retained (five peer-reviewed articles, two conference abstracts/posters). Geographically, studies were conducted in the United Kingdom (N=4), United States (N=3) and/or the Netherlands (N=2). Both static (N=5) and dynamic (N=2) models were used, but the proportion of high-risk patients (i.e., COPD) was only considered in three static models. Both dynamic (N=2)
and static models (N=2) included non-medically-attended RSV symptomatic episodes, however, the associated quality-adjusted life year (QALY) losses were not evaluated in the sensitivity analyses. All static models used one-year/one-season time horizon because of the assumed one-season vaccine protection. Vaccine characteristics (efficacy, price) and RSV-related burden (community incidence, hospitalisation and mortality rates) were generally the influential parameters.

Conclusion: For upcoming RSV economic evaluations, age- and risk-specific RSV-related burden are crucial. QALY losses of non-medically-attended episodes shall be investigated given these episodes can be large in number. The duration of protection and waning of immunity shall be evaluated, which would require >1 year time horizon.

Keywords: RSV, cost-utility analysis, cost-effectiveness analysis, economic evaluation, older adult vaccine, literature review

Conflict of Interest: This project is funded by PROMISE (Preparing for RSV Immunisation and Surveillance in Europe). PROMISE has received funding from the Innovative Medicines Initiative 2 Joint Undertaking under grant agreement No 101034339. This Joint Undertaking receives support from the European Union’s Horizon 2020 research and innovation programme and EFPIA. All authors report no potential conflicts of interest.

### 69. ADJUSTING FOR UNDERASCERTAINTY OF RSV INFECTIONS IN RSV-ASSOCIATED ACUTE INFECTION HOSPITALISATION BURDEN ESTIMATION IN OLDER ADULTS IN HIGH-INCOME COUNTRIES

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Background: Previous studies suggest diagnostic testing characteristics (ie, variations in clinical specimens and diagnostic tests) can contribute to underestimation of RSV disease burden. We aimed to estimate RSV-associated acute respiratory infection (ARI) hospitalisation burden in older adults (aged ≥65 years) in high-income countries and adjust for potential underascertainment of RSV infections.

Methods: We conducted a systematic literature review to identify data on RSV-associated ARI hospitalisation burden in older adults in high-income countries. We estimated unadjusted RSV-associated ARI hospitalisation incidence by age group through generalised linear mixed-effects meta-analysis, and then adjusted incidence for underascertainment of RSV-specific ARI based on RSV testing methodology.

Results: Based on six studies, we estimated the pooled unadjusted annual RSV-associated ARI incidence among older adults as 157 per 100,000 (95% CI: 98–252); the incidence was adjusted to 398 per 100,000 (222–572) after accounting for RSV underascertainment (~2.5 times unadjusted estimate). The adjusted rate could be translated into 0.9 (0.5–1.6) million RSV-associated ARI hospitalisations among adults aged ≥65 years in high-income countries during 2019. Stratified analysis by age group showed that the annual adjusted incidence increased from 265 per 100,000 among persons aged 65–74 years to 792 per 100,000 in persons >85 years (Table). Conclusion: This study provides the adjusted RSV-associated hospitalisation incidence in older adults by explicitly accounting for the potential underascertainment of RSV infections and has implications for better understanding the potential impact of RSV vaccine candidates for older adults if these are licensed.

Acknowledgement: This study receives funding support from Pfizer.

Keywords: Burden; older adult; hospitalisation; under-ascertainment

Conflict of Interest: Elizabeth Begier and Bradford Gessner are employees of Pfizer.

### Table. Unadjusted and adjusted estimates of RSV-associated ARI hospitalisation burden (rate and number) in older adults in high-income countries

<table>
<thead>
<tr>
<th>Age group</th>
<th>Method</th>
<th>Number of studies</th>
<th>Number of data points</th>
<th>Rate (per 100,000)</th>
<th>Number (±95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>65–74 years</td>
<td>Unadjusted</td>
<td>6</td>
<td>14</td>
<td>237 (96–252)</td>
<td>351 (222–572)</td>
</tr>
<tr>
<td></td>
<td>Adjusted</td>
<td></td>
<td></td>
<td>398 (228–695)</td>
<td>902 (516–1576)</td>
</tr>
<tr>
<td>75–84 years</td>
<td>Unadjusted</td>
<td>1</td>
<td>6</td>
<td>505 (195–1230)</td>
<td>129 (113–148)</td>
</tr>
<tr>
<td></td>
<td>Adjusted</td>
<td></td>
<td></td>
<td>695 (386–757)</td>
<td>127 (92–205)</td>
</tr>
<tr>
<td>&gt;85 years</td>
<td>Unadjusted</td>
<td>1</td>
<td>6</td>
<td>791 (557–230)</td>
<td>144 (125–166)</td>
</tr>
<tr>
<td></td>
<td>Adjusted</td>
<td></td>
<td></td>
<td>803 (615–970)</td>
<td>86 (65–110)</td>
</tr>
</tbody>
</table>

70. RSV TESTING AMONG CHILDREN <5 YEARS DURING A RESPIRATORY VIRUS SURGE IN THE UNITED STATES, SEPTEMBER–NOVEMBER 2022

Ruth Link-Gelles (1)*, Morgan Najdowski (1), Talia Spark (2), Akintunde Akinseye (2), and Katherine Fleming-Dutra (1) for the VISION Network
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Background: Respiratory viral activity decreased in the United States during the COVID-19 pandemic; however, as social distancing restrictions eased, increased rates of respiratory syncytial virus (RSV) and other respiratory illnesses have resulted in surges of care seeking during fall 2022.

Methods: VISION is a multisite, electronic healthcare records network including emergency department and urgent care (ED/UC) facilities, and hospitals across 10 US states. Originally designed to evaluate COVID-19 vaccines, the network also collects RSV testing data in persons presenting with COVID-like illness (CLI) and receiving SARS-CoV-2 testing. We explored RSV testing practices among children 6 months–4 years old presenting to ED/UCs or hospitalized with CLI during September 1 through November 6, 2022.

Results: Among 4 sites contributing data, 11,097 children in ED/UC and 882 children hospitalized presented with CLI and received a SARS-CoV-2 test. 8,494 (77%) of this study population also received molecular testing for RSV in the ED/UC and 882 (83%) in the hospital, with 2,075 (24%) and 321 (36%) testing positive, respectively. Hispanic and non-Hispanic white children were more likely to be tested for RSV, as were those with ≥1 underlying medical conditions. Weekly RSV percent positivity ranged from 5–44% in the ED/UC and 15–70% in the hospital.

Conclusions: In fall 2022, most children presenting with CLI and receiving SARS-CoV-2 tests. We explored RSV testing practices among children 6 months–4 years old presenting to ED/UCs or hospitalized with CLI during September 1 through November 6, 2022.

Results: Among 4 sites contributing data, 11,097 children in ED/UC and 882 children hospitalized presented with CLI and received a SARS-CoV-2 test. 8,494 (77%) of this study population also received molecular testing for RSV in the ED/UC and 882 (83%) in the hospital, with 2,075 (24%) and 321 (36%) testing positive, respectively. Hispanic and non-Hispanic white children were more likely to be tested for RSV, as were those with ≥1 underlying medical conditions. Weekly RSV percent positivity ranged from 5–44% in the ED/UC and 15–70% in the hospital.

Conclusions: In fall 2022, most children presenting with CLI and receiving SARS-CoV-2
testing received RSV testing and almost one-third were positive in both settings. Monitoring testing practices during a surge in respiratory infections in children is important for understanding and interpreting RSV disease burden and seasonality to inform prevention measures.

Keywords: testing practices, viral surge, COVID-19, influenza

Conflict of Interest: None declared

71. 2022/2023 EPIDEMIC CIRCULATION OF HUMAN RESPIRATORY SYNCYTIAL VIRUS OBSERVED EARLIER IN SOUTHERN CHINA THAN NORTHERN: PRELIMINARY OBSERVATION FROM A SEASONALITY SURVEILLANCE STUDY IN CHINA


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Background: The reported burden of Human Respiratory Syncytial Virus (HRSV) is high in infants and young children but under-ascertained. There is an urgent need to set up systematic surveillance in China.

Methods: A prospective observational study is conducted in sentinel hospitals from 7 cities of different geographical regions in China. About 10 severe acute respiratory infection (SARI) cases <2 years old are randomly selected weekly for 3 years. This analysis was based on the samples initially collected from July to October 2022. Respiratory specimens were preliminary tested for HRSV according to local requirements of regular clinical practice and then sent to National Institute for Viral Disease Control and Prevention (IVDC), China CDC for final PCR tests. HRSV seasonality would be determined based on the HRSV positive rate from final PCR tests.

Results: From July to October, a total of 746 SARI children <2 years old were enrolled in the study and received the preliminary HRSV tests. Monthly HRSV positive rates were 5.84%, 5.34%, 4.95%, and 6.97% from July to October, respectively. Positive rates of HRSV in hospitals in southern China were higher than those in the northern sentinel hospitals. The highest positive rates were observed in Shenzhen, from 17.50% in July, and steadily increased to 21.05% in October.

Conclusion: Overall, HRSV positive rate increased in October. HRSV epidemic has started in southern China, earlier than northern region in 2022/2023. Continuous monitoring is required given the impact of recent surge in the USA.

Keywords: Human Respiratory Syncytial Virus, Seasonality, Surveillance, China

Conflict of Interest: None declared

72. IMPACT OF COVID-19 PANDEMIC ON RSV CIRCULATION IN HOSPITALIZED AND OUTPATIENTS CASES OF ACUTE RESPIRATORY INFECTIONS (ARI)

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4. Commission of Investigations of the Province of Buenos Aires

Introduction: Respiratory viruses are the main cause of ARI in the pediatric population. In March 2020, WHO declared a state of pandemic (COVID-19) with a high impact. Globally, changes in post-pandemic circulation patterns were observed.

Objective: To compare the viral circulation pattern in ARI cases under 18 years of age with and without hospitalization criteria in a pediatric hospital in Buenos Aires between EW 1-33 of 2022.

Methods: Observational, cross-sectional, descriptive study of patients with respiratory symptoms with and without requiring hospitalization in 2022. Virological diagnosis was made by RT-PCR of nasopharyngeal aspirates.

Results: During the year 2022, a total of 305 hospitalized ARI cases were reported, 68% tested positive for viruses, being metapneumovirus (36.5%) the predominant followed by RSV (32.2%), rhinovirus (17.1%), Influenza A (7.1%), Adenovirus (3.3%), COVID-19 (3.3%) and Parainfluenza (0.5%). The onset of viral circulation was late, from EW 20. During the same period, 3,517 outpatient consultations for respiratory infection were recorded, 909 (25.8%) with viral isolation, being influenza A (39.3%) the predominant followed by rhinovirus (24.3%), RSV (14.6%), metapneumovirus (6.3%), SAR-Cov-2 (5.5%), adenovirus (4.1%), CoV (3.6%), Parainfluenza 3 (1.8%) and Influenza B (0.1%). There was a predominance of influenza in outpatient cases and RSV in hospitalized cases. Hospitalized cases were older, with higher frequency of focal pneumonia as clinical presentation, comorbidities and history of previous hospitalizations for respiratory causes compared to outpatients.

Conclusion: After COVID-19 pandemic, changes in respiratory viruses epidemiological pattern, seasonality and in the number of hospitalizations were observed.

Keywords: RSV, epidemiological surveillance, acute respiratory infection

Conflict of Interest: None Declared

73. THE COST AND HEALTH BURDEN ATTRIBUTABLE TO RESPIRATORY SYNCYTIAL VIRUS (RSV) IN CHILDREN AND OLDER ADULTS IN EUROPE

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Background: Using the most recent evidence we aim to estimate Respiratory Syncytial Virus (RSV) -related costs and Quality-Adjusted Life Year (QALY) losses in infants (< 1 year), children (<5 years) and older adults (> 65 years) for the European Union (EU27) as a whole, as well as for each EU country separately.

Methods: We obtained population sizes, age-specific life expectancies, RSV-mortality, RSV-incidence, average cost and QALY losses per RSV episode from Eurostat, World Bank and the RESCEU project. We assigned distributions to all RSV-specific parameters, made 1000 random draws and produced probabilistic estimates (mean and 95% Confidence Interval) of the RSV-related direct medical and total costs (direct + indirect costs), and QALY losses.

Results: We estimated the annual pre-Covid-19 RSV direct medical cost [total cost] burden (in million) on infants, children, and older adults in EU27 at €64.28 (28.05,117.34) [€80.50 (34.82,147.81)], between €70.10 (38.02, 120.07) and €122.39 (66.38, 209.35), and €10.22 (1.29, 24.73) [€21.27 (7.62, 43.49)], respectively. The total QALY lost was estimated to be 159,987.71 (105,177.13, 230,368.83), between 814,044.22 (354,600.54, 1,173,120.59) and 814,131.69 (334,568.74, 1,173,313.63), and 18,620.97 (2,443.34, 55,458.03) in infants, children, and older adults, respectively, of which about 98% represents QALY loss due to RSV mortality.
Conclusion: The RSV burden is substantial in Europe, with a much larger cost and health burden observed for infants than for older adults, and with mortality contributing the most to QALY losses.

Acknowledgement: The authors thank the Respiratory Syncytial Virus Consortium in Europe (RESCEU) investigators for their work in providing relevant data.

Keywords: RSV; disease burden, cost; quality-adjusted life-years; infants; children; older adults; Europe

Conflict of Interest: None declared.

74. RSV, INFLUENZA, AND CORONAVIRUS INTERACTION WITHIN A 10-YEAR LONGITUDINAL COHORT STUDY

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Background. Alternating patterns of RSV and influenza peaks at the community level, or viral interference, have been observed in surveillance data over large regions. Inference from these studies, however, is often challenged by their ecologic nature. To examine RSV-influenza interference more closely in a defined population, we compared infection patterns in over ten years of a longitudinal household cohort study.

Methods. The Household Influenza Vaccine Evaluation (HIVE) study has prospectively enrolled and followed families with children in southeast Michigan since 2010. Household participation continues over multiple years until no longer eligible. Participants are actively followed for acute respiratory illness, including illnesses not requiring medical attention, and a combined nasal-throat swab is collected at symptom onset. Specimens are tested by RT-PCR for respiratory viruses including influenza A and B, RSV, and coronavirus types 229E, HKU1, NL63, and OC43. Seasonal patterns were graphically evaluated.

Results. From 2010-2020, RSV circulation preceded that of influenza in 7 of the years (Figure). In each of these 7 years, the decline of RSV infection coincided with the rise of influenza. Similar alternating peak patterns were not observed when comparing RSV to coronaviruses.

Conclusions. This analysis supports other findings suggesting interference of RSV infection by influenza. We have shown this pattern within a defined and systematically followed group of individuals with testing that is independent of healthcare visits and clinician-directed testing. Understanding virus-virus interactions at the community level will continue to be important for monitoring the changing epidemiology of RSV.

Keywords: RSV, influenza, coronaviruses, seasonality

Conflict of Interest: ETM has received grant funding from CDC, NIH, FLULAB and Merck.

75. THE BURDEN OF RESPIRATORY SYNCYTIAL VIRUS IN INFANTS IN THE OUTPATIENT AND INPATIENT SETTING IN SPAIN

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5. Consorcio de Investigación Biomédica de Epidemiología y Salud Pública (CIBERESP), Spain.

BACKGROUND: Respiratory syncytial virus (RSV) infection is the most common cause of acute lower respiratory infection (ALRI) in infants. Our study aimed to estimate the burden of medically attended ALRI cases potentially related to RSV in Spanish infants.

METHODS: Electronic medical records of public providers from two Spanish regions from 09/2017 to 06/2018 were used - covering 8,006 children aged <12 months. Three case definitions were considered: (a) RSV-specific; (b) RSV-specific and unspecified acute bronchiolitis (RSV-specific and Bronchiolitis), and; (c) RSV-specific and unspecified ALRI (RSV-specific and ALRI).

RESULTS: We identified 1,076 medically attended ALRI cases potentially due to RSV, of which 202 (18.8%), 151 (14.0%), and 723 (67.2%) coded with RSV-specific, unspecified acute bronchiolitis, and unspecified ALRI codes, respectively. Cases per 1,000 infants were 25.2, 44.1 and 134.4, for RSV-specific, RSV-specific and Bronchiolitis, and RSV-specific and ALRI definitions. On average, RSV-specific cases had 9.4 Primary Care (PC) visits during their episode, 2.4 visits to the Emergency Department (ED) and 1.3 visits to specialists. Almost all RSV-specific cases were hospitalized for RSV (99.0%), visited PC (96.0%), and the ED (99.5%). Infants aged <6 months accounted for most cases (78.2%). Risk factors were observed in 11.9% of RSV-specific cases, with most infants being healthy. Mean direct healthcare cost was € 3,362 per RSV-specific case, of which 72.9% from hospitalizations.

CONCLUSIONS: RSV is a major healthcare demand driver in infants in Spain. Most cases were observed in otherwise healthy infants, supporting the use of RSV protective options for the broad infant population.

Keywords: Respiratory syncytial virus; Spain; Burden; Epidemiology; acute lower respiratory infection

Funding: This study was funded by Sanofi.

Conflict of Interest: Martín-Torres F, Díez-Domingo J and García-Sánchez M received honoraria from Sanofi for taking part in expert meetings.

76. BURDEN OF RESPIRATORY SYNCYTIAL VIRUS (RSV) IN CHILDREN IN SWEDEN (BRICS) - A RETROSPECTIVE OBSERVATIONAL COHORT STUDY USING POPULATION-BASED REGISTER DATA: RATIONAL AND DESIGN (NCT05622331)

Anton Holmgren (1,2,3), Malin Ryd Rinder (4, 5), Mathieu Bangert (6), Oliver Martyn* (7), Lena Svensson (8), Anna Fornwall (9), Hanna Fues Wahl (9), Martina Aldvén (9), Lena Jacobs (9), Sven-Arne Silfverdal (10)
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2) Department of Paediatrics, Halland Hospital, Halmstad, Sweden.
3) The research and development unit, Region of Halland, Sweden.
4) Astrid Lindgren Children’s Hospital, Karolinska University Hospital, Stockholm, Sweden.
5) Department of Women’s and Children’s Health, Karolinska Institutet, Stockholm, Sweden.
Background: RSV is a leading cause of hospitalization amongst children under 2 years, with the vast majority occurring in otherwise healthy children. In Sweden, the estimated incidence of hospitalized RSV infection during the first year of life is 17.4 per 1,000 persons, and 0.6 per 1,000 persons in children aged 1-4 years. Despite the common nature of RSV infections, few studies have been performed using register data covering the majority of Sweden. We present the rationale and design of the BRICS study, which aims to estimate the burden of RSV in children using national and regional registers.

Materials and methods: The BRICS study is a retrospective observational cohort study of RSV infection in children <5 years old using pseudonymized patient data from Swedish national and regional registers. The study includes data on all inpatient and specialist outpatient hospital care, prenatal, delivery and neonatal care since 2001; and pharmacy dispensed medications since 2005. Children are linked to parents/caregivers to examine variables for socioeconomic status and work absence to care for sick child (VAB leave). Primary care and RSV-related laboratory data from >2 Swedish regions are included. Sequelae of RSV infection will be compared to other common respiratory pathogens.

Results and Conclusion: Findings from the BRICS study are expected to improve the understanding of epidemiological aspects and burden associated with RSV infections, to help guide future health policies and the implementation of RSV interventions in Sweden and internationally. Full results are expected in the second half of 2023.

Keywords: Epidemiology, Burden of Disease, Healthcare resource utilization, Sweden, complications

Funding: Sanofi

Conflict of Interest: AH reports having received consultancy remuneration from Sanofi as a scientific expert to support the design, conduct and interpretation of the BRICS (RSV00046) study. MR reports having received consultancy remuneration from Sanofi as a scientific expert to support the design, conduct and interpretation of the BRICS (RSV00046) study; involvement in RSV clinical trials sponsored by Janssen; and having stock holdings in Astra Zeneca and Pfizer. SS received consultancy remuneration as a scientific expert from Sanofi to support the design, conduct and interpretation of the BRICS (RSV00046) study; involvement in clinical trials sponsored by Sanofi and GSK; receiving honoraria for speaking engagements from GSK; and participation in Advisory Boards or Data Safety Monitoring Boards for Sanofi, Pfizer, GSK and Bergen University. MB, OM and LS are employees of and may own shares in Sanofi. AF, MA and LJ are employees of and may own shares in Quantify Research AB, which has been contracted by Sanofi to conduct the BRICS study. HW is a former employee of and may own shares in Quantify Research AB.

Sérgio Massora (1)*, Leocadia Vilanculos (1), Hélio Mucavele (1), Percy Efrain Pantoja (2), Elena Marbán-Castro (2) Aneslio Cossa (1), Avertino Benedito (1), Nelson Teme (2), I. Mandomando (1), Clara Menéndez (1), (2), (4), (4) and Azucena Bardaji (1), (2), (4).

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3. Instituto Nacional de Saúde, Ministério de Saúde, Maputo, Moçambique.

Background and Aims: Respiratory syncytial virus (RSV) is a leading cause of under-5 morbidity and mortality. Low and middle-income countries concentrate most (90%) of the RSV burden. We aimed to determine the incidence of RSV acute lower respiratory infections (ALRI), and associated mortality and risk factors, among African children.

Methods: A health facility-based prospective observational study was carried out in children aged 0-60 months hospitalized with WHO-defined clinical criteria for pneumonia at the Manhiça District Hospital (MDH), in Southern Mozambique. Clinical and demographic data was collected through standardized questionnaires. A nasopharyngeal aspirate (NPA)/swab (NP) was collected from all study children at enrolment. Respiratory samples were analyzed for RSV detection by molecular methods (TaqMan Array). In this area, HIV prevalence in pregnant women attending ANC is high (21%), and 30% of admitted children at MDH are HIV positive.

Results: A total of 330 children admitted with WHO-defined criteria for severe pneumonia were recruited between October 2019 and September 2022. NP and NPA are being tested at Centro de Investigação em Saúde de Manhiça (CISM) using TaqMan Array Card technology, and primers and probes specific for RSV-A and RSV-B using RT nested PCR. Analyses of clinical and microbiological data are currently ongoing, and will be presented at RSVVW’23 meeting.

Conclusion: An RSV maternal immunization strategy is being considered for the prevention of severe RSV disease in infants. This study is expected to contribute to the development of a RSV vaccine for children under 6 months of age.

Keywords: Incidence, Respiratory syncytial virus, children, risk factor, mortality.

Conflict of Interest: None declared

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Background: Respiratory Syncytial Virus (RSV) is the most common cause of bronchiolitis and lower respiratory tract infection in children in the first year of life, disproportionately affecting infants in developing nations. Previous studies have found that the nasopharyngeal microbiome of infants with RSV infections has specific characteristics that impact the severity of disease, including lower biodiversity, perturbations of the microbiota and differences in relative abundance. These studies have focused on infants seen in a clinical or hospital setting, predominantly in developed countries.

Methods: To address this gap, we conducted a microbiome analysis within a cohort of post-mortem RSV+ infants with age at death ranging from 4 days to 6 months and matched RSV- deceased Zambian infants all of whom died in the community and were previously enrolled in the Zambia Pertussis and RSV Infant Mortality Estimation (ZPRIME) study. As part of the ZPRIME study procedures, all infants underwent one-time, post-mortem nasopharyngeal sampling. The current analysis explores the differences between the microbiome profiles of RSV+ and RSV- infants using 16S ribosomal DNA sequencing.
Results: We found that Haemophilus and Moraxella were more abundant in the microbiome of RSV+ infants than in RSV- infants. Additionally, Gemella, Staphylococcus and Streptococcus were less abundant in RSV+ infants than in RSV- infants.

Conclusion: These results support previously reported findings of the impact of RSV on the nasopharyngeal microbiome in other cohorts and suggest that changes in abundance of these microbes are likely specific to RSV and may indicate the severity of disease.

Keywords: nasopharyngeal microbiome, respiratory syncytial virus, infant, post-mortem

Conflict of Interest: None declared

### 70. THE INFLUENCE OF SEASONALITY ON THE CLINICAL COURSE OF RSV BRONCHIOLITIS IN THE MIDST OF THE COVID-19 PANDEMIC IN ISRAEL

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Background: The SARS-2 COVID-19 pandemic had greatly influenced the well documented seasonal pattern of Bronchiolitis caused by Respiratory Syncytial Virus (RSV). Normally RSV appears during the autumn and winter but was not present in our hospital at all during the COVID19 pandemic lockdown (3.2020-4.2021) and reemerged in the spring and summer after the lockdown was lifted. We hypothesized that the clinical and epidemiologic characteristics of the disease will be influenced by these changes.

Methods: In this retrospective study, the computerized medical files of children admitted with bronchiolitis or respiratory symptoms and positive RSV PCR between 10.2017 and 10.2021 were analyzed. Two different time periods were considered: pre-COVID19 (10.2017-2.2020) and post-COVID19 lockdown (5.2021-10.2021).

Results: 1284 patients were initially screened. Of those 770 had a positive RSV PCR without other pathogens isolated. Epidemiologic, laboratory and clinical features were obtained and analyzed.

646 patients were assigned to the pre-COVID19 group and 124 were assigned to the post-COVID19 lockdown group. Patients of both groups were similar in age, gender and in length of hospital stay. Post COVID19 lockdown patients had lower rates of oxygen supplementation (57.3 vs 67.2% in pre COVID19 patients, p=0.039) but higher rates of non-invasive ventilation (NIV) support (14.5 vs 8.4% in pre COVID19 patients, p=0.042). There was no statistically significant difference in ICU admission rates, complications and serum inflammatory markers.

Conclusion: our preliminary analysis suggests that patients with RSV bronchiolitis admitted after the COVID19 lockdown had a more severe disease, as shown by the higher rate of NIV support.

Keywords: RSV, Bronchiolitis, COVID19, Seasonality

Conflict of Interest: None declared

### 80. OUTCOMES OF PREGNANT WOMEN HOSPITALIZED WITH RSV INFECTION, RSV-NET, 2014-2022

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Background: Respiratory syncytial virus (RSV) causes a significant number of hospitalizations among infants and older adults; less is known about RSV among pregnant women. To estimate the frequency of severe outcomes among pregnant women hospitalized with RSV, we analyzed data from the Respiratory Syncytial Virus Hospitalization Surveillance Network (RSV-NET) during 2014-2022.

Methods: RSV-NET is an active, population-based surveillance system that tracks RSV-associated hospitalizations. RSV-NET cases are RSV infections in residents of a defined catchment area who test positive for RSV through a clinician-ordered laboratory test within 14 days before or during hospitalization. In this analysis, we included annual surveillance data collected during the RSV season (October 1 to April 30) during 2014-2022. Pregnancy status and severe outcomes were assessed in women aged 18-49 years (2019-2020 season was excluded from analysis due to missing pregnancy status). A severe outcome was defined as ICU admission or in-hospital death.

Results: Among 953 women aged 18-49 years hospitalized with RSV (Figure), 199 (20.9%) were pregnant. Ten (5.0%) pregnant women required ICU admission and one (0.5%) died in-hospital compared to 157 ICU admissions (21.7%) and 8 deaths (1.1%) among non-pregnant women. Most pregnant women (80.0%) and non-pregnant women (88.9%) hospitalized with RSV infection who had a severe outcome had ≥1 underlying medical condition.

Conclusions: Severe outcomes among pregnant women hospitalized with RSV were uncommon. Most women aged 18-49 years with severe outcomes had ≥1 underlying medical condition, regardless of pregnancy status. Further investigation of how RSV infection affects pregnancy and newborn outcomes is needed.

Keywords: Pregnant women, Hospitalization

Conflict of Interest: Kimberly Yousey-Hindes: The CDC provides grant funding for the Connecticut Emerging Infections Program, which pays my salary. E.J.A has consulted for Pfizer, Sanofi Pasteur, GSK, Janssen, Moderna, and Medscape, and his institution receives funds to conduct clinical research unrelated to this
81. PEDIATRIC HOSPITALIZATIONS ASSOCIATED WITH RESPIRATORY SYNCYTIAL VIRUS (RSV), SARS-COV-2, AND INFLUENZA VIRUSES BEFORE AND DURING THE COVID-19 PANDEMIC, NEW VACCINE SURVEILLANCE NETWORK, 2016-2022

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Background: The COVID-19 pandemic disrupted seasonal circulation patterns of respiratory syncytial virus (RSV) and influenza in the United States and characterization of pediatric hospitalizations during the pandemic has been limited.

Methods: We enrolled children aged <18 years hospitalized with acute respiratory illness at 7 surveillance hospitals during December 2016 to February 2020 (pre-pandemic) and March 2020 - October 2022 (pandemic). Routine surveillance data sources included parent/ guardian interviews, medical chart review, and collection of midturbinate nasal and/or throat swabs for testing by reverse transcription polymerase chain reaction. We compared demographic characteristics, underlying conditions, and severity markers among children with RSV, influenza, or SARS-COV-2 infections.

Results: Among 16,327 children hospitalized in the pandemic period, 4,279 (26%) tested positive for RSV and 995 (6.1%) for influenza; in the pandemic period, among 9,931 children hospitalized, 1,851 (18.6%) tested positive for RSV, 841 (8.4%) for SARS-COV-2, and 180 (1.8%) for influenza. During the pandemic, infants less than 2 months and those born prematurely were more likely to be hospitalized for RSV than for SARS-COV-2 (p<0.01) or influenza (p<0.01). Children with RSV were more likely to require supplemental oxygen (64.1%) than children with influenza (37.8%, p<0.01) or SARS-COV-2 (38.2%, p<0.01), and more likely to be admitted to the ICU (21.8%) than children with influenza (13.3%, p<0.01) or SARS-COV-2 (18.1%, p<0.03). There was no difference in frequency of mechanical ventilation or death.

Conclusion: In the pandemic period, RSV remains a leading cause of hospitalization among children with higher relative severity than those hospitalized with SARS-COV-2 or influenza.

Table 1: Characteristics of children hospitalized with respiratory syncytial virus, SARS-COV-2, or influenza viruses during pre-pandemic and pandemic periods, New Vaccine Surveillance Network, December 2016 – October 2022

82. EPIDEMIOLOGICAL EVIDENCE OF NON-SPECIFIC BENEFICIAL EFFECTS OF RESPIRATORY VACCINES AGAINST RESPIRATORY SYNCYTIAL VIRUS–HOSPITALISATIONS IN INFANTS USING POPULATION-BASED DATA

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Background: In the pre-RSV-vaccine era, we aimed to assess the real-world effectiveness of the existing pneumococcal conjugate vaccine (PCV) and seasonal influenza vaccine on RSV-hospitalisations.

Methods: We conducted a population-based cohort study of 360,994 Western Australian births 2000-2012, using probabilistically linked individual-level immunisation, perinatal, hospitalisation and RSV testing data. For PCV, we performed adjusted Cox proportional hazard models with time varying exposure (receipt of infant PCV doses) against the first RSV-confirmed hospitalisation in infants <12 months. For influenza, we exploited a quasi-natural experiment created from the 2008 state-funded preschool influenza vaccination program to conduct an instrumental variable method to mitigate biases and reverse causality.

Results: Following universal funding in 2005, PCV coverage ranged from 73-85%. Influenza vaccine coverage was low prior to 2008 but increased to 36% in children aged 6 months–2 years in 2009. Receipt of PCV or influenza vaccines reduced RSV-hospitalisations in young children. Remarkably, receipt of 23 PCV doses in the universal funded period was associated with a 30% reduction in RSV-hospitalisation in Aboriginal infants (aHR 0.70 [95% CI 0.46-1.06]) and 21% reduction in non-Aboriginal infants (aHR 0.79 [95% CI 0.63-0.99]) compared with unvaccinated infants. The state-funded preschool seasonal influenza program resulted in 1,193 fewer cases of RSV-hospitalisations with 67% of those in children aged ≤ 2 years.

Conclusions: Our population-based analyses using two distinct methodologies, suggest that universal childhood PCV and seasonal influenza vaccination provide non-specific protection against infant RSV-hospitalisations. If confirmed, the findings support broader implementation of currently approved PCV and influenza vaccines.
Keywords: RSV-hospitalisation; infant; non-specific vaccine effects; epidemiology; population; influenza vaccine; pneumococcal conjugate vaccine

Conflict of Interest: HCM and PCR have been paid institutional honariums for participation in industry forums and are in receipt of funding through investigator initiated studies

8.3. IMPACT OF RELAXATION OF COVID-19 PREVENTIVE MEASURES ON RESPIRATORY SYNCYTIAL VIRUS (RSV) INFECTION AMONG THE ABORIGINAL TRIBAL CHILDREN (NICOBARESE) IN REMOTE ISLAND IN INDIA.

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Introduction: Car-Nicobar Island is a home for an aboriginal tribe, Nicobarese. There has been no systematic surveillance study from this far-flung Indian island on the prevalence of respiratory viral pathogens.

Method: In light of this tribe’s vulnerability and geographical location of this island, a prospective hospital-based surveillance (ICMR funded) study was conducted between June 2019 and May 2022 to evaluate the prevalence of RSV and other respiratory viruses among Nicobarese reporting to the health facilities with Influenza-Like Illness (ILI).

Results: A total of 2609 tribal children with ILI reported to the health facility, which include infants (13.7%), toddlers (19.9%), preschool children (14.5%), middle-aged children (28.0%), and adolescents (34%). Compared to inpatient cases, outpatient cases were high. Of these total ILI cases, 429 were screened for viral etiology and 219 children were found to be infected with at least one respiratory virus, whereas six had co-infections. RSV-A was the most common viral etiology among children (N = 122), especially toddlers than infants and preschool children. The most common symptoms were fever, chills, cough, and nasal discharge.

RSV-A infection peaked in October and November 2021, when the schools were reopened after the decline of COVID-19 cases at Car-Nicobar Island.

Conclusions: With the relaxation of public health measures after the decline of COVID-19 cases at Car-Nicobar, an upsurge of RSV-A infections was reported among Nicobarese children. In view of the vulnerability of this tribe a continuous surveillance of viral respiratory pathogens and necessary preventive measures are needed in place.

Keywords: Relaxation of COVID-19 preventive measures; RSV infection among the aboriginal tribal children

Conflict of Interest: Authors have No Conflict of Interest

8.4. SEASONALITY OF INFANT LOWER RESPIRATORY TRACT INFECTIONS, INCLUDING THOSE CAUSED BY RSV, WAS ALTERED DURING THE COVID-19 PANDEMIC: RESULTS FROM FOUR US HEALTH SYSTEMS

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Introduction: Respiratory syncytial virus (RSV) is the leading cause of infant hospitalizations and lower respiratory tract infections including bronchiolitis. Surveillance shows that since the start of the COVID-19 pandemic and the implementation of associated non-pharmaceutical public health (PH) measures beginning in March 2020, seasonal respiratory illnesses, including infant Bronchiolitis caused by RSV, have been disrupted.

Objective: To show infant bronchiolitis and RSV bronchiolitis incidence trends across four health systems during the COVID-19 pandemic.
Methods: We assessed EHR data from infants age <12months in the State University of New York (SUNY) Upstate Medical University health system, the Duke University Health System (DUHS), Tampa General Hospital (TGH), and the Renown Regional Medical Center Health System (Renown). We examined all encounters for ICD-10-CM codes and laboratory testing to estimate the incidence of respiratory illness due to bronchiolitis and RSV from October 2015 to November 2022.

Results: Prior to March 2020, bronchiolitis and RSV exhibited typical seasonality. With the onset of COVID-19 in 2020, there was sporadic seasonal illness followed by an interseasonal peak in mid-2021. In 2022, an early seasonal peak occurred in all four health systems. (Figures 1 and 2). Most cases are seen in emergency and outpatient settings (Figure 3).

Conclusion: During the COVID-19 pandemic, typical seasonal periodicity of bronchiolitis and RSV incidence has been altered, likely by non-pharmaceutical public health measures. 2022 trends indicate a return to typical seasonality. Continued monitoring is needed to determine the impact of the pandemic on disease seasonality to aid future efforts at prevention.

Keywords: Lower Respiratory Tract Infection, Bronchiolitis, Respiratory Syncytial Virus, COVID-19

Conflict of Interest: ZQ and EW are employees of Clinetic, Durham, NC, USA. MS and JF are employees of EpidStrategies, A Division of ToxStrategies. CBN is an employee of Sanofi.

83. INFANT HOSPITALIZATIONS AND ICU ADMISSIONS FOR BRONCHIOLITIS AND RSV-BRONCHIOLITIS ARE AT HISTORIC HIGHS DURING 2022 EARLY SEASONAL DISEASE: RESULTS FROM FOUR US HEALTH SYSTEMS

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Background: In the US, respiratory syncytial virus (RSV) is the leading cause of infant hospitalization and lower respiratory tract infections including bronchiolitis. Surveillance shows that since the start of the COVID-19 pandemic in March 2020, bronchiolitis and RSV-bronchiolitis epidemiology among US infants has been changing.

Objective: To assess trends in hospitalizations and ICU admissions for infant bronchiolitis and RSV-bronchiolitis since the start of the COVID-19 pandemic, across four US health systems.

Methods: We assessed electronic health record (EHR) ICD-10-CM and laboratory testing data from the Duke University Health System, Renown Health System, USF Health/Tampa General Hospital, and SUNY Upstate Medical University from October 2015 to November 2022.

Results: During the recent early 2022 RSV season, infant hospitalizations (Figures 1a, 1b), and ICU admissions and mechanical ventilation use (Figures 2a, 2b) for bronchiolitis and RSV-bronchiolitis have reached the highest levels since the start of our surveillance period in 2015.

Conclusion: The recent 2022 early bronchiolitis and RSV-bronchiolitis season has resulted in historically high levels of severe disease among infants. Continued monitoring of RSV-bronchiolitis trends is needed.

Keywords: Lower Respiratory Tract Infection, Bronchiolitis, Respiratory Syncytial Virus, infant, hospitalized, ICU, COVID-19, healthcare utilization

Conflict of Interest: ZQ and EW are employees of Clinetic, Durham, NC, USA. MS and JF are employees of EpidStrategies, A Division of ToxStrategies. CBN is an employee of Sanofi.
86. RSV INFECTION IN CHILDREN ADMITTED TO A PEDIATRIC INTENSIVE CARE UNIT IN GHANA AMID COVID-19 PANDEMIC

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Background: Respiratory syncytial virus (RSV) infection is a seasonal illness that affects about 97% of children by the age of 2 years. Although RSV infection can be life threatening, there are limited data available on the burden of RSV in critically ill children. The current study assessed the burden of RSV among children in a pediatric intensive care unit (PICU) in Ghana.

Methods: Children below age 24 months with severe respiratory tract infections who were admitted at the PICU of the Korle Bu Teaching Hospital were recruited with parental consent. Nasal swabs were obtained and tested for RSV and Influenza virus using the ID NOW POC and then confirmed by real time PCR at the NMIMR. Samples were also investigated for the presence of other viral agents.

Results: Twenty-eight children were enrolled from June to November 2021. RSV was confirmed in 9/28 (32%) of the children who were all below age 12 months. Among the RSV-positive group, infants <3 months old had a higher incidence of infection (67%, p<0.01). RSV A predominated 7/9 (78%) cases. One patient each tested positive for Influenza virus and SARS-CoV-2. Two patients (22%) were preterm and 5 (56%) had congenital abnormalities. The average length of stay on PICU was 19.11 days and 1 RSV death occurred.

Conclusions: RSV remained an important cause of severe respiratory illness during the COVID-19 outbreak in Accra. The PICU burden of RSV was heavy on infants during the first year of life. Interventions targeted against severe RSV disease are needed.

Keywords: Respiratory Syncytial Virus(RSV), Pediatric Intensive Care, Severe Respiratory Infections, Infants Hospitalizations, Ghana

Conflict of Interest: None declared

87. ESTIMATION OF HOSPITALIZATIONS ATTRIBUTABLE TO RSV INFECTION IN ADULTS OVER 50 YEARS OLD IN FRANCE USING A MODEL-BASED APPROACH, 2010-2020

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The epidemiology of respiratory syncytial virus (RSV) is poorly described and underestimated among older adults due to insufficient testing. The objective of this study was to estimate the epidemiological burden of RSV infection in adults over 50 years old in France, with a focus on 65 years and older.

Poison cyclic regressions were applied to estimate the weekly number of age- and cause-specific hospitalizations attributable to RSV from July 2010 to February 2020. Outcome data were extracted from the national hospital discharge database. Indicators of RSV and influenza activities, time trends, and seasonal terms were included in the models.

Over the study period, the average annual hospitalization rates attributable to RSV in adults 65 years and older were 181 hospitalizations per 100,000 inhabitants for respiratory causes and 345/100,000 for cardio-respiratory causes, representing 21,776 and 41,529 yearly hospitalizations respectively. The percentages of respiratory and cardio-respiratory hospitalizations estimated to be RSV-related were 6.3% and 3.2% respectively. The RSV-related hospitalization rates increased with age. Rates for respiratory causes were 44, 106, 258/100,000 for 50-64 years, 65-74 years and 75 years and older respectively. Rates for cardio-respiratory causes were 117, 251, 441/100,000 for 50-64 years, 65-74 years and 75 years and older respectively (Table).

The initial results of this study demonstrated RSV infection is responsible for a significant hospital burden in France among adults over 50 years old, particularly those 75 years and older. Additional work will be performed to evaluate the impact of model parameters on results.

Keywords: Respiratory syncytial virus, RSV, Hospitalization, France, epidemiology, modelization, adults, elderly

Conflict of Interest: V. Barbet and M. Lemaitre are employees of Horiana, with which Pfizer contracted to support data acquisition and analysis for this study. J.-S. Casallegno does not have conflicts of interest. L. Watier, P. Loubet, P. Vanhems and H. Lilliu received honoraria from Pfizer and/or other pharmaceutical companies. C. Nuttens, S. Fieuzev, E. Blanc and E. Begier are employees of Pfizer and may hold stock or stock options.

Estimated average annual numbers of hospitalizations (95% CI) attributable to RSV infection and associated rates per 100,000 inhabitants by age group in France, July 2010 to February 2020

88. RSV COINCIDENTS WITH OTHER RESPIRATORY VIRUSES IN HOSPITALIZED CHILDREN, GHANA

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Background: Respiratory syncytial virus (RSV) infections are common in children and a major cause of hospitalization among infants. Children with RSV infections are exposed to a variety of other respiratory viruses with a similar seasonal pattern. The study aimed to established if RSV coinfections contributed to severity of disease in pediatric patients seeking acute medical care at the Child Health Department of KBTH and PML Children Hospital in Accra.

Methods: Nasal swabs prospectively collected from symptomatic children less than 5 years of age were investigated for multiple viruses and RSV. Samples were also investigated for the presence of other viral agents.

Results: Twenty-eight children were enrolled from June to November 2021. RSV was confirmed in 9/28 (32%) of the children who were all below age 12 months. Among the RSV-positive group, infants <3 months old had a higher incidence of infection (67%, p<0.01). RSV A predominated 7/9 (78%) cases. One patient each tested positive for Influenza virus and SARS-CoV-2. Two patients (22%) were preterm and 5 (56%) had congenital abnormalities. The average length of stay on PICU was 19.11 days and 1 RSV death occurred.

Conclusions: RSV remained an important cause of severe respiratory illness during the COVID-19 outbreak in Accra. The PICU burden of RSV was heavy on infants during the first year of life. Interventions targeted against severe RSV disease are needed.

Keywords: Respiratory Syncytial Virus(RSV), Pediatric Intensive Care, Severe Respiratory Infections, Infants Hospitalizations, Ghana

Conflict of Interest: None declared
were more frequent in the RSV coinfection group (p<0.001). Duration of symptoms was longer for both RSV single and coinfections, lasting about 2 days longer in single infections. RSV single infection group was of a younger age than the coinfection group.

Conclusions: RSV coinfections were frequent among the study cohort. Overall RSV infection either alone or in combination with other viruses do not present greater severity but have mixed clinical features.

Keywords: Respiratory syncytial virus, viral coinfections, acute respiratory infections, hospitalized children, Ghana

Conflict of Interest: None declared

89. CLINICAL CHARACTERISTICS AND DISEASE BURDEN OF RESPIRATORY SYNCYTIAL VIRUS INFECTION AMONG HOSPITALIZED ADULTS IN THE VALENCIA REGION OF SPAIN, 2014 – 2019

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Background: Burden of disease of respiratory syncytial virus (RSV) in the adult population has not been well characterized. Studying this disease in adults is key to help establish public health policies and strategies for future vaccines.

Methods: A multicentre prospective observational study within the Valencia Hospital Surveillance Network for the Study of Influenza and Other Respiratory Viruses Diseases (VAHNSI, Spain) framework was conducted during 2014/2015-2016/2019. Adults ≥50 years of age admitted in hospital with a respiratory complaint were included in the study if meeting the influenza-like illness (ILI) case definition, and were tested by RT-PCR for RSV and other 7 respiratory viruses.

Results: From the 12,308 included patients, 4,201 (34%) were positive for any virus and 505 (4%: 12% of total positives) were RSV+. RSV positivity in people 50-64, 65-74, 75-79, 80-84, 85-89 and ≥90 was 3%, 3%, 4%, 5%, 4% and 5%, respectively (among positives, 10%, 10%, 13%, 14%, 12% and 14%). 92% of overall RSV+ had at least one chronic condition. The most frequently encountered comorbidities among RSV+ were heart disease (58%), bronchitis/EPOC/respiratory disease other than asthma (36%) and diabetes (31%).

Conclusions: RSV was responsible of 12% of viral ILI-hospitalizations in ≥50. 9/10 RSV+ were detected in adults with chronic conditions.

Keywords: RSV, Epidemiology, Adults
Funding: This study was partly funded by Fisabio, the FIE and Sanofi Pasteur.

Conflict of Interest: None declared

80. VIRAL CO-INFECTIONS IN PEDIATRIC HOSPITALIZATIONS WITH RESPIRATORY INFECTION DURING 5 SEASONS, 2014-2018, VALENCIA REGION (SPAIN)

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Background: We aim to investigate the rate, age pattern and severity of viral coinfections, as well as viruses involved in mixed infections, in children hospitalized with respiratory diseases.

Methods: A multicentre prospective observational study within the Valencia Hospital Surveillance Network for the Study of Influenza and Other Respiratory Viruses Diseases (VAHNSI, Spain) framework was conducted during 2014/2015-2018/2019. Children <5 years of age admitted in hospital with a respiratory complaint were included in the study if the respiratory symptoms had an onset within 7 days prior to admission and were tested by RT-PCR for RSV and other 7 respiratory viruses.

Results: From the 3,251 included patients, 2,175 (67%) were positive for any virus and 242 (7%; 11% of total positives) were viral coinfections. Coinfections rate decreased within age, being 8% and 3% in children of 0 and 4 years of age, respectively. The most frequent coinfection was RSV + Rhinovirus/Enterovirus (24% of total coinfections) followed by RSV + Coronavirus (19%). RSV was involved in 64% and Rhinovirus/Enterovirus in 50% of the total coinfections. No association was detected between viral coinfection and presence of comorbidities. Coinfections did not result in more severe cases (in terms of ICU and mechanical ventilation) in comparison to monoinfections.

Conclusions: Viral coinfections represented 11% of total viral detections in pediatric hospitalizations. RSV was the main causative, followed by Rhinovirus/Enterovirus.

Keywords: RSV, Epidemiology, children, coinfections
Funding: This study was partly funded by Fisabio, the FIE and Sanofi Pasteur.

Conflict of Interest: None declared
91. BURDEN OF RESPIRATORY SYNCYTIAL VIRUS (RSV) INFECTION AMONG ADULTS OVER 60 YEARS IN NURSING AND CARE HOMES: A SYSTEMATIC REVIEW

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Introduction: Respiratory syncytial virus (RSV) is a major cause of acute respiratory infections (ARI) in infants and older adults. Older adults in nursing and care homes (NCH) are vulnerable to severe RSV infection, morbidity and mortality.

Methods: We searched MEDLINE, EMBASE and Global Health databases to identify articles published between 2000 and 2022. Observational and experimental studies conducted among adults ≥60 years in NCH requiring assistive care and reporting RSV outbreaks or infections were included and relevant data were extracted.

Results: We screened 18,690 articles. Thirty were selected for full-text review and 18 included (sample size range: 42–1,469 and mean participant age: 67.6–88 years). Non-outbreak RSV disease incidence (n=11 studies) ranged from 0.5–8.9%, and prevalence (n=5) from 2–10%. Outbreak-related attack rates (n=7) ranged from 13.5–47.6%. RSV ARI (n=1) and lower respiratory tract infection (n=1) annual incidence rates were 4,580 and 3,040 cases per 100,000 respectively. Proportion of hospitalised RSV-ARI (n=3) ranged from 10.3–20%, length of stay (18.5 days [IQR: 14–37]). Non-outbreak case fatality ratio (n=3) ranged from 7.7–20%. Commonly reported chronic comorbidities among RSV cases (n=6) included COPD, heart failure, ischemic heart disease, coronary artery disease, hypertension, diabetes, kidney dysfunction, cerebrovascular accident, malignancies, dementia and Charlson comorbidity score > 6.5.

Conclusion: Data on RSV infection among NCH residents are limited and largely heterogeneous but document a high risk of illness, frequent hospitalisation and high mortality. Nationally representative epidemiologic studies and NCH-based viral pathogen surveillance are needed to assess the burden in this high-risk population.

Keywords: RSV, burden, outbreak, nursing and care home, older adults

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92. CIRCULATION PATTERN OF RESPIRATORY SYNCYTIAL VIRUS IN CHILDREN UNDER 2 YEARS OLD, IN MAPUTO, MOZAMBIQUE (2015-2018)

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Background: Respiratory Syncytial Virus-RSV is the leading cause of lower respiratory tract infections in children globally, with the highest burden in low-and middle-income countries where the association between RSV activity and climate remains unclear. This study aimed to describe the Circulation Pattern of RSV in Children under 2 years old, in Maputo 2015-2018.

Methods: Were included 1545 children under two-years old, with mild (ILI) and Severe Acute Respiratory Infection (SARI), 136 (8.8%) and 1409 (92%) were ILI and SARI children, respectively. Were collected samples of nasopharyngeal swabs. The RSV detection and typing were done using real-time qRT-PCR. Of all 368 RSV positive samples, 333 were typed.

Results: RSV was detected in 23.9% (368/1545) of all patients, of which 26% (367/1409) were SARI. The median age of RSV cases was lower than non-RSV cases [5 months (0-13), vs 10 months (0-23); p=0.047]. Among SARI cases, the positivity was higher in children under 6 months (40.6%, 185/456). Cough was two-times likely to occur in RSV patients than non-RSV [86.2% 352/366; OR=2.5 (1.4-4.4); p=0.001], and fever was recorded in 44% (158/358). The RSV positive rate varied between years. RSV A and RSV B co-circulated through the years, but only one predominated in each year. Analysis of RSV cases between SARI children showed higher detection rates occurring consistently in the first half of the year, but peaks and amplitude varied between epidemic seasons. The phylogenetics analyses revealed genotype GA2 for RSV A and genotype GBS for RSV B circulated in Maputo (2015 and 2018).

Keywords: Mild Acute Respiratory Infection, Severe Acute Respiratory Infection, Respiratory Syncytial Virus and Children

Conflict of Interest: No Conflict of Interest

93. INCIDENCE OF RSV IN ADULTS: A COMPREHENSIVE REVIEW OF OBSERVATIONAL STUDIES AND CRITICAL GAPS IN INFORMATION

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Background: RSV is an important cause of lower respiratory tract disease in adults overall and among those with underlying conditions. Understanding the disease burden can inform future vaccination strategies. We conducted a comprehensive literature review of observational studies reporting RSV incidence in adults globally, and highlight current evidence gaps.
Methods: PubMed and Embase were searched for English-language publications (2000-2022) and congress abstracts (2019-2021) reporting RSV incidence rates or incidence proportions. Cross-sectional studies, case series, and other designs estimating only the frequency of RSV in the population were excluded. The search included all geographic areas, and data were extracted by age group and underlying condition when available.

Results: Of 528 records identified, 37 primary studies were relevant to this analysis. Fifteen studies included or focused exclusively on the incidence of RSV in adult populations with underlying conditions. Approximately two-thirds of the studies reported RSV incidence in the hospital setting (Figure). Studies varied in their measurement of incidence; age categorizations and RSV incidence were highly variable within and between geographic regions. RSV incidence tended to increase with age and was highest in adults with underlying conditions. Additionally, most evidence was from high-income regions with few studies from low- and middle-income regions, particularly the Middle East, Central Europe, Central America, South America, and Africa.

Conclusion: Estimates of RSV incidence are highly variable across populations and geographies. Further research with well-defined case definitions is needed for accurate estimates of RSV incidence, particularly in the areas identified by the gap analysis.

Keywords: RSV; Literature Review; Incidence; Adults; Gap analysis

Conflict of Interest: Catherine Panozzo and Parinaz Ghaswalla are employees of Moderna, Inc., and holds stock/stock options in the company. Rhonda Bohn is an employee of Bohn Epidemiology, LLC. and was contracted by Moderna, Inc., to conduct this review. Benjamin Doty is a consultant at Bohn Epidemiology, LLC, and was contracted by Moderna, Inc., to conduct this review.

94. CLINICAL CHARACTERISTICS AND OUTCOMES OF RSV DISEASE BY SUBTYPE AMONG HOSPITALIZED CHILDREN UNDER 5 YEARS, NEW VIRUS SURVEILLANCE NETWORK (NVSN), UNITED STATES, 2016 – 2020

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Background: Respiratory syncytial virus (RSV) is a major cause of severe acute respiratory illness in young children [1, 2]. RSV can be categorized into two major antigenic subtypes (A and B), with multiple genotypes within each subtype [3-5]. Studies of the relationships between RSV subtypes and clinical severity are conflicting. [5]

Methods: We compared characteristics of RSV-positive children <5 years old hospitalized with fever and/or respiratory symptoms from December 01, 2016, to April 01, 2020 at seven surveillance sites by RSV subtype. Surveillance included parent/guardian interviews, medical chart review, and collection of mid-turbinate nasal and/or throat swabs for multipathogen assay (e.g., RSV, Rhinovirus, Adenovirus) testing by reverse transcription polymerase chain reaction among all children enrolled in NVSN.

Results: Among 3,941 hospitalized RSV-positive children aged <5 years, 2,281 (58%) had subtype RSV-A and 1,660 (42%) had subtype RSV-B infections. Patient characteristics and risk factors (e.g., race/ethnicity, smoking exposure in the home, underlying medical conditions) did not differ significantly by RSV subtype. Measures of illness severity (e.g., ICU admission, intubation, number of days in hospital) were not statistically different by RSV subtype. The most common symptoms were cough (99%) followed by congestion or runny nose (95%); no significant differences in symptoms by subtype were identified (Figure).

Conclusion: We found no evidence of significant differences in patient characteristics, disease severity, or clinical presentation between RSV subtypes A and B among children aged <5 years.
Keywords: RSV, RSV Subtypes, RSV-A, RSV-B, Children, Hospitalized, New Vaccine Surveillance Network, Disease severity, Clinical Outcomes

Conflict of Interest: Janet A. Englund reports support from AstraZeneca, GSK (GlaxoSmithKline), and Pfizer, Inc., and consulting fees from Sanofi Pasteur, Meissa Vaccines, and AstraZeneca. Natasha B. Halasa reports grant support from Sanofi Pasteur and Quidel and an education grant from Genetech. Christopher J. Harrison reports institutional support from GK Merck, and Pfizer, Inc., and honoraria from Pediatric News. Rangaraj Selvarangan reports grants from Hologic, BioFire Diagnostics, Becton Dickinson, Lumix, and Cepheid and serves on the GSK advisory board. Geoffrey A. Weinberg reports consulting fees from ReViral and honoraria from Merck for writing textbook chapters in the Merck Manual. John V. Williams reports grant support from the National Institutes of Health (for work unrelated to the report), consulting fees from Quidel’s scientific advisory board, and honorarium from the Infectious Disease of Children for a conference presentation, participation on a GSK independent data monitoring committee and on a data safety monitoring board for the National Institute of Allergy and Infectious Diseases IMPAACT Study.

95. EPIDEMIOLOGICAL CHARACTERIZATION AND MODELLING FOR SHORT-TERM PREDICTION OF BRONCHIOLITIS IN CATALONIA, SPAIN

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Since the COVID-19 pandemic began, the future epidemiology of the most common respiratory viral infections (RVI) is uncertain. The seasonal pre-pandemic respiratory syncytial virus (RSV) epidemic has changed its pattern after SARS-CoV-2’s irruption in 2020. In Catalonia, two under-pandemic epidemics started in May 2021 and October 2021, respectively, and the most recent wave in November 2022 has the greatest magnitude historically observed. Our aim was to characterize and predict RSV epidemics.

Epidemiological data of <5-year-old children with clinical bronchiolitis diagnoses were obtained from the public Primary Care Services Information System (SISAP) (September 2012-November 2022), and data from attended children with RSV infection were collected from the University Hospital Vall d’Hebron (September 2013-December 2021). With both systems, bronchiolitis related to RSV infections were estimated for modelling seasonal epidemics. The logistic model was adjusted for each RSV season. Successive fittings were carried out with incremental data to test the model’s predictive capacity, and the difference between predicted and real day of peak was calculated.

The logistic model successfully described RSV epidemics in Catalonia. For every studied season, the epidemic peak can be anticipated by 20 days with less than 7 days of error, and the peak’s magnitude was anticipated with less than 10% of error. Besides, the worst outcome corresponds to 2020-2021 and 2021-2022 seasons, which are precisely the under-pandemic ones (Figure 1).

The current dynamics are reminiscent of pre-pandemic seasons.

Keywords: Respiratory Syncytial Virus, RSV, mathematical models, logistic equation, epidemiology, bronchiolitis

Conflict of Interest: None declared

Figure 1. Pointed in red, the 7-days moving average of the estimated epidemiological data of bronchiolitis caused by RSV. Dashed in blue, the logistic model adjusted to the data. The blue areas correspond to the confidence intervals of the model. For (A) seasons 2012-2013 to 2016-2017 and (B) seasons 2017-2018 to the yet uncompleted 2022-2023.
96. SEASONALITY OF RESPIRATORY SYNCYTIAL VIRUS INFECTION IN INFANTS AND YOUNG CHILDREN IN LUSAKA, ZAMBIA

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Introduction: Respiratory Syncytial Virus (RSV) is the leading cause of acute lower respiratory infections in young children. RSV is considered to be a seasonal pathogen, though seasonality data are sparse from African countries.

Methods: We examined RSV infection longitudinally by leveraging previously collected data from four studies based in Lusaka, Zambia: PERCH, SAMIPS, ZPRIME and the Mobile Bedside Ultrasound for the Diagnosis of Pediatric Pneumonia (mBSUS) study. In each study, we collected nasopharyngeal swabs on infants and young children. RSV positivity was confirmed using singleplex RT-PCR with a cycle threshold value ≤40. We report RSV prevalence in Lusaka by month over most of an eight-year span.

Results: We have observed that the patterns of RSV seasonality in Lusaka are variable, with somewhat predictable “starts” of the RSV season being in the winter and early start of spring. Counts of RSV are highest in the rainy season (February-April) and tend to decline during the cool dry season (May to August). The lowest counts of RSV infection occurred in the hot dry season (September to November). In 2020, we observed a delayed onset of RSV “season” which may be a consequence of COVID-related lockdowns.

Conclusions: By understanding the seasonality of RSV transmission, we can optimize strategies for preventing RSV infection and improving the outcomes of these infections among the most vulnerable infants.

Keywords: Respiratory Syncytial Virus, immunization, seasonality, public health

Conflict of Interest: None declared.

97. SURVEILLANCE AND EVOLUTION OF HUMAN RESPIRATORY SYNCYTIAL VIRUS BY WHOLE GENOME SEQUENCING DURING THE 2015-2022 SEASONS IN BARCELONA, SPAIN

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Background: Human respiratory syncytial virus (HRSV) causes a major health problem, being the most important aetiologic agent of lower respiratory tract infections in children.

Methods: Respiratory specimens from patients with acute respiratory infection were collected from October/2013 to May/2022 at Hospital Universitari Vall d’Hebron. Whole-genome sequencing was performed in randomly-selected samples.

Results: 102,064 specimens were collected, of which 5,925 (5.8%) were HRSV laboratory-confirmed. HRSV showed a marked seasonality, which only changed upon the SARS-CoV-2 pandemic, not circulating during 2020-2021 winter, and describing an unexpected peak during summer 2021. Both genetic groups (HRSV-A and HRSV-B) co-circulated showing a triennial shift in predominance BBBA. A total of 315 whole-genome sequences (181 HRSV-A and 134 HRSV-B) were obtained. All HRSV-A genomes belonged to ON1 genotype, and all HRSV-B, to BA (132 BA9 and 2 BA10). Within the antigenic site II (F protein), no mutations seemed to be fixed in the viral population, and no palivizumab-resistance-related mutations were reported. Within the antigenic site Ø, the epitope for nirsevimab, K65R increased in prevalence in HRSV-A; while I206M and Q209R became fixed and S211N increased in prevalence in HRSV-B, none related to reduced susceptibility to nirsevimab.

Conclusions: HRSV presents a significant prevalence in our hospital. Though presenting a clear seasonality, SARS-CoV-2 pandemic displaced the HRSV’s epidemic peak during the 2020-2021 season. No known mutations associated with monoclonal antibodies resistance were reported. Due to the imminent widespread administration of nirsevimab to the youngest population, HRSV genomic surveillance must be strengthened to monitor potential circulating escape mutant viruses.

Keywords: epidemiology, palivizumab, nirsevimab, mutations, evolution

Conflict of Interest: None declared.
98. INFLUENZA AND OTHER RESPIRATORY VIRUSES' EPIDEMIOLOGY DURING THE COVID-19 PANDEMIC

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Background: Respiratory viral illnesses have decreased significantly since the COVID-19 pandemic. A very few flu cases have been documented over the globe. We performed cross-sectional study at the National Influenza Center (NIC) in Pune, India. Objective: To determine the epidemiological change in influenza and other respiratory tract viruses from the nasopharyngeal swab samples collected during the COVID-19 period. Methods: We investigated nasopharyngeal swabs for respiratory viruses between January 2020 and March 2022 during the two years of the pandemic in Pune, India. Multiplex real-time PCR was used to detect the respiratory viruses viz. influenza A, B, influenza A H1N1, rhinovirus/enterovirus, parainfluenza (PIV) 1, 2, 3, 4, human metapneumovirus, respiratory syncytial virus (RSV) A/B, and adenovirus. Results: Retrospectively analyzed the results of 4894 NS samples. The average age of 2885 (58.9%) male and 2009 (41.1%) female patients between the ages of 0–92 was 34.8 years. The maximum number of participants (31%) were between 15 and 45 years of age. A total 1391 (28.4%) of the samples were positive for viruses. SARS-CoV-2 was the most common virus, with 683 (14%), in all age groups. RSV was the next common viral pathogen seen among 351 (7%) of cases, mostly pediatric. The influenza positivity rate during the two years of the pandemic was very minimum of 3.8%. In the rest of the ORV, the percent positivity was below 2%. Conclusion: Findings showed that the epidemiology of respiratory viruses changed significantly during the pandemic. Flu activity has dropped dramatically and rise in RSV was noted.

Keywords: Influenza, RSV, COVID surveillance, Respiratory viral illnesses

Conflict of Interest: None declared

99. ASSOCIATION BETWEEN SOCIAL VULNERABILITY INDEX SCORE AND OUTCOMES IN CHILDREN <2 YEARS OLD WITH RESPIRATORY SYNCYTIAL VIRUS

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Background: Respiratory syncytial virus (RSV) is a common cause of childhood morbidity and mortality. Children with a high social vulnerability index (SVI) score are potentially disproportionately affected. Our aim is to determine the association between SVI score and clinical outcomes in children <2 years old with RSV.

Methods: We retrieved the records of all patients at Vanderbilt University Medical Center tested using the BioFire FilmArray Respiratory 2.0 Panel, which is a provider-ordered multiplex PCR assay for common respiratory pathogens, including RSV. We included children <2 years old who tested positive for RSV. Any child who presented >14 days following a previous presentation was considered a distinct case.

Results: From 1/2018 to 11/2022, 59,719 patients were tested, and 16,025 (26.8%) were <2 years old, of whom 2,390 (14.9%) were RSV-positive. We used the two-sample t-test with unequal variances to compare the 2020 SVI score—retrieved using address data—by clinical outcomes.

Conclusion: Children <2 years old with RSV who reside in census tracts with higher social vulnerability had worse outcomes. Further studies are required to explore this disparity.

Keywords: RSV, Social Vulnerability Index Score, RSV outcomes, Intubation, ICU admission

Conflict of Interest: Natasha B. Halasa reports grant support from Sanofi Pasteur and Quidel and an education grant from Genetech.

100. RESPIRATORY SYNCYTIAL VIRUS SEASONALITY DURING AND AFTER THE COVID-19 PANDEMIC IN THREE LMIC SETTINGS

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Background: During the COVID-19 pandemic the epidemiology of respiratory syncytial virus (RSV) has significantly changed in many high income countries. However, little is known about post-COVID-19 RSV seasonality in low- and middle-income countries (LMICs). The RSV GOLD III - ICU Network study aims to describe clinical, demographic and socioeconomic characteristics of children admitted to the pediatric intensive care unit (PICU) in 10 LMICs and provided a good opportunity to describe post-COVID-19 RSV seasonality.
Methods: Children <2 years of age with respiratory symptoms fulfilling the WHO “extended severe acute respiratory infection (SARI)” criteria are tested for RSV during two local RSV seasons. Epidemiology and clinical characteristics of children at three study sites (Ghana, Nepal and Nigeria) that have already finished two study seasons are compared.

Results: Between April 2021 – November 2022, a total of 1319 children have been tested for RSV. Of these, 326 (25%) were RSV-positive. While in Ghana no seasonal changes have occurred, a minor delay in Nepal (6 weeks) and a major delay in Nigeria (4 months) has been observed in 2022. Children being admitted post-COVID were older than those during the first RSV study season in 2021 (median age 178 days vs. 85 days). Presence of comorbidities and length of stay were similar.

Conclusions: We observed variable shifts in RSV seasonality in 3 LMICs after the COVID-19 pandemic although non-pharmaceutical interventions were less used in these countries. Data from other LMICs are needed to clarify to what extent COVID-19 has changed seasonality in these countries.

Keywords: Respiratory syncytial virus; LMICs; COVID-19; Epidemiology; Seasonality

Conflict of Interest: LJB has regular interaction with pharmaceutical and other industrial partners. She has not received personal fees or other personal benefits. LJB is chair and expert board member of the ReSViNET Foundation. NIM has regular interaction with pharmaceutical and other industrial partners. She has not received personal fees or other personal benefits. HN reports grants from Innovative Medicines Initiative and National Institute of Health Research; personal fees and grants from WHO and Sanofi; and personal fees from the Bill & Melinda Gates Foundation, Janssen, Abbvie, and Revival.


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Background: In Brazil, RSV monitoring is carried out using the reporting system for hospitalized acute respiratory distress syndrome (ARDS), initially designed for Influenza surveillance; therefore, many infants infected by RSV may not be tested.

Objective: We assessed time trends in RSV hospitalization rates among Brazilian infants in the last 10 years.

Methods: This retrospective study includes all hospitalized ARDS cases in infants <2 years in Brazil between 2013-2022 with lab-confirmed RSV infection (78% confirmed by PCR). Hospitalization rates were estimated by 100,000 persons, using population denominators from the Brazilian Institute of Geography and Statistics. Joinpoint regression model was used to estimate annual percent changes (APC) in rates (2013-2022) and corresponding 95% confidence intervals (95% CI).

Results: 40,542 hospitalized RSV cases were reported. Significant increasing trends in RSV hospitalization rates were registered in Brazil (APC=+32.8%, 95% CI +19.8; +47.3%), and in the Northeast (APC=+49.9%, 95% CI +30.1; +72.7%), Midwest (APC=+35.0%, 95% CI +10.0; +65.6%), and Northeast (APC=+27.1%, 95% CI +13.6; +42.1%) regions. Higher hospitalization rates post-COVID-2022 (2021-2022) were observed in South (399.5/100,000) and Midwest regions (259.6/100,000), followed by those registered in the Southeast (136.6/100,000), Northeast (53.8/100,000), and North (37.1/100,000). A higher percentage of RSV cases reported by public hospitals was noted in 2021 (post-COVID-19 =57.9%) compared to 2019 (pre-COVID-19=47%).

Conclusions: The COVID-19 pandemic and the need for differential diagnosis for other causes of respiratory illness have likely caused an increase in RSV testing and reporting. This scenario may support RSV awareness, revealing the actual burden on infants in Brazil.

Keywords: Respiratory Syncytial Virus Infections, public health surveillance, infants, hospitalization/trends, Brazil

Conflict of Interest: Karina Braga Ribeiro, Sheila Homsani, Aline Tolardo = Sanofi, Vaccines Unit = employees

102. RSV DEATH PREDICTORS AMONG BRAZILIAN HEALTHY FULL-TERM INFANTS – FINDINGS FOR ASSERTIVE PUBLIC HEALTH INTERVENTIONS

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Background: Recent evidence shows that the respiratory syncytial virus (RSV) significantly affects healthy full-term babies. This study aimed to identify predictors of death among healthy infants in Brazil.

Methods: This is a retrospective cohort study of all hospitalized acute respiratory distress syndrome (ARDS) cases in healthy full-term infants <2 years of age in Brazil between 2019-2022 with lab-confirmed RSV infection retrieved from the national surveillance system (SIVEP-Gripe) (n=12,916).

We assessed age, sex, race/ethnicity, birth out of the RSV season, symptoms, type of hospital, hospital region, ventilatory support, and ICU admission. Chi-square test was used to evaluate the association between variables and death. Logistic regression was used to estimate crude and adjusted odds ratios (aOR) and 95% confidence intervals.

Results: 141 deaths were registered. In the univariate analysis race/ethnicity (p<0.001), dyspnea (p=0.015), cough (p=0.015), hospital region (p<0.001), ventilatory support (p<0.001), and ICU admission (p<0.001) were significantly associated with death. Multivariate model identified ventilatory support (Non-invasive, aOR=2.38, 95% CI 1.16-4.89; Invasive, aOR=14.13, 95% CI 6.61-30.18), ICU admission (yes, aOR=1.75, 95% CI 1.15-2.67), and hospital region (Northeast vs South, aOR=3.59, 95% CI 1.91-6.75; North vs South, aOR=2.88, 95% CI 1.44-5.74) as independent predictors of death. Compared to white, indigenous presented a marginal increased risk of death (aOR=2.87, 95% CI 0.87-9.42).

Conclusions: Indigenous infants and those hospitalized with RSV in regions North and Northeast are at a higher risk of death. Assertive public health interventions are required to reduce disparities in outcomes among healthy full-term infants affected by RSV.

Keywords: Respiratory Syncytial Viruses, infant, term birth, death, risk factors, Brazil

Conflict of Interest: Karina Braga Ribeiro, Aline Tolardo, and Sheila Homsani = Sanofi, Vaccines = employees

103. MATERNAL RISK FACTORS FOR RESPIRATORY SYNCTIAL VIRUS LOWER RESPIRATORY TRACT INFECTION (LRTI) IN OTHERWISE HEALTHY PRETERM AND TERM INFANTS – A SYSTEMATIC REVIEW

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Background: Maternal risk factors, such as smoking while pregnant, can contribute significantly to the risk of an infant having RSV-LRTI. To date, no formal assessment of all maternal risk factors for RSV-LRTI in infants has been published.
Objective: To undertake a systematic literature review (SLR) to answer the research question: What maternal risk factors are associated with an increased risk of RSV-LRTI in infants?

Methods: The SLR used systematic and explicit methods to identify, select, and critically appraise relevant research, and to collect, analyse and report data from the included studies according to the PRISMA guidelines. The PubMed (Medline), Embase, and Cochrane Library databases were searched (November 2022) using the following search terms (combined with “Medical Subject Headings” [MeSH] in PubMed and “Subject Headings” in Embase): (1) “Respiratory syncytial virus”, RSV, “lower respiratory tract infection”, bronchiolitis, “acute respiratory tract infection”, LRTI, LRI, ARTI, ARI, ALRI; AND (2) risk, risk factor*; AND (3) pregnant, woman, women, maternal, pregnant*, gestation. Study inclusion/exclusion criteria are shown in Table 1.

Results: A total of 3130 citations were identified from the three databases (PubMed: 1172, EMBASE: 1729; Cochrane: 229), of which, after removal of duplicates, 2349 were reviewed. Screening by title and abstract removed 1902 citations, with 447 undergoing full paper review.

Conclusions: A greater understanding of maternal risk factors and their relative contribution to RSV-LRTI in infants will enable more accurate assessments of the impact of preventive strategies. The full results of the SLR will be presented for the first time at RSVVV’23.

Keywords: RSV; risk factors; pregnancy; perinatal; maternal

Conflict of Interest: PM has received research funding and/or compensation as advisor/lecturer from AbbVie, AstraZeneca, Janssen Pharmaceuticals, Medimmune, and Sanofi and is a member of RESVINET. ML has received research funding and/or compensation as advisor/lecturer from AbbVie, AstraZeneca, and Sanofi. RI and EAM are employees of Pfizer and may hold stock in Pfizer. BRG and NW employers have received payment from AbbVie and AstraZeneca for work on various projects. EV and BM have nothing relevant to disclose.

104. THE ROLE OF BACTERIAL CO-INFECTIONS IN THE SEVERITY OF HOSPITALIZED ACUTE RESPIRATORY INFECTIONS AMONG CHILDREN INFECTED WITH RESPIRATORY SYNCYTIAL VIRUS

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7. EpiUnit, Instituto de Saúde Pública, Universidade de Porto.

VigRSV network:

Background: During autumn/winter respiratory syncytial virus (RSV) epidemics, bacterial co-infection is common and affects the severity of disease. However, there is limited understanding on the relationship between RSV-bacterial co-infections and clinical severity during off-season epidemics.

Methods: We conducted a prospective, sentinel surveillance study at 20 sites in Portugal, in children < 2 years hospitalized with RSV, during April 2021-October 2022. The effect of testing positive for bacteria on the length of hospitalization and disease severity (defined by the need for ventilation or admission to an intensive care unit) was investigated using multivariate linear and logistic regression models. Age group (<6 months, >6 months) and prematurity (yes, no) were included in models as potential confounders.

Results: We report two RSV off-season epidemics: June 2021-February 2022 and May-October 2022. Among 403 RSV hospitalizations, 63% occurred in children < 6 months and 17% in pre-term; 24% tested positive for bacteria; median length of hospitalization was 5 days (interquartile range, 3-7 days); 11% had severe disease. Most common bacteria were Haemophilus influenzae and Streptococcus pneumoniae. Children who tested positive for bacteria had an increase of 3.4 days in hospitalization length (p<0.01) and a 12-fold risk of having severe disease (risk ratio: 12.3, 95% confidence interval: 6.3-24.3).

Conclusion: RSV-bacterial co-infection was associated with increased length of hospitalization and severe illness during off-season epidemics. This risk is probably overestimated as laboratory testing for bacterial infections is usually higher in severely ill-appearing children. Measures to prevent outgrowth of pathogenic bacteria within the respiratory tract should be discussed.

Keywords: Respiratory Syncytial Virus infections/epidemiology; Respiratory Syncytial Virus Infections/prevention and control; Respiratory Syncytial Virus, Human

Conflict of Interest: Inês Azevedo has received fees, not directly related to this work, from Sanofi Vaccines Portugal as a speaker for presenting data on RSV infections in Portugal at medical conferences, has received financial support from Sanofi Vaccines Portugal to attend online medical meetings and is President of the Portuguese Paediatric Society. Teresa Bandeira received fees, not directly related to this work, from Sanofi Vaccines Portugal as a speaker for presenting data on RSV infections and preventing measures at medical conferences and meetings in Portugal, and has received financial support from Sanofi Vaccines Portugal to attend medical meetings in Portugal. Ana Paula Rodrigues has received fees, not directly related to this work, from AstraZeneca as a speaker for presenting data on RSV infections in Portugal at medical conferences.
105. RSV INFECTION AND CLINICAL OUTCOMES AMONG PEDIATRIC HEMATOPOIETIC CELL RECIPIENTS (HCT) AND SOLID ORGAN TRANSPLANT RECIPIENTS (SOT): A MULTI-SITE U.S. STUDY

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Background: RSV is one of the most common causes of lower respiratory tract infection in children. Patients undergoing transplant are at increased risk for severe disease.

Methods: Pediatric (< 18 years old at transplant) HCT and SOT recipients from 22 U.S. transplant centers who underwent transplant (2010-2019) and had RSV detected within 365 days of transplant were eligible. Descriptive statistics were used to characterize the clinical course and outcomes of RSV infection.

Results: Among 311 patients, 199 received HCT, and 112 SOT. Over half (55.6%) were male, Caucasian (57.0%) with a median age of 4 years old. Most HCT recipients underwent allogeneic transplant with 137 (69.2%) receiving a myeloablative conditioning, and 47 (24.4%) t-cell depletion. Among SOT recipients, the most transplants were liver (41%), heart (28.6%), and kidney (23.2%). Over 50% reported RSV related hospitalization, 63 (20.4%) in <1 month, 135(21.1%) in 1 month, 100(15.6%) in 2 months, 54(8.4%) in 3 months and 45(7.0%) in 4 months. The rest of children from 5 months till 24 months represented 228 individuals (35.6%).

Three deaths (1%) related to RSV were reported. Conclusion: RSV is associated with high rates of hospitalization and lower respiratory tract infection. Further studies to determine the risk factors for severe disease and poor clinical outcomes are needed to guide preventive and early therapeutical interventions.

Keywords: RSV, respiratory tract infection, pediatrics, pediatric immunocompromised, pediatric transplantation, transplantation, Pediatric Hematopoietic Cell Recipients, Pediatric solid organ Recipients

Conflict of Interest: None declared

106. PHYLOGENETIC ANALYSIS OF RSV IN CHILDREN UNDER 5 YEARS OLD WITH SUSPECTED SARS-COV2 AT BAHRAAMI CHILDREN’S HOSPITAL, TEHRAN, IRAN FROM JANUARY TO MAY 2022

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Human respiratory syncytial virus (RSV) is a major cause of acute lower respiratory tract infections in children. The COVID-19 pandemic and strict restrictions have impacted the spread and transmission of RSV, and subsequently the rate of hospital admissions among children at a young age. Therefore, the prevalence of RSV and the circulating genotypes need to be updated. Between January and May 2022, nasopharyngeal swabs were taken from 196 children under 5 years old with suspected SARS-CoV2 at the pediatric ward of Bahrami Children’s Hospital in Tehran. All samples were analyzed with a real-time PCR assay using the Tagman RT-PCR kit to confirm viral infection. RSV-positive specimens were tested for the HRSV-G gene using a conventional one-step RT-PCR kit. The HRSV-G gene was sequenced and virus genotypes were confirmed by phylogenetic analysis by the MEGA X program. Of the 196 specimens suspected of having SARS-CoV2 (114 inpatients and 82 outpatients), SARS-CoV2 and RSV were detected in 24 (12.24%) and 23 (11.73%), respectively. Approximately 70% of the RSV-positive specimens were children under one-year-old and hospitalized. Among the RSV-positive cases, 52.2% were male and 47.8% were female. Common symptoms in RSV-positive patients were fever, cough, and dyspnea. By the time the abstract was submitted, 10 samples had been sequenced. According to phylogenetic analysis, all belonged to RSV-A strains and were assigned to the ON1 genotype. Continuous and long-term molecular-epidemiological surveys for the early detection of circulating and emerging genotypes are necessary to gain a better understanding of their epidemic potential.

Keywords: RSV, Phylogenetic analysis, ON1 genotype, children, Outpatient, Hospitalized, SARS-CoV2, Iran

Conflict of Interest: None declared

107. DIFFERENCES IN THE HOSPITALIZATION BURDEN CAUSED BY RSV IN CHILDREN <2 YEARS OLD. A 10 YEAR TIME SERIES

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Background: RSV is an especially dangerous virus in the first two years of a child’s life. However, there are differences within this age group, with younger children being at higher risk of hospitalization due to complications. The objective of this study is to analyze the differences in the burden of hospitalization for laboratory-confirmed RSV in <2 years in a period of 10 years.

Methods: We conducted a retrospective and descriptive study analyzing the number of laboratory-confirmed cases of RSV infection in hospitalized children <2 years at the Hospital Clínico Universitario de Valladolid (Spain) in the 2010-2019 period. The median and IQR of the number of hospitalized cases in this period were analyzed in each month of the first two years of life of children.

Results: In the 10 years analyzed, a total of 641 hospitalizations with laboratory-confirmed RSV infection were analyzed in children <2 years; 78(12.3%) in <1 month, 135(21.1%) in 1 month, 100(15.6%) in 2 months, 54(8.4%) in 3 months and 45(7.0%) in 4 months. The rest of children from 5 months to 24 months represented 228 individuals (35.6%).

Conclusions: The greatest burden of hospitalization in children <2 years occurs in the first 4 months of life, with 64.4% of hospitalizations occurring in this age group. These data show that these children could be the most benefited through actions such as the use of passive immunization through monoclonal antibodies, as well as vaccinating the pregnant mother to protect the baby during lactation.

Keywords: Respiratory Syncytial Virus; Burden of hospitalization; Children;

Conflict of Interest: The authors confirm no conflict of interest
108. EPIDEMIOLOGY OF HOSPITALIZATIONS WITH LAB-CONFIRMED RSV INFECTION IN DIFFERENT AGE GROUPS: A 12-YEAR TIME SERIES

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Background: RSV is a virus that affects both the youngest and the oldest. However, there is a lack of studies that clearly show the relative hospitalization burden caused by this virus in different age groups.

Methods: We conducted a retrospective and descriptive study analyzing the number of laboratory-confirmed cases of RSV infection in hospitalized at the Hospital Clínico Universitario de Valladolid (Spain) in the 2010-2021 period. The variables of the date of diagnosis and age were collected from the microbiology databases. A descriptive analysis was performed in five age groups: 0-2 years, 3-5 years, 6-17 years, 18-59 years, and ≥60 years.

Results: In the 12 years analyzed, a total of 1,183 hospitalizations with laboratory-confirmed RSV infection were analyzed; 733(62.0%) in 0-2 years, 337(28.0%) in 3-5 years, 16(1.4%) in 6-17 years, 50(4.2%) in 18-59 years and 301(25.4%) in ≥60 years. In the 0-2 group, a significant increase in hospitalization was observed in most years in November, while in ≥60 years this increase occurs about two months later, around February. The rest of the age groups do not show a significant hospitalization burden.

Conclusions: In the 12 years analyzed, 87.4% of RSV hospitalizations occurred in aged 0-2 years and in ≥60 years, with children being the group with the greatest burden. The hospitalizations in children aged 0-2 years precede the cases in ≥60 by two months, so there seems to be a pattern that is probably related to coexistence at Christmas and to the care of the children by the grandparents.

Keywords: Respiratory Syncytial Virus; Hospitalization burden; Children; Elderly;

Conflict of Interest: The authors declare no conflict of interest.

109. DETERMINING THE TRUE INCIDENCE OF SEASONAL RESPIRATORY SYNCYTIAL VIRUS-CONFIRMED HOSPITALISATIONS IN PRETERM AND TERM INFANTS IN WESTERN AUSTRALIA

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Background: Acute lower respiratory infections caused by respiratory syncytial virus (RSV) contribute to significant morbidity and mortality in infants and other at-risk groups such as preterm infants <33 weeks gestational age (wGA). We used a previously developed statistical prediction model to estimate RSV-hospitalisation rates in the first year of life by birth month and degree of prematurity.

Methods: We analysed observational, population-based cohort data using probabilistically linked state-wide health data, including birth records, perinatal and death registry data, hospital admissions, and respiratory microbiology testing data from 2000 - 2012. Predicted incidence rates of the first RSV-confirmed hospitalisation were calculated as rates per 1000 child-years by degree of prematurity (<28 weeks wGA, 29-32 wGA, 33-36 wGA, ≥37 wGA), birth month (January to December), and calendar age sub-groups (<6 months, 6-12 months) in infants.

Results: The cohort consisted of 367,728 infants and 272,013 admissions, of which 20,730 (20.7%) admissions temporally linked to an RSV testing record, and 5,800 (28.0%) were positive. Overall, predicted RSV-hospitalisation rates were highest in autumn-born births (March-May) in infants aged <6 months (56-
73/1,000 child-years) and varied with degree of prematurity. Preterm infants born at 29-32 wGA between March-May had the highest RSV-hospitalisation rates (267-311/1,000 child-years), whereas infants born >33 wGA had peak RSV-hospitalisation rates in birth months May-June, similar to term births.

Conclusion: RSV-hospitalisation burden is highly seasonal and varies with degree of prematurity. Accurate estimates of RSV-hospitalisation in high-risk subgroups are essential to inform the optimal timing by birth month for close-to-market RSV vaccines and antibody treatments.

Keywords: Respiratory syncytial virus, prematurity, hospitalisation, seasonal trends, infants, palivizumab, niruvimab

Conflict of Interest: Acknowledgement: Supported in part by a research grant from Investigator Initiated Studies Program of Merck Sharp & Dohme (Australia). The opinions expressed in this paper are those of the authors and do not necessarily represent those of Merck Sharp & Dohme (Australia).

### 110. MALNUTRITION AND THE DEVELOPMENT OF SEVERE OR VERY SEVERE RSV LRTI IN INDIAN CHILDREN: A COHORT STUDY IN MEGLHAT TRIBAL AREA OF INDIA.

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3. National Institute of Virology, Indian Council of Medical Research, Pune, India;
4. Colorado School of Public Health, Aurora, CO, USA.

Background: RSV is important cause of severe lower respiratory tract infection (LRTI) and LRTI mortality globally. Malnutrition as a risk factor for severe RSV LRTI is unclear.

Methods: Active surveillance of children younger than 2 years of age (U2C), with weekly home visits was conducted in 93 villages and all hospitals of Melghat, India for acute LRTI, from 2016 to 2020. We collected nasopharyngeal swabs from U2C with severe LRTIs and all who died, and did RTPCR for respiratory viruses. Periodic anthropometry of all U2C in the entire cohort were measured. The WHO Anthro Analyzer Tool was used to calculate z-scores of weights for age (WFA). The growth trajectories of U2C with severe RSV LRTI were compared with those of 5 control U2C. A regression model of quadratic growth was used to estimate a fitted curve and 95% CIs for both the RSV LRTI cases and controls. A secondary analysis compared the growth trajectories of the cases with controls.

Results: We compared 477 RSV cases with 5542 controls. 140/477 (29.4%) U2C with RSV LRTI had a WFA <-3z compared to the control U2C 897/5542 (16.2%), p-value < .000001. The growth trajectories are shown in Figure 1. The control group shows z-score below zero starting at around -1.5 at birth and dropping to -2 at 24 months. RSV LRI cases demonstrate a significantly lower z-score, also showing a decline over 24 months of life.

Conclusions: Even in severely malnourished children (SMC), the most SMC tend to get the most severe RSV LRTI.

Keywords: Growth trajectories, LRTI, Malnutrition, RSV

Conflict of Interest: EAFS reports grants to the institution from AbbVie, AstraZeneca, Bill and Melinda Gates Foundation, Merck, Pfizer, Regeneron and Roche, and consulting fees paid to the institution from Alere Cidara, Merck, Pfizer and Sanofi Pasteur. All other authors report no disclosures and no conflicts of interest.

### 111. ESTIMATING UNDER-RECOGNIZED RSV INFECTIONS AMONG CHILDREN WITH ACUTE RESPIRATORY ILLNESS IN AN EMERGENCY DEPARTMENT

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Background: Respiratory syncytial virus (RSV) infection is a leading cause of acute respiratory illness (ARI) in children. Published estimates based on ICD-10 codes and standard of care (SOC) testing might underestimate RSV burden without appropriate adjustment for limited testing and coding.

Methods: We conducted prospective, year-round, active surveillance with laboratory confirmation of RSV infection in children with ARI seen in Children’s Mercy Kansas City emergency department (ED) during 2017-2021. Medical chart reviews for ICD-10 codes were compared with surveillance-based (SB) RSV testing to estimate sensitivity and specificity of ICD-10 codes (RSV codes J12.1, J20.3, J21.0 and J01.4; ARI codes J06; J11; J12; J18; J20; J21; J22) for RSV infection. RSV detection rates were compared between SOC versus SB RSV testing.

Results: Among 4464 children enrolled in an ED setting, 4323 (96.8%) had SB RSV test results. RSV was detected in 557 (12.9%) children; detections were more frequent in 1162 children <1 year of age (18.3%) than 3161 children >1 year of age (10.9%). RSV ICD-10 codes were less sensitive (20.8%) and more specific (99.8%) than ARI ICD-10 codes for RSV infection (64.1% and 62.6%, respectively) (Table 1). RSV was detected in 109 of 315 children who received SOC testing, which represented only 19.6% of 557 RSV detections by SB testing.

Conclusion: RSV ICD-10 codes and SOC testing underestimated RSV infections in ARI children receiving care in an ED setting. Active surveillance with SB testing could improve estimation of RSV rates in children to support vaccine and prophylaxis efforts.

Keywords: RSV, Children, Emergency Department, ICD-10, Laboratory Testing

Conflict of Interest: None declared
### 112. PREVALENCE AND PREDICTORS OF RESPIRATORY SYNCTIAL VIRUS AMONG CHILDREN PRESENTING WITH ACUTE RESPIRATORY INFECTIONS ON THE ALONG KENYA-UGANDA BORDER

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Acute respiratory infections (ARIs) are a leading cause of under-five mortality globally. East Africa in general, the reported prevalence of respiratory syncytial virus (RSV) infections has varied widely. Our study sought to determine the prevalence of RSV infection in children admitted with ARI fulfilling the WHO criteria for bronchiolitis. Additionally, predictors of RSV in the cross border population residing within the study site were established. This was a prospective cross-sectional prevalence study in 10 hospitals that lie within 45KM of the Kenyan-Ugandan border on either sides of the countries. Five hospitals on either side were sampled. Six hundred and twenty five children were enrolled. The overall RSV positive rate was 10.2%, was reported. Age, religion, parity and income status were strongly associated with RSV status of the children. Health system factors seemed to play a key role in determining disease outcomes in children.

**Keywords:** Prevalence, Predictors, RSV

**Conflict of Interest:** None declared

### 115. RESPIRATORY SYNCTIAL VIRUS (RSV) INFECTION IN INFANTS AND QUALITY OF LIFE OF FAMILIES – A MULTI-COUNTRY STUDY

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Background: RSV infection in infants not only affects the child itself, but also their parents and caregivers. Sufficient information on the overall impact and burden of the disease on the entire family is scarce.

Aim: The primary objective of the study is to investigate the health-related quality of life of parents and/or caregivers of children hospitalised for RSV with a comprehensive caregiver-specific approach in Germany, France, Italy and Sweden.

Methods: The multi-country observational study is specifically addressed to parents and caregivers of children aged < 24 months hospitalised for RSV. Children’s comorbidities and symptoms, health-related quality of life of the family (via the PedsQLTM FIM) and related dimensions are assessed during the hospital stay or shortly after as well as six weeks later again.

Results: The study is currently in the recruitment process which is taking place from September 2022 until May 2023. For this abstract, interim analysis of preliminary data will be presented.

Discussion: The results will contribute to acquiring new knowledge on the burden of RSV and its multidimensional impact on affected families and thereby help raise awareness for the virus infection in young populations, its consequences and challenges for the family and their social network.

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**Keywords:** Respiratory syncytial virus, RSV, quality of life, parents, infants, children

**Conflict of Interest:** The authors declare no personal conflict of interest. EFCNI received a research grant from Sanofi in support of this independent study.

### 116. RESPIRATORY SYNCTIAL VIRUS AND UNSPECIFIED BRONCHIOLITIS MORTALITY IN BRAZIL, 2000-2021: A HIDDEN DISEASE BURDEN AMONG HEALTHY INFANTS?

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Background: In developing countries, acute respiratory infections are a significant public health problem, responsible for one-third of deaths in children. In Brazil, few studies demonstrate respiratory morbidity and mortality associated with RSV in infants.

Objective: We aimed to describe deaths caused by RSV or unspecified bronchiolitis among Brazilian infants.

Methods: This is a descriptive epidemiological study based on the National Mortality System, including all deaths with RSV or unspecified bronchiolitis (ICD J12.0, J20.5, and J21.9) cited as the underlying cause, occurring in infants <1 year between 2000-2021. We evaluated the frequency of prematurity (P05–P07), chronic lung disease (P19–P29), and congenital heart disease (Q20–Q28) as associated causes of death, as well as gestational age.

Results: 973,276 deaths were registered. RSV and unspecified bronchiolitis were the underlying cause on 413 and 3614 infants, respectively. Chronic lung disease, congenital cardiopathies, and prematurity codes were contributing factors in < 10% of the deaths caused by RSV or unspecified bronchiolitis. In addition, 51.1% and 43.7% of RSV and bronchiolitis deaths occurred in full-term babies. The peak of RSV and bronchiolitis deaths occurred in June and May, respectively, while the distribution according to the birth month showed a high percentage for those born in May and March.

Conclusions: Our results suggest that RSV and unspecified bronchiolitis are a significant cause of death in healthy full-term infants in Brazil. Epidemiological characteristics of unspecified bronchiolitis deaths suggest that they can be miscoded RSV deaths.

**Keywords:** Respiratory Syncytial Virus Infections, bronchiolitis, morality/trends, infants, term babies, Brazil

**Conflict of Interest:** Aline Tolardo, Sheila Homsani, Karina Braga Ribeiro = Sanofi, Vaccines Unit = employees.
115. EVALUATING THE DISEASE BURDEN OF RSV INFECTIONS IN YOUNG CHILDREN IN PRIMARY CARE: A SYSTEMATIC LITERATURE REVIEW

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Background: The burden of RSV in hospitalized children <5 years is substantial, but limited data are available on RSV in young children in primary care. This study presents preliminary results on the disease burden (incidence rates) of RSV in children <5 years in primary care settings.

Methods: A systematic literature review was performed in PubMed and Embase from 2000 to 2022. Studies reporting on the incidence rate of RSV infections in children <5 years in primary care settings were included. Two reviewers independently completed data extraction and assessed the methodological quality of included studies. We plan to present incidence rates by age, primary care setting and world region.

Results: A total of 3774 records were screened and a preliminary analysis identified 25 eligible studies among children <5 years. These studies were mainly performed in high income countries (n = 20) in Europe (n = 9) and North America (n = 11) within different primary care settings (emergency and outpatient departments; GP and pediatric offices). Clinical heterogeneity between studies was high. Preliminary results demonstrate a significant burden of RSV in primary care with incidence rates ranging between 5.57 to 360 per 1000 children, with the highest incidence rates reported in infants <1 years.

Conclusions: This is the first study that aims to present estimates of the disease burden of RSV in children <5 years in primary care settings. These results can be used to support informed decision-making regarding the introduction of future passive immunization programs in young children in the community.

Keywords: Children; Disease Burden; Primary care; Outpatient department

Conflict of Interest: JvS and JP declare that Nivel has received unrestricted research grants from WHO, Sanofi and the Foundation for Influenza Epidemiology outside the submitted work. JvS and JP declare that Nivel received a grant from the Respiro Syncytial Virus Consortium in Europe (RESCEU) project of the ‘Innovative Medicines Initiative 2 Joint Undertaking’ grant agreement No 116019 and a grant from the Preparing for RSV Immunisation and Surveillance in Europe (PROMISE) project of the ‘Innovative Medicines Initiative 2 Joint Undertaking’ grant agreement No 101034339. This Joint Undertaking gets support from the “European Union’s Horizon 2020 research and innovation programme” and the “European Federation of Pharmaceutical Industries and Associations”. MB and RK are employees of Sanofi and may hold shares and/or stock options in the company.

Funding: This collaborative study is funded by Sanofi and Astrazeneca. There is an agreement that all epidemiological analyses are completed in collaboration with the team from Sanofi, but all public health implications and conclusions are determined by Nivel.

116. INCIDENCE OF ALL-CAUSE PICU ADMISSIONS FOR RESPIRATORY INFECTION: A RETROSPECTIVE STUDY IN KATHMANDU, NEPAL

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4. Respiratory Syncytial Virus Network (ReSViNET) Foundation, Zeist, the Netherlands

Background: Severe Acute Respiratory Infection (SARI) is one of the leading causes of morbidity and mortality in children under 5 years old worldwide. Currently, limited individual patient data are available from lower-middle-income countries, where disease burden is highest. This retrospective study investigates the incidence and mortality of SARI-related intensive care unit (ICU) admissions in children under 2 years old within the catchment area of Kanti Children’s Hospital (KCH) and Tribhuvan University Teaching Hospital (TUTH) in Kathmandu, Nepal.

Methods: Children <2 years of age who met the WHO SARI-case definition were included. The WHO manual for estimating disease burden associated with Influenza was used, combined with national census data to calculate the incidence and mortality.

Results: In total, 302 children were admitted with SARI-related symptoms to KCH and TUTH between June 2019 and March 2021. The average age was 6.3 months and 67.9% (205/302) were male. 479.230 children lived in the catchment area of the hospitals at this time. The SARI-related ICU admission incidence per 100,000 children <2 years was 63.0 ((302/479.230)*100,000) and the mortality rate was 9.6% (29/302).

Conclusions: We showed that the WHO manual for estimating disease burden associated with Influenza can be used to estimate the incidence of PICU admission for all-cause respiratory infection. This study has a number of limitations. The SARI diagnoses were based on clinical judgement and were not laboratory confirmed. In the catchment areas of KCH and TUTH are multiple other NICU’s and PICU’s. Since the exact number is unknown, we were unable to correct for this. Many mortality cases may have been missed since most pneumonia deaths in low- and middle-income countries occur outside of the hospital. The admission incidence and mortality rate are therefore mere estimates.

Keywords: SARI; Incidence; Mortality; Disease Burden; Nepal; PICU; NICU

Conflict of Interest: Prof. Dr. L. Bont MD/PhD: Louis Bont has regular interaction with pharmaceutical and other industrial partners. He has not received personal fees or other personal benefits. UMCU has received major funding (>€100,000 per industrial partner) for investigator-initiated studies from AbbVie, MedImmune, Janssen from 2015-2017 (total annual estimate less than €20,000). LJB is the founding chairman of the ReSViNET Foundation.

117. DISTINCT SEASONALITY AND REDUCED DISEASE SEVERITY IN THE FIRST RSV SEASON TO RESURGE DURING THE COVID-19 PANDEMIC

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8. Pediatric Pneumology, Children’s Hospital at Marien-Hospital Wesel, Wesel, Germany
Background: The COVID-19 pandemic induced significant shifts in seasonality of common airway pathogens such as respiratory syncytial virus (RSV). Previously, no systematic data on disease severity of hospitalized “off-season” RSV infections had been collected.

Methods: Since September 2020, our multicentric, prospective PAPI study has analyzed rates and phenotypes of hospitalized RSV patients ≤24 months old in five German hospitals. For the RSV seasons from 2017-2020, cases from these hospitals retrospectively were analyzed. (Total cases n=906).

Results: After a complete absence in 2020/2021, RSV returned approximately 15 weeks earlier than usual in 2021. Duration and total case numbers were comparable to previous seasons. No significant shifts in age, gender, or other risk factors occurred. Palivizumab immunization rates in 2021/2022 were lower than in previous seasons (0.9% vs. 2.5%). However, the mean duration of hospitalization was significantly shorter in 2021/2022 (mean 4.8 days vs. 5.4 days in previous seasons, p 0.0004). Additionally, rate and duration of O2 supplementation in 2021/2022 were significantly lower than during prepandemic seasons. (In 2021/2022, O2 supplementation was 48.9% vs. 57.1% in previous seasons; mean duration of O2 supplementation was 2.3 days in 2021/2022 vs. 4.4 days in previous seasons, p<0.0001.) The rate of patients needing ventilation during 2021/2022 also was lower.

Conclusion: We present first data on disease severity and risk profiles of children hospitalized with RSV bronchiolitis during the COVID-19 pandemic. This shows distinct seasonality and reduced disease severity during the last, atypical season. Our analysis may assist preparation for future, atypical waves of airway pathogens

Keywords: RSV, resurgence, SARS CoV2, epidemiology, surveillance

Conflict of Interest: none declared

118. SIMPLIFIED DETECTION AND CHARACTERIZATION OF RESPIRATORY SYNCYTIAL VIRUS FROM CLINICAL SALIVA SAMPLES

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Introduction: With RSV vaccines progressing through clinical trials, large-scale post-vaccine surveillance studies will be required, and full-length genome data will be key to monitoring vaccine effectiveness. We developed a full genome Oxford nanopore sequencing protocol for respiratory samples.

Methods: Paired nasopharyngeal and saliva specimens were collected from children (<5y) with medically attended respiratory infections admitted to Wilhelmina Children’s Hospital (the Netherlands). Samples were processed by both RNA-extraction-free and full RNA extraction methods, then tested in PCR for RSV. Sensitivity of detection was compared across sample type and extraction method. RSV-positive samples were subtyped. cDNA was amplified using PCR. Fragments (4000-6500 bp) generated using primer-pairs spanning the entire genome, according to subtype, were used to modify the amplicon-based Oxford Nanopore SARS-CoV-2 sequencing workflow for RSV.

Results: Of 28 children sampled, 13 (46%) tested RSV-positive, all from both their nasopharyngeal and saliva specimens, with no significant difference in Ct values (p=0.62). RSV detection in raw saliva remained stable for 72 hours at +4°C, ~19°C and 37°C. We sequenced RSV from nasopharyngeal and saliva specimens with 80-95% coverage, with minimal modifications to the SARS-CoV-2 protocol.

Conclusion: Due to its non-invasive collection and low-resource requirement relative to swabbing, saliva is an attractive sample type for large-scale surveillance studies. Our findings suggest that saliva is at least equally sensitive for the detection of RSV in infants. The ability to sequence virus from different specimen types with a cost-effective method increases surveillance capacity and will increase the number of near-complete genomes available for monitoring seasonal epidemics.

Keywords: saliva, genome sequencing, surveillance, PCR

Conflict of Interest: This study was funded by a research grant from Merck to Louis Bont.
119. EFFICIENCY OF TRANSPLACENTAL TRANSFER OF NATURALLY-ACQUIRED RSV MATERNAL ANTIBODIES IN PRETERM AND FULL TERM INFANTS

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BACKGROUND: Maternal immunization (MI) requires efficient transplacental transfer (TPT) of maternal antibodies. While full term infants (≥37 weeks gestational age [wGA]) are generally born with cord/maternal titer ratios (CMRs) >1.0, preterm infants are generally expected to have lower CMRs, and are also at increased risk of severe RSV. Observational RSV antibody TPT data by wGA are needed to model vaccine-induced antibody transfer and potential vaccine effectiveness in preterm infants, as deliveries <35 wGA are rare in trial participants.

METHODS: Via a collaborative multi-site seroepidemiology project, TPT of naturally-acquired RSV neutralizing antibody was assessed by wGA at birth. These data will be analyzed descriptively and incorporated with US preterm birth and Tdap MI rates by wGA (as proxy for RSV MI uptake), and RSVpref (Pfizer) vaccine immunogenicity and antibody half-life data to model potential TPT of vaccine-induced antibody across wGA.

RESULTS: RSV-A titers from 287 mother-infant dyads born across a range of wGA ([≥37: 7%, 28-31: 15%, 32-36: 47%, ≥37: 31%]) were included in this interim analysis. Geometric mean RSV-A CMR was 1.01 overall but increased (along with proportion CMR>1.0) as wGA at birth increased.

CONCLUSION: Enrollment is ongoing; modeling will assess what proportion of infants born preterm may receive sufficient vaccine-induced RSVPref maternal antibody to provide protection against severe RSV in early life.

Keywords: Transplacental Antibody transfer, preterm infants, vaccine effectiveness

Conflict of Interest: J.A.: Consultant for Pfizer, Sanofi Pasteur, Janssen, Moderna, and Medscape, and his institution receives fees to conduct clinical research unrelated to this manuscript from MedImmune, Regeneron, PaxVax, Pfizer, GSK, Merck, Sanofi Pasteur, Janssen, and Mercon. He also serves on a safety monitoring board for Kentucky BioProcessing, Inc. and Sanofi Pasteur. He serves on a data adjudication board for WCG and ACI Clinical. His institution has also received funding from NIH to conduct clinical trials of COVID-19 vaccines. L.A.A. has done paid consultancies on RSV vaccines for Bavarian Nordic, Janssen, and AdvVac; his laboratory is currently receiving funding through Emory University from Pfizer for laboratory studies for RSV surveillance studies in adults, Sciogen for animal studies of RSV vaccines, and Advaccine Pharmaceuticals, Ltd for RSV neutralizing antibody studies; he is a co-inventor on several CDC patents on the RSV G protein and its CX3C chemokine motif relative to immune therapy and vaccine development; and is co-inventor on a patent filing for use of RSV platform VLPs with the F and G proteins for therapeutic vaccines. B.B. has regular interaction with pharmaceutical and other professional partners. He has not received personal fees or other personal benefits. UMCU has received major funding (>100,000 per industrial partner) for investigator initiated studies from AbbVie, MedImmune, Janssen, Pfizer, the Bill and Melinda Gates Foundation and MeMed Diagnostics. UMCU has received major cash or in kind funding as part of the public private partnership IMfunded RESCU project from GSK, Novavax, Janssen, AstraZeneca, Pfizer and Sanofi. UMCU has received major funding from Julius Clinical for participating in the INFORM study sponsored by MedImmune. UMCU has received minor funding for participation in trials by Regeneron and Janssen from 2015-2017 (total annual estimate less than €20,000). UMCU received minor funding for consultation and invited lectures by AbbVie, MedImmune, Ablynx, Bavaria Nordic, MabImmune, Novavax, Pfizer, Janssen (total annual estimate less than €20,000). Dr. Bont is the founding chairman of the ReSVINET Foundation. J.E.: Consultant for Sanofi Pasteur, AstraZeneca, Meissa Vaccines, and Moderna. Research support to my university from Pfizer, GlaxoSmithKline, AstraZeneca, and Merck. A.K.: Unpaid consultant for GSK. Consultant for Pfizer. Receives grant support from Pfizer and Merck.

120. AD26.RSV.PREF/RSV PREF PROTEIN VACCINE INDUCES A BROAD RANGE OF RSV-SPECIFIC HUMORAL AND CELLULAR IMMUNE RESPONSES IN OLDER ADULTS

Arangassery Rosemary Bastian (1)* Christy A. Comeaux (1) Ann R. Falsey (2) John Ervin (4) Joris Menten (5) Els De Paepe (5) Sjouke Vandenberghe (5) Esther Heijnen (1) Benoit Callendret (1) on behalf of the CYPRESS Investigators

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5. Janssen Infectious Diseases, Beerse, Belgium

Background: In CYPRESS (phase 2b; NCT03982199), Ad26.RSV.pr (Pfizer) vaccine induced a broad range of humoral and cellular immune responses in adults ≥65 years. We present broader immunogenicity profiling from CYPRESS.

Methods: Participants were randomized 1:1 (vaccine:placebo). Immune markers relevant for protection against RSV infection were assessed in the immunogenicity subset (n=195). Assessments included serum and mucosal RSV pref IgA antibody titers (ELISA); RSV-specific Fc-effector functional antibody responses (antibody-dependent complement deposition [ADCD], cellular phagocytosis [ADCP], natural killer cell activation [ADNK], and neutrophil phagocytosis [ADNP]); nAbs against RSV A and B clinical isolates (virus neutralization assay); RSV-F-specific memory B-cell responses (ELISPot); and proportions of RSV-F-specific CD4+ T-cell and Th1/Th2 CD4+ T-cell responders (intracellular cytokine staining). Results: Day 15 vaccine-group fold increases were 24.6 and 2.4 for serum and mucosal RSV pref IgA antibodies, respectively; 7.8 (ADCD), 1.9 (ADCP), 2.5 (ADNP), and 2.6 (ADNK) for Fc-effector functional antibodies; and 10.4-11.9 for nAbs against RSV clinical isolates. Median RSV-F-specific memory B-cell frequency increased from 94 spot-forming cells (SFC)/10⁶ PBMCs at baseline to 833 SFC/10⁶ PBMCs at Day 15 and remained above baseline at Day 169. At Day 169, 63.6% and 27.3% showed CD4+ and CD6+ T-cell responses; 65.9% showed a Th1-biased CD4+ T-cell response. Placebo recipients showed no substantial immune responses.

Conclusions: Single-dose Ad26.RSV.pref/RSV pref protein induced a broad range of humoral and cellular immune responses in adults ≥65 years.

Keywords: B cells, clinical trials, functional antibodies, immunogenicity, polyfunctionality, respiratory syncytial virus, system serology, T cells, vaccine

Conflict of Interest: A.R.B., C.A.C., E.H., and B.C. are employees of Janssen Vaccines & Prevention B.V. A.R.F. has received research grants from Janssen, Merck Sharp & Dohme, Pfizer, BioFire Diagnostics, and CyanVac; consulting fees from Arrowhead; and personal fees for serving on a Data Safety Monitoring Board for Novavax. S.B. has nothing to disclose. J.E. is under contractual agreement for the Alliance for Multispecialty Research - KCM regarding payment for the conduct of the protocol. J.M., E.D.P., and S.V. are employees of Janssen Infectious Diseases.
121. RSV G PROTEIN MONOClonAL ANTIBODIES TARGETING THE CX3C MOTIF IMPROVE THE ANTIVIRAL RESPONSE AND PROTECT AGAINST RSV MUCogenic DISEASE

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Respiratory syncytial virus (RSV) is a major cause of serious lower respiratory disease with no vaccine available and limited therapeutic choices. Most candidate vaccines target the fusion (F) protein to induce neutralizing antibodies (Abs) and do not control attachment (G) protein and aid in finding a highly effective therapeutic setting. Here, we present an interim analysis (IA) from a pivotal phase 3 clinical trial in adults aged ≥60 years assessing mRNA 1345, an investigational mRNA vaccine encoding the membrane-anchored RSV F glycoprotein stabilized in the prefusion conformation.

Methods: The ongoing phase 3, randomized, observer-blind, placebo-controlled, case-driven study in adults aged ≥60 years (NCT05127434) enrolled participants from 22 countries; participants were randomized 1:1 to receive 1 dose of mRNA-1345 50 µg or placebo. The primary efficacy endpoints were the prevention of a first episode of RSV-associated lower respiratory tract disease (RSV-LRTD) with ≥2 or ≥3 symptoms in 14 days and 12 months post-injection.

Results: The IA included 35,538 participants (mRNA-1345, n=17,792; placebo, n=17,746). The mean age was 68.1 years, 50.9% were male, 36.1% were non-White, and 34.5% were Hispanic or Latino. A single dose of mRNA-1345 was well-tolerated and no safety concerns were identified. The primary efficacy endpoints for the study were: mRNA-1345 was efficacious in preventing the first episode of RSV-LRTD in participants with ≥2 and ≥3 symptoms. Conclusion: A single dose of mRNA-1345 had a favorable safety and tolerability profile and was efficacious in preventing RSV-LRTD with ≥2 and ≥3 symptoms in adults aged ≥60 years.

Keywords: RSV, monoclonal antibodies, interferon, immune response, mucogenic disease

Conflict of Interest: All authors are employees of Janssen Pharmaceutica NV and may be Johnson & Johnson stockholders, except Brecht Bonneux (University of Antwerp). The research is funded by Janssen Pharmaceutica/VLAIO (Flanders innovation and entrepreneurship agency).

122. RESISTANCE MUTATIONS TO SMALL MOLECULE INHIBITOR REVEAL NEW INSIGHTS INTO RSV POLYmerase FUNCTIONING.

Brecht Bonneux (1,2)*, Marcia Van Ginderen (1), Suzanne De Bruyn (1), Nick Verheyen (1), Carl Van Hove (1), Nadia Neto (1), Kim Thys (1), Edgar Jacoby (1), Dirk Roymans (1,3), Florence Herschke (1), Peter Rigaux (1,3)

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2. University of Antwerp, Belgium
3. Currently working for other companies

While prophylactic vaccines and monoclonal antibodies seem around the corner, treatments against Respiratory Syncytial Virus (RSV) remain scarce. In the therapeutic setting, polymerase inhibitors offer the advantage of targeting already infected cells. To elucidate the mechanism of action of a novel small molecule inhibitor replication inhibitor, we investigated the functionality of escape mutations identified during resistance selection experiments and subsequent plaque purifications. Several resistance mutations (R999G, D1026N, C1388G, I1381S/T, Y1361F) were found in the capping domain of L, molecule replication inhibitor, we investigated the functionality of escape mutations. These results contribute to the overall understanding of the general RSV biology, a pivotal phase 3 clinical trial in adults aged ≥60 years assessing mRNA 1345 was efficacious in preventing the first episode of RSV and cell cytotoxicity procedures were used to assess the anti-RSV and cell cytotoxicity properties of Nauclea latifolia (NL) extract in Hep-2 and Vero cells of human origin. A recombinant strain of rgRSV that expresses the green fluorescent protein (rg) was used to evaluate the

Keywords: polymerase inhibitor, small molecule, resistance mutations, capping domain, RdRp, modeling, inter domain interaction

Conflict of Interest: All authors are employees of Janssen Pharmaceutica NV and may be Johnson & Johnson stockholders, except Brecht Bonneux (University of Antwerp). The research is funded by Janssen Pharmaceutica/VLAIO (Flanders innovation and entrepreneurship agency).

123. SAFETY AND EFFICACY OF MRNA-1345, AN MRNA-BASED VACCINE AGAINST RESPIRATORY SYNCYTIAL VIRUS, IN ADULTS 60 YEARS AND OLDER

Eleanor Wilson, Jaya Goswami, Sonia K. Stoszek, Runa Mithani, Shraddha Mehta, Archana Kapoor, Wemuei Huang, Lan Lan, Laila El Asmar, Catherine A. Panozzo, Parinaz Ghaswalla, Allison August*, Christine A. Shaw, Jacqueline Miller, Grace L. Chen

Moderna, Inc., Cambridge, MA, USA

Background: There is a substantial unmet need for a respiratory syncytial virus (RSV) vaccine in older adults. Here, we present an interim analysis (IA) from a pivotal phase 3 clinical trial in adults aged ≥60 years assessing mRNA-1345, an investigational mRNA vaccine encoding the membrane-anchored RSV F glycoprotein stabilized in the prefusion conformation.

Methods: The ongoing phase 3, randomized, observer-blind, placebo-controlled, case-driven study in adults aged ≥60 years (NCT05127434) enrolled participants from 22 countries; participants were randomized 1:1 to receive 1 dose of mRNA-1345 50 µg or placebo. The primary efficacy endpoints were the prevention of a first episode of RSV-associated lower respiratory tract disease (RSV-LRTD) with ≥2 or ≥3 symptoms in 14 days and 12 months post-injection.

Results: The IA included 35,538 participants (mRNA-1345, n=17,792; placebo, n=17,746). The mean age was 68.1 years, 50.9% were male, 36.1% were non-White, and 34.5% were Hispanic or Latino. A single dose of mRNA-1345 was well-tolerated and no safety concerns were identified. The primary efficacy endpoints for the study were: mRNA-1345 was efficacious in preventing the first episode of RSV-LRTD in participants with ≥2 and ≥3 symptoms. Conclusion: A single dose of mRNA-1345 had a favorable safety and tolerability profile and was efficacious in preventing RSV-LRTD with ≥2 and ≥3 symptoms in adults aged ≥60 years.

Keywords: RSV, monoclonal antibodies, interferon, immune response, mucogenic disease

Conflict of Interest: All authors are employees of Janssen Pharmaceutica NV and may be Johnson & Johnson stockholders, except Brecht Bonneux (University of Antwerp). The research is funded by Janssen Pharmaceutica/VLAIO (Flanders innovation and entrepreneurship agency).

124. ANTVIRAL ACTIVITY OF NAUCLEA LATIFOLIA ROOT EXTRACT AGAINST THE HUMAN RESPIRATORY SYNCYTIAL VIRUS INVITRO

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Globally, respiratory syncytial virus (RSV) continues to be the most frequent cause of viral lower respiratory tract infection in newborns and children, as well as the elderly. Medicinal plants have already been identified as a possible source for the development of anti-RSV therapies. In this present study, viral plaque reduction and cell viability procedures were used to assess the anti-RSV and cell cytotoxicity properties of Nauclea latifolia (NL) extract in Hep-2 and Vero cells of human origin. A recombinant strain of rgRSV that expresses the green fluorescent protein (rg) was used to evaluate the
associated setup for antiviral activity. Using immunocytochemical approach, the antiviral effects against the RSV A2 strain were also evaluated. By using a plaque reduction test, antiviral activity of extracts were investigated before and after viral inoculation at various times.

The results of the preliminary data of NL extract showed anti-RSV activities with IC50 = 75.62 µg/ml when tested against the recombinant strain rgRSV expressing the green fluorescent protein. Corresponding assay for the cytotoxic effect of NL extract against utilized cell lines gave TC50 = 333.82 µg/ml. Further screening of NL against the circulating RSV A2 strain established their promising anti-RSV utility. Time of addition studies for elucidation of possible mechanism of action gave 74.38, 69.42, and 71.90 % reduction of RSV plaque forming units at 0, 2, and 4 hours post-infection addition times.

Our findings reveal that the screening exercise of NL extracts has anti-RSV activity. Moreover, cellular protection from RSV-induced cell cyto-pathology represent another desirable property of NL.

**Keywords:** Respiratory syncytial virus (RSV), antiviral, cytotoxicity, Nauclea latifolia extracts, anti-RSV, viral inhibition, cell viability.

**Conflict of Interest:** None declared

### 125. THE RESPIRATORY SYNCYTIAL VIRUS PREFUSION F PROTEIN CANDIDATE VACCINE (RSVPreF3 OA) ATTENUATES THE SEVERITY OF RSV IN BREAKTHROUGH INFECTIONS IN ADULTS ≥60 YEARS OF AGE

Desmond Curran (1)*, Sean Matthews (2), Elizar Sabater (1), Silvia Narejos Pérez (3), Lina Pérez Brea (4), Mika Rämet (5), Laura Helman (6), Dae Won Park (7), Daniel Molnar (1), Lusine Kostanyan (1), Veronica Hulstrøm (1), on behalf of the AReSVi-006 study group

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2. Freelance c/o GSK, Wave, Belgium
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4. FISABIO-Public Health, Valencia, Spain
5. FVR, Finnish Vaccine Research, Finland
6. MROC Research, Mishawaka, IN, United States
7. Korea University Ansan Hospital, Ansan, Korea

Background: RSV is a contagious pathogen causing acute respiratory infections (ARIs). RSV-related symptoms range from mild upper respiratory tract infections to potentially life-threatening lower respiratory tract disease (LRTD). Physical functioning (PF) declines during RSV-ARI, and it may continue to be impacted even after recovery from RSV infection. RSVPreF3 OA vaccine efficacy was 71.7% against RSV-ARI and 82.6% against RSV-LRTD, in adults ≥60 years old (AReSVi-006/NCT04886596). We present the patient-reported outcomes (PRO) collected during October 2021/April 2022 season, within the same trial.

Methods: PRO assessments (secondary endpoints) included the InFluenza PRO (FLU-PRO), Short Form-12 (SF-12), and EuroQol 5-dimension (EQ-5D) health questionnaires. The maximum FLU-PRO (Max-FLU-PRO) Chest/Respiratory score during the first 7 days from ARI onset was calculated for participants with confirmed RSV-ARI episodes and compared between study groups using a Wilcoxon test. Least Squares mean (LSMean) of SF-12 PF and EQ-5D Utility scores at ARI visit were calculated using mixed effects models.

Results: Overall, 27 RSV-ARI episodes were reported in RSVPreF3 OA (N=12,466) and 95 in Placebo (N=12,494) group. Statistical analysis of the Max-FLU-PRO Chest/Respiratory scores showed significantly lower median values in RSVPreF3 versus Placebo group (Table). LSMean of SF-12 PF and EQ-5D Utility scores during RSV-ARI episode seemed higher for RSVPreF3 versus Placebo group (Table).

Conclusions: Max-FLU-PRO Chest/Respiratory scores suggest that RSVPreF3 OA, in addition to preventing RSV infection, attenuated the severity of RSV-associated symptoms in breakthrough infections. The observed reduction in symptoms translated into trends of reduced impact of RSV infection on PF and quality of life utility.

**Keywords:** Infection control and prevention; Quality of life; Public health and surveillance; Vaccinology; Older adults; Respiratory syncytial virus; Acute respiratory infections

**Funding:** GlaxoSmithKline Biologicals SA

**Conflict of Interest:** DC, DM, ES, SM, LK and VH were employees of GSK at the time the study was designed, initiated, and/or conducted. DC, ES, DM and LK hold shares/stock options in GSK as part of their employee remuneration. MR reports grants and other support from GSK to his institution. LH reports payment for completing the study work and support for attending meetings and/or travel. SNP was involved as principal investigator in clinical trials with different sponsors.

### 126. PRETERM BIRTH SIGNAL IN A MATERNAL IMMUNIZATION STUDY WITH A RESPIRATORY SYNCYTIAL VIRUS PREFUSION F PROTEIN VACCINE CANDIDATE

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In 2020, GSK initiated a phase 3, double-blind, 2:1-randomized, placebo-controlled trial (RSV MAT-009; NCT04605159) in 24 countries to assess an RSV prefusion F maternal vaccine candidate (RSVPreF3 Mat) administered to 18–49-year-old women in the late second or third trimester of pregnancy. The study assessed vaccine safety and efficacy against RSV-associated lower respiratory tract illness in young infants. In February 2022, after 3,557 pregnant women had been vaccinated with RSVPreF3 Mat and 1,771 with placebo, GSK stopped enrollment and vaccination in this study and all other ongoing RSVPreF3 Mat studies because of an imbalance in the proportions of preterm births and neonatal deaths between the vaccine and the placebo groups. The imbalance in preterm births was statistically significant (relative risk [RR] at the day 43 post-delivery analysis: 1.38; p=0.009, Table). The imbalance in neonatal deaths was considered a consequence of the imbalance in preterm births. No other safety signal was observed in infants or mothers. The preterm birth imbalance peaked from August to December 2021 and was not observed consistently from January 2022 onward. The imbalance was more associated with low- and middle-income countries (RR: 1.57, 95% confidence interval [CI]: 1.17–2.10) than high-income countries (RR: 1.04, 95% CI: 0.68–1.58). No association was found with the administered
vaccine lot, gestational age at vaccination, time between vaccination and delivery or various risk factors for preterm birth. Investigation into the safety signal and safety follow-up of the mothers and infants are ongoing.

Keywords: maternal vaccination, RSV, prefocus F protein, preterm birth, safety signal

Funding: GlaxoSmithKline Biologicals SA

Conflicts of interest: ID, PRD, JHK, SL, CS, JUS and PW are employees of GSK. ID, PRD, JHK, SL, JUS and PW hold stock options/shares in GSK. PRD also holds long-term stock incentives in Pfizer. GSK declares payments from GSK for her role as chair of an independent data monitoring committee for RSV vaccine trials in pregnancy; payments from Pfizer for her role as chair of an independent data monitoring committee for GBS vaccine trials in pregnancy; royalties as an author on a textbook section on Listeria infection in pregnancy; and funding paid to her institution from an NIH-NIAID federal contract and a CDC federal contract. GSK also declares participating in a data safety monitoring board for HPV vaccine trials by the National Cancer Institute and being the president of the Infectious Diseases Society for Obstetrics and Gynecology without receiving compensation.

127. SAFETY AND PHARMACOKINETICS OF NIRSEVIMAB FOR PREVENTION OF RSV DISEASE IN CHILDREN WITH CONGENITAL HEART DISEASE OR CHRONIC LUNG DISEASE OF PREMATURITY

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Background: A single dose of nirsevimab, an extended half-life monoclonal antibody against RSV, showed favorable safety and pharmacokinetics (PK) through the first RSV season in the Phase 2/3 MEDLEY trial in infants with congenital heart disease (CHD), chronic lung disease of prematurity (CLD), or born preterm. We report the safety and PK of a second dose of nirsevimab administered prior to the second RSV season.

Methods: Before Season 1, infants with CHD or CLD or those born ≤35 weeks gestational age without CHD/CLD were randomized 2:1 to nirsevimab or palivizumab. Before Season 2, children with CHD/CLD randomized to nirsevimab for Season 1 received 200 mg nirsevimab (N/N); those randomized to palivizumab were re-randomized 1:1 to either 200 mg nirsevimab (P/N) or 15 mg/kg palivizumab (P/P). Adverse events (AEs), anti-drug antibodies (ADA) and PK were evaluated for 2150 days post-dose.

Results: Of 262 infants in Season 2 (42 P/P, 40 P/N, 180 N/N), 252 completed ≥150 days post-dose. AE incidence was similar across treatments (P/P: 29 [69.0%]; P/N: 29 [72.5%]; N/N: 126 [70.0%]), with no deaths or AEs of special interest reported. ADA prevalence was low in children receiving N/N (Day 31: 1.1% [1/90]; Day 151: 0% [0/158]). Mean nirsevimab serum concentration on Day 151 was 52.3 µg/mL (pooled N/N and P/N). No RSV lower respiratory tract infections occurred through Day 151.

Conclusions: Following a second dose of nirsevimab prior to Season 2, children with CHD/CLD achieved nirsevimab serum exposures at efficacious levels and the safety profile remained favorable.

Keywords: nirsevimab, respiratory syncytial virus, congenital heart disease, lung disease

Conflict of Interest: J Domachowskie has received grant/research support from AstraZeneca and consulting fees for Sanofi, Y Chang, RJ Kubiak, A Leach, VS Mankad, T Takas, T Villafana, Wählby Hamrén are employees and shareholders of AstraZeneca. I Banu, M Shroff are employees of AstraZeneca. V Atanasova, F Cabañas, K Furuno, K Nguyen have no conflicts of interest to disclose.

128. PROTECTIVE EFFICACY OF AN INACTIVATED WHOLE VIRUS RSV VACCINE IN MICE

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The respiratory syncytial virus (RSV) is one of the leading causes of acute lower respiratory infections in children associated with numerous paediatric hospitalizations, and no approved vaccine available.

Previously our group showed the development of a safe and efficacious vaccine produced by a versatile and non-chemically electron beam inactivation (ELLI). Since the formaldehyde-inactivated RSV vaccine applied intramuscularly induced an unwanted enhanced disease in children after natural RSV infection, we questioned if ELLI-inactivated RSV delivered by a mucosal application is able to induce a strong and immune-balanced immune response associated with protective efficacy. Therefore, the ELLI-inactivated RSV was formulated with different liposomes to optimize mucosal uptake and protection upon RSV-challenge. Immunogenicity and protective efficacy were tested in a murine challenge-model after homologous vaccination via intranasal route. Serum samples were taken before and three weeks after prim and boost immunization. One month after boost mice were challenged with 1*10^6 focus forming units of RSV and scored for five days.
We observed immunogenicity in ELLI mucosal immunized animals by detecting RSV-binding and -neutralizing antibodies in serum samples. In addition, protective efficacy was proven by a statistically significant 352-fold reduction of viral load compared to control animals. Moreover IFN-γ and IL-6 cytokine levels were statistically significantly reduced in BALs of ELLI-mucosal immunized animals in comparison to vehicle controls.

In conclusion, we found a promising inactivated vaccine-candidate for a mucosal application against RSV. After optimization we will translate the mucosal inactivated vaccine delivery into clinical trials to evaluate safety and efficacy against RSV in humans.

Keywords: RSV, vaccine, mucosal protection, mucosal vaccine, formulation, RSV mouse model

Conflict of Interest: None declared

129. EFFICACY OF AD26.RSV.PREF/RSV PREF PROTEIN VACCINE AGAINST RSV IN A PHASE 2B STUDY OF ADULTS AGED ≥65 YEARS OVER 3 SEASONS


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7. Janssen Global Services, LLC, Ranitan, NJ, USA

Background: In CYPRESS (a randomized, double-blind, placebo-controlled, phase 2b trial; NCT03982199), an AD26.RSV.pref/RSV pref protein vaccine demonstrated 80% and 70% efficacy for prevention of RSV-mediated lower respiratory tract disease (LRTD) and acute respiratory infection (ARI), respectively, in adults aged ≥65 years. We report the final vaccine efficacy (VE) analysis through 3 RSV seasons.

Methods: Participants (N=5782) were randomized 1:1 to receive vaccine or placebo before the first RSV season. The primary endpoint was first occurrence of RT-PCR-confirmed RSV LRTD after the first RSV season. To assess VE durability, the first occurrence of RSV LRTD or ARI was evaluated in the overall study population during RSV seasons 1, 2, and 3.

Results: The per-protocol efficacy set included 2124 and 864 vaccine recipients and 2126 and 881 placebo recipients in seasons 2 and 3, respectively. In seasons 2 and 3, RSV LRTD was observed in 4 participants in the vaccine group and 17 in the placebo group (RSV ARI: 9 and 21 participants, respectively). In the study population overall, VE for prevention of RSV LRTD was 76.1% (95% CI: 26.9%, 94.2%) for seasons 2 and 3 combined and 78.7% (57.3%, 90.4%) across 3 seasons. VE for prevention of any RSV ARI was 56.6% (95% CI: 1.2%, 82.5%) in seasons 2 and 3 combined and 65.7% (43.5%, 79.9%) across 3 seasons.

Conclusions: A single dose of the AD26.RSV.pref/RSV pref protein vaccine was efficacious against RSV LRTD and RSV ARI through ≥3 RSV seasons in adults aged ≥65 years.

Keywords: Acute respiratory infection; lower respiratory tract disease; respiratory syncytial virus; vaccine

Conflict of Interest: A.R.F. has received research grants from Janssen, Merck Sharp & Dohme, Pfizer, BioFire Diagnostics, and CyanVac; consulting fees from Arrowhead; and personal fees for serving on a Data Safety Monitoring Board for Novavax. C.A.C., T.H., M.D., B.C., and E.H. are employees of Janssen Vaccines & Prevention B.V. and may own stock or stock options. S.B. has nothing to declare. J.E. has a contractual agreement with The Alliance for Multispecialty Research – KCM regarding payment for the conduct of the study protocol. E.D.P and S.V. are employees of Janssen Infectious Diseases and may own stock or stock options. M.N. is an employee of IQVIA RDS Netherlands B.V., a research organization paid by the study sponsor for the conduct of the protocol. E.K.H.C. is an employee of Janssen Global Services, LLC, and may own stock or stock options.

150. PROGRAMMATIC SUITABILITY AND USER ACCEPTABILITY EVALUATION OF DELIVERY SYSTEMS FOR THE PREVENTION OF RESPIRATORY SYNCYTIAL VIRUS IN INFANTS

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Background: Respiratory syncytial virus (RSV) causes significant morbidity and mortality in young infants, with most deaths occurring in low- and middle-income countries (LMICs). Though no RSV prevention products are yet available for all infants globally, extended half-life monoclonal antibodies (mAbs) are currently in development for children of all gestational ages.

Methods: To inform product development efforts of infant RSV mAb products, PATH conducted a programmatic suitability and acceptability assessment to evaluate which delivery systems will be most suitable for LMIC contexts. Using a mixed-methods approach, we conducted stakeholder interviews, focus group discussions, and an online survey to evaluate five delivery systems broadly categorized as prefilled and non-prefilled devices.

Results: Participants included global stakeholders (n=21), country decision-makers (n=29), and country end-users (n=29). Overall, 82% of participants preferred the prefilled devices (n=64), highlighting their ease of use, acceptability, improved safety, reduced wastage, and simplified logistics. Some stakeholders (n=14) preferred the non-prefilled devices due to vaccinator familiarity and smaller cold chain volume. Ease of use was ranked as the most important product attribute across stakeholder groups. Global stakeholders also highlighted cost as a key consideration; country end-users emphasized minimizing the cold chain volume particularly at lower levels of the supply chain.

Conclusion: Our results suggest that prefilled devices will be preferred for infant RSV mAbs in LMICs due to their multiple advantages including ease of use. To optimize the mAb delivery system to better meet LMIC needs and improve uptake, future studies should evaluate cost-effectiveness, usability, secondary packaging, and labeling/temperature monitoring requirements.

Keywords: RSV prevention, monoclonal antibodies, user needs, global health, programmatic suitability, delivery devices, infants, country stakeholders, packaging and delivery technologies, health equity

Conflict of Interest: None declared
131. AN IMMUNOINFORMATICS-BASED APPROACH TO DESIGN A POPULATION-SPECIFIC VACCINE AGAINST RSV

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Respiratory syncytial virus (RSV) is the leading cause of acute lower respiratory infections in young infants around the world. Although the development of an effective vaccine has been a priority for the past 50 years, it is not yet available. Here, we analyzed previous RSV-vaccine clinical trials results in order to propose rational alternatives for future formulations.

We analyzed data comprising an RSV-vaccine phase 3 clinical trial of an adjuvanted F subunit vaccine candidate (1). Results showed no difference in RSV infection in infants born to pregnant women vaccinated with RSV F vaccine or placebo. Interestingly, data stratification according to country income level uncovers varying efficiencies, which are greater in low-income countries vs high-income countries, leading us to analyze whereas this difference could be (at least) partially ascribed to genetic differences regarding HLA population frequencies.

We found that the populations of countries grouped as high income countries share the distribution of most frequent HLA while the populations classified as low income countries exhibit a different HLA distribution profile.

Finally, employing state-of-the-art immunoinformatics techniques, we identified peptides that cover the entire proteome of RSV -both A2 and B1 strains- specifically predicted to encompass HLA from different populations, in order to trigger a strong T and B cell response. These results will be validated experimentally in our path to a rational design of a vaccine candidate.

This computational approach constitutes a cost-effective first step for generating a prototype vaccine candidate, aiming to contribute to the equitable access of a final universal formulation.

Keywords: RSV, Vaccine design, HLAs, Novel Epitopes
Conflict of Interest: None declared

Figure 1. Efficacy analysis of RSV nanoparticle F-protein against RSV and all-cause-associated lower respiratory tract infections (LRTI) in infants born to pregnant women vaccinated with RSV F vaccine or placebo, by low and high income countries. Low income countries: Bangladesh, Mexico, Philippines, and South Africa. High income countries: Argentina, Australia, Chile, New Zealand, Spain, United Kingdom, and United States. Adapted from Madhi et al. (Supplementary appendix).

132. CLINICAL TRIAL SIMULATION PREDICTS HIGHER EFFICACY AGAINST RSV FOR CLESROVIMAB (MK-1654) THAN FOR MATERNAL VACCINATION

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Background: Passive immunization with neutralizing monoclonal antibodies, such as clesrovimab (MK-1654), is a proven approach for the prevention of RSV-associated lower respiratory tract infection in infants. Active maternal vaccination to prevent RSV disease in infants is also being explored.

Methods: A published model was adapted to predict serum neutralizing antibody (SNA) titer profiles in infants born to mothers who were vaccinated against RSV. Efficacy data, including those from a phase 3 trial (Novavax, NCT02624947) evaluating RSV maternal vaccination, were used to qualify the model’s ability to predict efficacy in infants. To do this, a virtual clinical trial was designed wherein mothers expected to deliver just before or during the RSV season were administered a hypothetical vaccine or placebo. Clinical trial simulation was used to predict efficacy, and thus, to evaluate how well the adapted model predicted efficacy for the prevention of RSV-associated hospitalization for 3 months.

Results: Model predictions accurately captured the efficacy for the published phase 3 trial. A 60-fold increase in infant titers at birth was predicted to provide efficacy comparable with that of a clinical dose of MK-1654 for 6 months and a 30-fold increase was necessary to achieve similar efficacy of MK-1654 for 3 months. Larger increases in titers were predicted to be necessary in mothers of preterm versus full-term infants to maintain a similar level of protection.

Conclusions: Based on these predictions, MK-1654 is likely to provide greater efficacy for prevention of RSV infection in infants than maternal vaccines being developed.

Keywords: respiratory syncytial virus, monoclonal antibody, drug therapy, infants, maternal vaccines, clinical trial simulation
Conflict of Interest: BM, KV, FG, LC, JN, AL, and JS are employees of Merck Sharpe & Dohme, Corp., a subsidiary of Merck & Co., Inc., Rahway, NJ, USA and may own and/or hold stock options in Merck & Co., Inc., Rahway, NJ, USA. The remaining authors declare no conflict of interest.

133. RSV’S DIRECT AND INDIRECT BURDENS HAVE PARENTS HOPING FOR PREVENTION OPTIONS

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Executive Director, National Coalition for Infant Health

While babies and young children experience the direct impact of RSV, families must cope with the indirect impact as well. The social, emotional and financial burden can weigh heavily on many families, leaving parents eager for a preventive measure to help protect their children.

The National Coalition for Infant Health recently partnered with YouGov, a global public opinion and data company, to survey parents on the experience of having a child contract RSV. Recruiting from a pool of known parents, the survey captured 340 responses from parents who confirmed at least one of their children had been sick with RSV. Of those respondents, 230 (68%) reported their sick child had also been hospitalized because of the virus.
Of the surveyed parents, 82% agreed that if an RSV preventive intervention, such as an immunization, was available to protect their child from RSV, they would have wanted their child to receive it.

Many parents are also willing to step up to protect their child from the harm of RSV. Of surveyed parents, 76% agreed that if an immunization was available to mothers during pregnancy that would protect a baby from RSV, they or their partner would have received it.

The survey results illustrate families’ multifaceted struggle with RSV and highlight the desire for prevention options to protect against the virus.

Keywords: RSV, Impact, Burden, Direct, Indirect, Hospitalization, Immunization, Prevention

Conflict of Interest: None declared

134. COST-EFFECTIVENESS OF RSV PREVENTION STRATEGIES IN ENGLAND AND WALES

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With a suite of promising new RSV prophylactics on the horizon, including a single-dose long-acting monoclonal, and vaccines aimed at older adults and pregnant women, it is likely that one or more of these will supplement or replace existing Palivizumab programmes, which currently cover very high-risk infants only. However, choosing the optimal intervention programme will require balancing the costs of the programmes with the health benefits accrued. In this study, we compare the impact and cost-effectiveness of the next generation of RSV prophylactics in England and Wales, by integrating an existing dynamic transmission model with an economic analysis. Assuming an ICER threshold of £20,000/QALY, we determined the maximum per-dose purchase price under which these large-scale intervention programmes would be cost-effective. If administered seasonally to all infants at birth, we found that the long-acting monoclonal, Nirsevimab, would have to be priced around £60 per dose or less to cost-effectively replace the current Palivizumab programme. In addition, we calculated the maximum purchase price per dose to cost-effectively supplement the Palivizumab programme with a seasonal elderly vaccination programme using the RSVPreF3 vaccine from GSK. As these new RSV prophylactics become commercially available, estimates for the maximum per-dose purchase price will allow advisory bodies, such as the Joint Committee on Vaccine and Immunisation (JCVI), to consider whether national RSV vaccination programmes should be implemented.

Keywords: RSV, modelling, cost-effectiveness analysis, vaccines

Conflict of Interest: None declared

135. PALIVIZUMAB FOR RESPIRATORY SYNCYTIAL VIRUS PROPHYLAXIS: AN UPDATED VIEW OF ITS USE IN SOUTHERN BRAZIL

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Aim In children Respiratory Syncytial Virus (RSV) is the primary pathogen responsible for severe respiratory infections, with approximately 34 million infections per year. Currently, immunoprophylaxis with the monoclonal antibody Palivizumab (PVZ) represents the only alternative for prevention. This study aims to evaluate the effectiveness of PVZ in preventing RSV infection in children up to two years of age, breakthrough infections, adherence, and clinical-epidemiological characteristics of infants eligible for PVZ.

Methods Prospective cohort study. Children aged 0 to 2 years, with eligibility criteria to use the PVZ, were included during two consecutive RSV seasonality periods. The study was carried out at a reference public health unit for PVZ application, in partnership with the Hospital Pequeno Principe (HPP), in Curitiba, Southern Brazil. Respiratory viruses (RV) were investigated by qRT-PCR.

Results A total of 296 children were included. The main criterion for PVZ was prematurity, weighing less than 1,500g. The average rate of adherence to the PVZ regimen was above 90%. A total of 34 million infections per year. Currently, immunoprophylaxis with the monoclonal antibody Palivizumab (PVZ) represents the only alternative for prevention. This study aims to evaluate the effectiveness of PVZ in preventing RSV infection in children up to two years of age, breakthrough infections, adherence, and clinical-epidemiological characteristics of infants eligible for PVZ.

Conclusions Most eligible children for PVZ use were premature infants. There was high adherence to the PVZ dose series and a good performance in preventing RSV infections. However, RSV breakthrough infections were observed, and possible PVZ resistance needs to be investigated. Future studies are necessary to deepen these findings.

Keywords: palivizumab, adherence, breakthrough infections, respiratory syncytial virus

Conflict of Interest: None declared

136. IDENTIFICATION OF A NOVEL BENZAMIDE DERIVATIVE AS A SMALL-MOLECULE INHIBITOR TARGETING THE ENTRY OF THE RESPIRATORY SYNCYTIAL VIRUS

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Targeting viral entry offers an attractive strategy for inhibiting virus infection at its early stage to address the unmet medical for effective antivirals. We, therefore, followed a structure-based approach to design a novel small-molecule inhibitor of RSV by performing screening and structure optimization, wherein a naturally occurring small molecule viral entry inhibitor served as a chemical starting point. The designed novel benzamide derivative inhibitor, designated as 2f, was selected for its improved stability and potent antiviral activity from a series of investigated structurally related compounds. 2f was well tolerated by cells and able to inhibit RSV infection with a half maximal inhibitory concentration (IC50) of 35 nM and a favorable selectivity index (SI) of 3,275. Although the exact
molecular target for 2f is unknown, in vitro investigations revealed that the mode-of-action of the compound targets the early stage of infection by interacting with RSV virion, thereby interfering primarily with the attachment and potentially with the virus-cell fusion step. Moreover, intranasal administration of 2f to mice simultaneously or prior to intranasal infection with RSV significantly reduced viral load in the lungs by 2.6 log10 and 0.5 log10, respectively, pointing to the in vivo potential of the compound. Our results suggest that 2f is a viable candidate for further preclinical development and evaluation as an antiviral agent against RSV infections.

Keywords: viral attachment, viral entry, antiviral, small molecule, inhibitor
Conflict of Interest: The presented compounds are part of an IP application (EP21184516.9).

157. THE QUEST FOR A RESPIRATORY SYNCYTIAL VIRUS VACCINE: THINKING BEYOND THE F PROTEIN

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Background: Vaccine candidates targeting RSV antigen pre-F have shown efficacy in adults ≥60 years in Phase 2/3 trials. However, the ability to target multiple antigens with a single vaccine offers the potential to protect against pre-F escape mutants. Furthermore, a robust T-cell response to internal antigens may be beneficial in preventing severe disease. We developed a multi-component Vaccine MVA-BN-RSV targeting 5 RSV antigens F, Ga, Gb, M2-1 and N.

Data: Human challenge trial (HCT) in healthy 18-50 years (NCT04752644) and Phase 2 trial in ≥55 years (NCT02873386).

Results: In the HCT, MVA-BN-RSV vaccinated subjects showed a significant reduction in clinical RSV symptoms post-challenge, demonstrating a vaccine efficacy of 79–88.5% in preventing symptomatic RSV infection. Participants displayed ~4-fold increases in IgA and IgG GMTs 2-weeks after vaccination. IFN-γ-producing PBMCs increased 2- to 6-fold in response to the various stimulating pools 7-days after vaccination. Immune responses were durable and above baseline 6 months post-vaccination; notably T-cell responses against internal antigens were >2-fold baseline levels at 6-months.

Durability of immune responses are corroborated by Phase II data in adults ≥55 years; T-cell responses at week 1 were 5.4 to 9.7-fold above baseline, and for pool N and F remained 2- to 2.7-fold higher at week 56. Most participants responded to multiple RSV proteins simultaneously, demonstrating broad MVA-BN-RSV–induced humoral and T-cell responses.

Conclusion: MVA-BN-RSV activates various adaptive immune responses against RSV, which contribute to the high vaccine efficacy observed in the HCT. MVA-BN-RSV is being evaluated in a Phase 3 trial (NCT05238025).

158. PREVENTION OF INFANT RSV ILLNESS WITH A BIVALENT RSVPREF VACCINE IN PREGNANCY: RESULTS FROM A GLOBAL EFFICACY TRIAL

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6. Pfizer Worldwide Research, Development and Medical, Pearl River, NY, USA

In an ongoing, global, phase 3, randomized, double-blind, placebo-controlled study, pregnant ≥49-year-olds between 24–36 weeks’ gestation were randomized 1:1 to receive RSVPref 120 µg (RSV subgroups A and B, 60 µg each) vaccine or placebo. Vaccine efficacy (VE) in infants was assessed against RSV-positive, medically-attributed severe LRTI (RSV-MA-sLRTI) and medically-attributed LRTI (RSV-MA-LRTI) occurring ≤90 and ≤180 days after birth. The study was performed in 18 countries in both hemispheres over 4 RSV seasons.

Overall, 3758 maternal participants received RSVPref at the time of the primary analysis; 3682 received RSVPref and 3676 received placebo; 3570 and 3558 infants were born to mothers who received RSVPref or placebo, respectively. VE against RSV-MA-sLRTI was 81.8% (95.9% CI 40.6–96.3) in infants within 90 days after birth and remained significant through 180 days (VE 69.4% [97.58% CI 43.4–84.1%]). RSVPref VE against RSV-MA-LRTI was 57.1% (95.5% CI 14.7–79.8%); RSVPref and 51.3% (97.5% CI 29.4–66.8%); RSVPref) within 90 and 180 days post-birth, respectively. At 90 days the lower-bound CI was <20%, therefore not meeting statistical success criterion for this endpoint. RSVPref was safe and well tolerated by maternal participants, with no safety signals detected in infants through up to 24-months after birth; adverse event incidences were similar in vaccine and placebo groups for mothers and infants. In conclusion, maternal vaccination with RSVPref was efficacious at preventing severe LRTI caused by RSV in infants through 6 months of age. Clinically important efficacy was observed for RSV-MA-LRTI through 6 months of age. No safety concerns were observed.

Keywords: RSV: Maternal Vaccination; Infant Efficacy
Conflict of Interest: Beate Kampmann*, PhD COI: Institution received funding from Pfizer for conduct of study. Shabir Madhi PhD COI: Institution received funding from Pfizer for conduct of study. Other non-study declarations in institutional grant funding from Pfizer, BMGF, Novavax, GSK, Minervax. Eric A. F. Simões, MD COI: Institution received funding from Pfizer for conduct of study. Iona Munjal, MD COI: Employee of Pfizer and holder of Pfizer stock and stock options. Barbara A. Pahud, MD, MPH COI: Employee of Pfizer and holder of Pfizer stock and stock options. David Radley, MS COI: Employee of Pfizer and holder of Pfizer stock and stock options. Emma Shittu, PhD COI: Employee of Pfizer UK and holder of Pfizer stock and stock options. Annaliese S. Anderson, PhD COI: Employee of Pfizer and holder of Pfizer stock and stock options. Kena A. Swanson, PhD COI: Employee of Pfizer and Shareholder of Pfizer stock. William C. Gruber, MD COI: Received salary, stock, stock options from Pfizer, Inc. Alejandra Gurtman, MD COI: Received salary, stock, stock options from Pfizer, Inc.

159. A PHASE I/IB RANDOMIZED, OBSERVER-BLIND, PLACEBO-CONTROLLED CLINICAL TRIAL TO EVALUATE THE SAFETY AND IMMUNOGENICITY OF A RESPIRATORY SYNCYTIAL VIRUS-LIKE PARTICLE SUBUNIT VACCINE IN HEALTHY ADULTS

Ilse De Coster1, Isabel Leroux-Roels2, Kanchanamala Withanage1, Valentino D’Onofrio3, Geert Leroux-Roels2, Pierre van Damme4, Max Clarlet5, Wasima Rida6, Judy Wenn7, Jennifer Price7, Niranjan Kanesa-thasan1

1. University of Antwerp1; Ghent University2; Icosavax4

Respiratory syncytial virus (RSV) causes lower respiratory tract disease in older adults. We evaluated the safety and immunogenicity of a single intramuscular dose of IVX-121, an RSV pref protein-based virus-like particle (VLP) candidate vaccine, in healthy young (18-45 years) and older (60-75 years) adults. A total of 90 young adults (Phase 1) and 130 older adults (Phase 1b) were randomized to receive either IVX-121 formulations (25, 75, and 250 µg VLP ± 500 µg aluminum hydroxide) or placebo. Local adverse events (AEs) were mild in young (53.6%) and older (32.4%) adults and increased with adjuvant or VLP concentration. Rates of solicited systemic AEs in older adults were similar for IVX-121 (14.3%) versus placebo (15.8%). No vaccine-related serious AEs or AEs of special interest were
reported up to 180 days postvaccination. No beneficial adjuvant effect was observed across all dosage levels in either age group. RSV-A neutralization antibody (NAb) geometric mean titers (GMTs) increased up to 10-fold (7687 IU/mL) from baseline to Day 28. RSV-B NAb titers were in comparable range to RSV-A NAb titers. A similar pattern was observed for RSV pref protein-binding IgG antibody GMTs. B and T cell-mediated immune responses to RSV pre-F peptides also increased postvaccination. At 6 months postvaccination, RSV-A and RSV-B NAb responses were sustained across all unadjuvanted dosage levels within ranges of 64-98% and 40-53%, respectively, relative to the Day 28 GMTs. No changes post-versus pre-vaccination were observed with placebo throughout 6 months. IVX-121 was well-tolerated and immunogenic in young and older adults.

### 140. SPECIFICITIES AND COMMONALITIES OF RSV DISEASE BURDEN IN US, FRANCE, UK AND SPAIN, AND EXPECTED MODELED IMPACT OF Nirsevimab

Alexia Kieffer (1)* Agathe Devèze (1) Juan-Luis Lopez-Belmonte (2) Richard Hudson (3) Jason Lee (4) Marie Le Pannerer (1) Céline Hoestlandt (1) Klas Bergenheim (5) Matthieu Beuvelet (1)

**Affiliations**

-Background: Respiratory syncytial virus (RSV) is a leading cause of hospitalization in all infants and is responsible for up to 80% of all hospitalizations for bronchiolitis during epidemics. Nirsevimab, an anti-RSV monoclonal antibody, has demonstrated protection against RSV medically attended lower respiratory tract infection (MA-LRTI) in all infants for at least 150 days.

-Objective: The objective of this modeling study was used to examine country specificities and commonalities associated with RSV healthcare utilization (HCU), related costs, and the expected impact of the introduction of nirsevimab to the US, France, UK and Spain.

-Methods: A static decision analytic model was used to estimate health and cost outcomes related to RSV with or without nirsevimab immunization in each country. Health outcomes considered included hospitalizations, emergency room, specialist and primary care visits.

-Results: The distribution of RSV MA-LRTIs presented consistent pattern across all countries, with the outpatient visits accounting for the largest segment of HCU [87%(UK)-94%(ES)], whereas the direct medical economic burden was principally due to RSV related hospitalizations [63%(ES)-92%(US)]. RSV inpatient events were distributed equally between infants born during the RSV season and infants born prior the season. The majority were in term infants [89%(FR)–93%(ES)]. Nirsevimab offered consistent protection across all subpopulations, regardless of individual risk, or age at the start of the season.

-Conclusion: The RSV clinical burden is consistent across countries, whereas more heterogeneity is observed in the economic burden. Timely immunization with nirsevimab accounting for country specific seasonality can offer consistent protection for all infants and reduce HCU.

**Keywords**: Impact model, Nirsevimab, Disease burden, Economic burden

**Conflict of Interest**: AK, AD, JLLB, RH, JL, MLP, CH and MB are employees of Sanofi and may hold shares and/or stock options in the company. KB is employee of AstraZeneca and may hold shares and/or stock options in the company.

### 141. PROJECTED IMPACT OF RSV VACCINE IN US ADULTS ≥ 60 YEARS OF AGE

Sandra Talbird (1) Cameron Cook (1) Jessica DeMartino (2) Luis Hernandez-Pastor (3) Girishanthy Krishnarajah (2)*

1. RTI Health Solutions, Research Triangle Park, US
2. Janssen Scientific Affairs, Titusville, US
3. Janssen Pharmaceuticals, Beerse, Belgium

**OBJECTIVE**: This analysis estimates the projected impact of a novel vaccine for the prevention of respiratory syncytial virus (RSV) among adults aged ≥ 60 years in the United States (US).

**METHODS**: A decision tree model followed a cohort of 74,629,409 adults aged ≥ 60 years and compared outcomes for RSV vaccine with no vaccine over a time horizon of 3 years.

The model used data from the CYPRESS phase 2 study, which showed an efficacy of 69.8% (year 1) and 56.6% (years 2 and 3) against RSV-positive acute respiratory infection (ARI). Other model input values were obtained from US sources.

The analysis assumed 50% vaccine coverage and focused on medically attended and nonmedically attended symptomatic RSV cases. Total and incremental health outcomes as well as the number needed to vaccinate (NNV) were reported undiscounted. One-way sensitivity and scenario analyses were also conducted.

**RESULTS**: The RSV vaccine resulted in 3,056,723 (-30.6%) fewer symptom cases, 1,745 per death avoided. Among all input parameters tested, the results were most sensitive to changes in annual RSV incidence and duration of protection conferred from the vaccine.

**CONCLUSION**: A durable RSV vaccine for adults that provides protection over multiple RSV seasons is expected to substantially reduce RSV cases, healthcare resource utilization, and deaths among adults aged ≥ 60 years in the US.

**Keywords**: Adult Vaccine, US, Respiratory Syncytial Virus, Burden of Illness Model

**Conflict of Interest**: SE Talbird and C Cook are both employees of RTI Health Solutions, which received funding for this analysis and publication; they maintained scientific control of analyses and have no other competing interests to declare. G Krishnarajah and JK DeMartino, are employees of Janssen Scientific Affairs. L Hernandez-Pastor is an employee of Janssen Pharmaceuticals. GK, JKD, and LHP hold stock/stock options in Johnson & Johnson.

### 142. US HEALTHCARE PROVIDERS’ PREFERENCES AND WILLINGNESS TO RECOMMEND NOVEL RSV PREVENTIVES TO PROTECT INFANTS: A DISCRETE CHOICE EXPERIMENT

Kathleen M. Beustrieren (1) Amy Law (2)* Lewis Kopenhafer (1) Martine C. Maculaitis (1) Patrick Olsen (1) Oliver Will (1) Brett Hauber (2) Jeffrey T. Vietri (2) Kari Yacisin (2) Joseph C. Cappelleri (2) Joshua Coulter (2) Kimberly Shea (2)

1 Cerner Enviros Inc.,
2 Pfizer Inc., New York, USA

**Background**: We assessed healthcare provider (HCP) preferences and willingness to recommend respiratory syncytial virus (RSV) preventives to protect infants in the United States (US).
Methods: An online survey including a discrete choice experiment was conducted among US HCPs who treated pregnant people (PP) or infants. RSV preventive attributes included effectiveness, duration of protection during RSV season, injection recipient/timing, preventive type, and type of visit required to receive injection. HCPs chose between two hypothetical preventive profiles (monoclonal antibodies (mAb), maternal vaccine) whose attributes varied across 12 choice tasks and a no-preventive option. Hierarchical Bayes models estimated attribute-level preference weights; attribute relative importance (RI) was computed as the difference between preference weights of most- and least-preferred levels of each attribute, standardized to a 0 (least)-100 (most) scale. HCPs were compared by patient population treated.

Results: Among 310 geographically-diverse HCPs, 49.0% treated infants (vs. PP). A preventive (vs. none) was chosen 96% of the time. Among attributes evaluated, effectiveness of the preventive had the most impact on preferences (RI=41.7; Figure 1). All else equal, vaccine was preferred over mAb, although preventive type was among the least important attributes (RI=7.2). Both HCP groups ranked RIs similarly; however, HCPs who treated infants (vs. PP) placed numerically greater importance on duration of protection during RSV season (RI=37.5 vs. 33.4, p=0.009).

Conclusions: HCPs strongly preferred an RSV preventive over none. Effectiveness and duration of protection were most important in RSV preventive choice. Assuming comparable effectiveness and duration of protection, both HCP groups preferred a vaccine over mAb.

Keywords: discrete choice experiment, healthcare provider preferences, infants, monoclonal antibodies, pregnant people, respiratory syncytial virus, United States, maternal vaccination

Conflict of Interest: Funding for this study (including abstract preparation) was provided by Pfizer, Inc. to Cerner Enviza, Inc. AL, BH, JTV, KY, JCC, and KS are employees of Pfizer, Inc. KMB, UK, MCM, PL, and OW, employees of Cerner Enviza, Inc.

145. RESULTS AT 12 MONTHS POST-VACCINATION WITH A RESPIRATORY SYNCYTIAL VIRUS (RSV) PREFUSION F PROTEIN INVESTIGATIONAL VACCINE (RSVPREF3 OA)

Tino F Schwarz (1), Shinn-Jang Hwang (2), Pedro Ylisastigui (3), Chiu-Shong Liu (4), Kenji Takazawa (5), Makoto Yono (6), John Ervin (7), Charles Andrews (8), Charles Fogarty (9), Tamara Eckermann (10), Delphine Collete (11), Magali de Heusch (12), Nathalie De Schrevel (11), Bruno Salaua (11), Axel Lambert (12), Céline Marechal (12), Phoebe Nakanwagi (12), Marc Lievens (12)*, Veronica Hulstrøm (12)

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2. En Chu Kong Hospital, New Taipei City, Taipei Veterans General Hospital, and National Yang Ming Chiao Tung University School of Medicine, Taipei, Taiwan
3. Alliance For MultiSpecialty Research, Fort Myers, United States
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5. Medical Corporation Shihanokai, Shihanokazaki Clinic, Tokyo, Japan
6. Nish-Kumamoto Hospital, Kumamoto, Japan
7. The Alliance for MultiSpecialty Research, Kansas City, United States
8. IMIA Research San Antonio, Texas, United States
9. Spartanburg Medical Research, South Carolina, United States
10. Praxis Dr. med. Irmgard Maier-Bosse, Munich, Germany
11. GSK, Rixensart, Belgium
12. GSK, Wavre, Belgium

Background: In an ongoing study (NCT04886596), RSVPref3 OA that contains 120 µg RSVPref3 and AS01E demonstrated high efficiency against RSV disease in adults ≥60 years. In the current study, RSVPref3 OA showed high immunogenicity and acceptable safety profile until month (M) 6. Here we present immunogenicity/safety results until M12.

Methods: This phase 3 multi-country ongoing randomized study (NCT04732871) enrolled adults ≥60 years to receive one RSVPref3 OA dose at day (D) 0. Overall and by age group humoral immunity (HI subset, RSVP-A/RSV-B neutralizing antibody geometric mean titers [Nab GMTs]) and cell-mediated immunity (CMI subset) were measured at pre-vaccination (D1), D31, M6 and M12. The CMI response was assessed in terms of frequency of RSVPref3-specific CD4+/CD8+ T-cells. Serious adverse events (SAEs) and potential immune-mediated diseases (pIMDs) related to vaccination were evaluated during M6-M12.

Results: 1653 participants received one RSVPref3 OA dose at D1. Overall, RSVP-A/RSV-B Nab GMTs increased 105.7/8-fold between D1 and D31, declined thereafter but remained 3.1/2.3-fold above pre-vaccination levels at M12. In all age groups, RSVP-A/RSV-B Nab GMTs followed a similar trend (Figure). RSVPref3-specific CD4+ T-cell median frequency (events/106 cells) increased to 1344 at D31, remaining above baseline by M12 (575). No new SAES and pIMDs related to RSVPref3 OA were reported during M6-M12.

Conclusion: In adults ≥60 years, one RSVPref3 OA dose was immunogenic and had an acceptable safety profile. HI and CMI responses were high at D31 and remained above pre-vaccination levels until M12 post-vaccination.

Keywords: prefusion F protein, neutralizing antibody, RSVP-A, RSVP-B, immunogenicity, safety, older adults

Funding: GlaxoSmithKline Biologicals SA
Background: Inactivated or recombinant influenza (IIV, RIV), tetanus toxoid, diphtheria toxoid, acellular pertussis (Tdap), and SARS-CoV-2 vaccines are recommended for use in pregnancy in many countries, and additional vaccines (RSV, GBS) are in development. As the number of antenatal vaccines increases, it will be critical for implementation to understand the extent to which they can be administered simultaneously.

Methods: We searched PubMed and Embase for studies evaluating immune responses to vaccines recommended in pregnancy when given simultaneously with other vaccines. Safety data were not a focus of this review. As pregnancy is often an exclusion criterion for participation in clinical trials, we also included studies conducted among male and female participants aged ≥14 to <50 years.

Results: We identified 271 studies; 30 met inclusion criteria. Five studies were conducted among pregnant women: only one included immunogenicity study endpoints. Vaccine combinations reviewed and their relevance during pregnancy are summarized in Figure 1. Nine studies evaluated some combination of IIV/RIV, Tdap, RSVpreF, or SARS-CoV-2. Of these, non-inferiority was established for most antigens during simultaneous administration, but reductions in immunogenicity of pertussis components were common.

Conclusion: Among males and pregnant and non-pregnant females, simultaneous administration generally did not result in inferior immune responses to vaccines recommended for antenatal use. The exception was acellular pertussis, however the absence of a correlate of protection for pertussis makes the clinical significance of this finding unclear. The paucity of available data and increasing number of antenatal vaccines supports the need for expanded coadministration studies in pregnant women.

Keywords: Maternal Immunization, Coadministration, Simultaneous administration, immunogenicity

Conflict of Interest: YA, MD, IM, KY, BG and JA are employees of Pfizer and may hold stock or stock options. CS has received consulting fees from Pfizer for this work.

### Summary of relevant publications

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Both vaccines in simultaneous evaluation recommended (or under investigation for use) during pregnancy

At least one (but not all) vaccines in simultaneous evaluation recommended (or under investigation for use) during pregnancy

No vaccines in simultaneous evaluation recommended (or under investigation for use) during pregnancy

### 145. NOVEL PREFUSOGENIC-F, G AND M PROTEIN-BASED VIRUS-LIKE PARTICLE AS VACCINE CANDIDATE FOR RESPIRATORY SYNCYTIAL VIRUS

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Respiratory syncytial virus (RSV) infection is a major cause of severe respiratory disease in infants and young children worldwide. There is no licensed vaccine and prophylactic treatment options are limited and expensive. RSV fusion (F) glycoprotein induces effective neutralizing antibodies, and is thus a focus for vaccine development efforts. Studies have shown that a partially cleaved, fusion-inactive F protein, termed prefusogenic F (preFg) is significantly more stable, immunogenic and produces high titer antibodies to both the prefusion and postfusion F structures that have limited neutralizing epitopes. Along with fusion protein, glycoprotein (G) also elicits potent neutralizing antibodies and matrix protein (M) plays a central role in viral assembly. Therefore, we have developed RSV virus-like particles (RSV-VLPs) using the baculovirus expression system consisting of preFg, G and M proteins. Electron microscopy imaging revealed formation of spherical VLPs sized between 70-100 nm with association of preFg, G and M proteins. IgG was elicited in mice immunized with intramuscular as well as various mucosal routes (sublingual, nasal and pulmonary). The VLPs induced both anti-F and anti-G IgG antibodies. IgG subclass analysis revealed balanced IgG2a and IgG1 response after immunization by intramuscular and pulmonary routes. Mice immunized with pulmonary route resulted in IgA in both nose and lungs while induction was limited to nose after nasal delivery. Sublingual delivery induced minimal IgA. Overall, we believe that we are the first ones to develop RSV-VLPs with prefusogenic F protein as a vaccine candidate that could be delivered by systemic and various mucosal routes.

Keywords: virus-like particles, prefusogenic-F, vaccine, pulmonary immunization

Conflict of Interest: None declared
146. SAFETY AND IMMUNOREACTIVITY OF A LIVE, ATTENUATED RSV VACCINE IN RSV-NAÏVE CHILDREN 6 TO 36 MONTHS OF AGE

Meissa Vaccines, Inc, Redwood City CA

Background: Respiratory syncytial virus (RSV) is a major cause of morbidity and mortality in infants and young children around the world, but no vaccine is available to directly protect young children. We developed a live, intranasal RSV vaccine attenuated by codon deoptimization or deletion of RSV genes associated with virulence and expressing a fusion protein with enhanced pre-fusion stability.

Methods: This is a randomized, single-blind, placebo-controlled dose-escalation Phase 1c study in children 6 to 36 months of age who tested negative for RSV neutralizing antibodies at screening. Subjects were administered dosages ranging from 10^6 PFU to 10^9 PFU, with some subjects given two doses 28 days apart of the 10^6 and 10^9 PFU formulations. Parents of study participants recorded solicited adverse events (AEs) daily for 14 days post-vaccination and unsolicited AEs for 28 days post-vaccination. Subjects were monitored for serious AEs (SAEs) and medically-attended AEs for the duration of their participation. Immunogenicity was assessed via serum neutralizing antibodies (nAb), serum SIV pre-f-specific binding IgG, and nasal pre-f-specific IgA.

Results: A total of 66 RSV-seronegative children have been enrolled to date. Vaccination was well-tolerated, and no safety signals have been identified. There were no SAEs and no study discontinuations due to AEs. The most common solicited AEs were rhinorrhea and cough, which were no more common in vaccine recipients than in placebo recipients. All solicited AEs in 10^9 PFU recipients were Grade 1 (mild). No virus virus shedding was detected in subjects given 10^9, 10^8, or 10^7 PFU dosages. Three of 22 subjects given the 10^9 PFU vaccine shed vaccine virus by dPCR, but none of them had any respiratory symptoms or fever associated with shedding. Two doses of 10^8 PFU induced a ≥4-fold rise in serum nAb in 78% and a ≥2-fold rise in nasal IgA in 44% of recipients, with a mean serum nAb GMT of 798 (214).

Conclusions: Meissa Vaccine’s intranasal, live, attenuated RSV vaccine was well-tolerated, and the amount of detectable vaccine virus shedding was infrequent and low. A two-dose regimen of vaccine vial size for this setting, data on number of women per day and proportion attending antenatal care (ANC) within the proposed gestational window for vaccine delivery is prerequisite.

147. ASSESSMENT OF GESTATIONAL AGE AT ANTENATAL CARE VISITS AMONG KENYAN WOMEN TO INFORM VIAL SIZE FOR RESPIRATORY SYNCYTIAL VIRUS VACCINE IN LOW- AND MIDDLE-INCOME COUNTRIES

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2. Kenya Medical Research Institute, Center for Global Health Research, Kisumu, Kenya
3. Kenya Medical Research Institute (KEMRI), Centre for Microbiology Research, Nairobi, Kenya.
4. University of Nairobi, Department of Microbiology, Nairobi, Kenya.
5. School of Life Sciences, University of Warwick, Coventry, UK
6. Center for Vaccine Innovation and Access, PATH, Seattle, USA

Background: Maternal respiratory syncytial virus vaccines that are likely to be implementable in low- and middle-income countries are in final stages of clinical trials. To inform vaccine uptake and guide the development of vaccine vial size for this setting, data on number of women per day and proportion attending antenatal care (ANC) within the proposed gestational window for vaccine delivery is prerequisite.

Methods: We undertook administrative review and abstraction of ANC timing visit records from 2019 registers of 24 selected health facilities in Kilifi, Siaya and Nairobi counties in Kenya. Data analysis involved descriptive summaries of the number and proportion of women attending ANC within the gestational window period of 28-32 weeks and 24-36 weeks.

Results: A total of 62153 ANC records were abstracted in health centres and 6 (4%) in primary health units. A total of 1699 (2.7%) women attended ANC within the gestational window period of 28-32 weeks and 24-36 weeks respectively were: 4 (2%) and 7 (4%) in primary health units and 2 (0.3%) and 9 (1.4%) in health centres.

Conclusion: The number of daily ANC attendees who are within the vaccine window varies between the levels of healthcare. A multidose vial size with about five doses per vial, approximates daily ANC attendance and would not incur possible wastage in similar settings.

Keywords: Respiratory syncytial virus, vaccine, low- and middle-income countries, maternal rsv

Conflict of Interest: None declared

148. FUNCTIONAL ROLE OF CDC AND ADCC FOR RSV-SPECIFIC ANTIBODIES FOLLOWING MATERNAL VACCINATION

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Introduction: Respiratory syncytial virus (RSV) is the most important cause of viral lower respiratory tract illness (LRTI) in infants and children worldwide. Currently, no safe and licensed vaccine against RSV exist. Maternal vaccination has been evaluated as a control strategy in the young. Antibody-mediated events including complement-dependent cytotoxicity (CDC) and antibody-dependent cellular cytotoxicity (ADCC) are antibody-mediated effector mechanisms and the principal means of control in post-maternal vaccination scenario. Therefore, this study was carried out to characterize how maternal-derived RSV-antibodies in mice pups mediate CDC and ADCC as antibody-dependent protection mechanisms.

Methods: Sera were collected from mice pups born by mother mice that were vaccinated in a prime-boost fashion using codon-optimized genetic vaccine expressing the fusion protein of RSV (RSV-F). Sera were analyzed for CDC by application of complement fixation test. ADCC was analyzed via FC-gamma receptor activation test through measurement of IL-2 release in BW5147 cells. Results: Following vaccination, a 512-fold increase in RSV-neutralizing antibodies, and a 100-fold reduction in RSV copy numbers were recorded in mice recipients. Serum antibodies in pups vaccinated mothers were found to activate and fix complement leading to a 5-fold increase in antibody fixation titre. FC-gamma receptors II (CD16) and IV (CD64) of BW5147 effector cells were both activated in response to RSV-specific antibodies leading to IL-2 release (≥10 OD). Conclusion: The results obtained suggest the positive role of CDC and ADCC and could explain in part the mechanism-specific basis of the efficacy of RSV vaccine in mice pups following maternal vaccination.

Keywords: RSV, Maternal Vaccination, Complement-dependent cytotoxicity (CDC), Antibody-dependent cellular cytotoxicity (ADCC), Mice pups

Conflict of Interest: None declared
149. RESPIRATORY SYNCYTIAL VIRUS AND VACCINATION IN KENYA; WHAT ARE THE HEALTHCARE WORKERS' PREFERENCE?

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1. Kenya Medical Research Institute, Center for Global Health Research, Kisumu, Kenya
2. Kenya Medical Research Institute, Wellcome Trust Research Programme, Kilifi, Kenya

Background: RSV is a major cause of childhood pneumonia, especially among infants aged below 6 months who bear the biggest burden of RSV disease. Little is known about healthcare workers’ (HCWs) knowledge and attitudes around RSV and vaccination. We investigated general and RSV-specific knowledge and attitudes of HCWs towards RSV and vaccination in two Kenyan counties.

Methods: Between September-October 2021, we conducted a cross-sectional survey among HCWs in eight health facilities (Siaya-5, Nairobi-3) and Ministry of Health (MoH) officials. We enrolled HCWs delivering services directly to mothers at the maternal and child health departments and MoH officials in-charge of vaccine distribution, policy and management.

Results: We interviewed 104 HCWs (from facilities-94 and officials-10; Siaya-60, Nairobi-44); 65 (62.5%) were nurses and 49 (47.1%) had 5-10 years of experience. In general, most participants would recommend maternal vaccination to protect the mother 91 (88.4%) and baby 76 (73.8%), a single-dose vaccine schedule 62 (59.6%) for maximal compliance 38/62 (61.3%) and single-dose/device vaccines 50/86 (58.1%) to prevent wastage and contamination. Of the 104, only 41 (39.4%) knew about RSV and 38/41 (92.7%) reported that pregnant women should be vaccinated against RSV. Nearly all (39/41) respondents were not aware of RSV vaccination products in the market but would recommend the vaccine if available.

Conclusion: There is a huge gap in knowledge around RSV and vaccination among Kenyan HCWs. Most HCWs would recommend maternal vaccination, preferring single-dose scheduling and single-dose vials/devices should the vaccines be available. We recommend creation of RSV awareness among the HCWs.

Keywords: Respiratory syncytial virus, health care workers, vaccination strategies, maternal vaccination, perceptions, vaccine schedule

Conflict of Interest: None declared

150. APPLICATION OF A MULTIDISCIPLINARY AND REFLECTIVE MULTI-CRITERIA DECISION ANALYSIS FOR THE ASSESSMENT OF NIRSEVIMAB FOR PREVENTION OF RESPIRATORY SYNCYTIAL VIRUS IN SPAIN

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11. Department of Pediatrics, Nazaret Healthcare Center, Valencia, Spain
12. Department of Quantitative Methods in Economics and Management, University Las Palmas de Gran Canaria. Las Palmas, Spain
13. Department of Virology, Scientific Advisory and Management (Director Emeritus), University of Valladolid, Castilla y León, Spain.

Background: Respiratory syncytial virus (RSV) is a highly infectious disease with a significant humanistic and socioeconomic burden. Nirsevimab is the first strategy for RSV prevention in children <12 months during their first RSV season. The multi-criteria decision analysis (MCDA) is an increasingly used instrument to inform preferences in a more consistent, explicit and transparent manner. The objective of this study was to develop a new MCDA framework for RSV preventative alternatives and to assess the value of nirsevimab in Spain within it, versus placebo and palivizumab.

Methods: An ad-hoc MCDA framework with 26 criteria was created to reflect multiple relevant attributes for the assessment of current and future preventive measures for RSV. The estimated value of nirsevimab was obtained by means of an additive linear model combining weights and scores assigned by a multidisciplinary committee of 9 experts. A re-test and two sensitivity analysis were conducted.

Results: Nirsevimab was evaluated by the committee as a measure that adds value to the current RSV Spanish scenario, by providing a high efficacy for prevention of all healthy late-preterm and term infants and a wider protection versus current alternatives. In addition, its implementation might increase the level of public health awareness among the general population, while reducing health inequities.

Conclusions: Nirsevimab has been evaluated as a measure which adds value for RSV prevention in children <12 months in Spain when compared to placebo or palivizumab. This exercise allows to understand where the value of preventive measures lies for the different agents.

Keywords: Respiratory Syncytial Virus, Prevention, Monoclonal antibodies, Multi-Criteria Decision Analysis, MCDA

Conflict of Interest: The authors declare that they have no competing interests.

151. BOVINE RESPIRATORY SYNCYTIAL VIRUS (BRSV) IN CALVES: A BETTER MODEL TO UNDERSTAND THE MECHANISMS OF HRSV IN HUMANS.

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1. Faculty of Sciences, Yahia Farès University, Medea Algeria.
2. VIDO: Vaccine and Infectious Disease Organization, Canada

Respiratory syncytial virus (RSV) is an important infectious agent and the leading cause of viral lower respiratory tract infection in young children worldwide. Clinical manifestations range from asymptomatic infection to bronchopneumonia, bronchiolitis, and pneumonia. Like human RSV (HRSV), bovine RSV (BRSV) is a negative-stranded RNA. The pathological lesions caused by HRSV and BRSV are very similar.

Vaccination of calves with formalin-inactivated BRSV (FI-BRSV) induces low levels of cellular immunity. Since inactivated and subunit vaccines formulated with CpG oligodeoxynucleotides (ODNs) have been shown to induce cellular immune responses, we studied the ability of a FI-BRSV vaccine formulated with CpG ODN to elicit cellular immunity against BRSV. Neonatal calves were immunized with FI-BRSV, FI-BRSV formulated with CpG ODN or medium and challenged with BRSV after two immunizations. Exacerbation of disease, characterized by increases in clinical signs of infection and BRSV-specific serum IgE and decreases in IFN-γ production, has been demonstrated in calves infected with BRSV following vaccination with FI-BRSV. It is thus hypothesized that BRSV-specific cellular immune responses, characterized by interferon-γ (IFN-γ) production and BRSV-specific IgG2, could be protective against subsequent infections.

Calves vaccinated with FI-BRSV formulated with CpG ODN developed increased numbers of IFN-γ secreting cells in the peripheral blood and broncho-tracheal lymph nodes and enhanced BRSV-specific serum IgG2 in comparison to FI-BRSV immunized animals. Calves that received FI-BRSV vaccine formulated with CpG
ODN also experienced a reduction in the amount of BRSV in the lung tissue. Thus, CpG ODN appears to be a suitable candidate adjuvant for inactivated BRSV vaccines.

**Keywords:** BRSV, HRSV, vaccine, CpG motifs, immunization.

**Conflict of Interest:** None declared

### 152. THE POTENTIAL PUBLIC HEALTH BENEFIT OF RESPIRATORY SYNCYTIAL VIRUS (RSV) VACCINATION IN OLDER ADULTS IN CANADA

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4Henry J. Kaiser Research Professor; Harvard T.H. Chan School of Public Health, Boston, MA, USA
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6Senior Director, Health Economics & Outcomes Research; Moderna, Inc. Cambridge, MA, USA
7Director, Health Economics & Outcomes Research; Moderna, Inc. Cambridge, MA, USA

**Background:** RSV causes Acute Respiratory Disease (ARD), including Lower Respiratory Tract Disease (LRTD), which can result in hospitalization and death in at-risk and older adults. The study objective was to estimate the potential public health benefit of an annual RSV vaccination strategy in older adults (>260 years) in Canada.

**Methods:** A decision-analytic model was developed to compare no vaccination to a hypothetical 1-dose vaccine administered prior to the RSV season with an assumed efficacy of 75% against outcomes of RSV-ARD, RSV-LRTD, and RSV-LRTD-hospitalizations. Canadian data were used to estimate RSV-related hospitalization rates and in-hospital mortality. Estimates from the United States were used to fill data gaps for RSV incidence and severity. Other outcomes included RSV-related deaths and number needed to vaccinate (NNV) to prevent one RSV-LRTD hospitalization or death.

**Results:** The model predicted 642,700 RSV-ARD cases annually in older adults in the absence of a vaccine; the vaccine would reduce RSV-ARD cases by 342,300 (53%). Compared to no vaccine, the vaccine would reduce RSV-LRTD cases, hospitalizations, and deaths by 144,100; 2,700; and 223, respectively, representing a 53% reduction for each outcome. The NNV to prevent one RSV-LRTD hospitalization or death is 3,600 or 42,900.

**Conclusions:** Data on the incidence and severity of RSV in the Canadian population are lacking and will be needed to better characterize the burden of RSV in Canada and to inform decision-makers on the value of forthcoming RSV vaccines. Despite these data limitations, an effective RSV vaccine will prevent significant morbidity and mortality in older adults.

**Keywords:** Respiratory Syncytial Virus, Vaccination, Canada

**Conflict of Interest**

**Table 1. Model Parameters**

<table>
<thead>
<tr>
<th>Model Parameter</th>
<th>Value</th>
<th>Data Source</th>
</tr>
</thead>
</table>
| 0-60 | 2,190,970 | 76%
| 60-69 | 1,280,930 | 76%
| 70-79 | 840,545 | 76%
| 80 & above | 801,205 | 76%

**Vaccination coverage**

**Percentage with symptomatic RSV**

| Percentage with RSV-LRTD* | 42.1% | GSK RSV OA candidate vaccine clinical trial data. Slide deck presented to AIHP October 2022. |

**Table 1. Model Parameters**

<table>
<thead>
<tr>
<th>Model Parameter</th>
<th>Value</th>
<th>Data Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>No treatment</td>
<td>80.5%</td>
<td>Calculated (100% - % with outpatient care)</td>
</tr>
<tr>
<td>Rate of RSV-LRTD cases requiring care</td>
<td>1.9%</td>
<td>Schneider (2018) Bunter-influenza, respiratory syncytial virus, and other respiratory viruses and the completeness of viral respiratory identification among respiratory inpatients, Canada, 2003-2016. Influenza and Other Respiratory Viruses 12:133-137.</td>
</tr>
<tr>
<td>No outpatient care</td>
<td>0%</td>
<td>Assumption (RNV-LRTD requires at least one outpatient visit)</td>
</tr>
<tr>
<td>Vaccine efficacy against RSV-ARD, RSV-LRTD, RSV-LRTD requiring inpatient care, and RSV-ARD requiring inpatient care</td>
<td>75%</td>
<td>Assumption</td>
</tr>
</tbody>
</table>

**Keywords:** RSV, Respiratory syncytial virus; LRTD: Lower respiratory tract disease; URS: Upper respiratory disease; ARD: Acute respiratory disease

* US data

### 155. PRE-FUSION RSV NANOPARTICLE VACCINE IMMUNE RESPONSES TARGET PRE-FUSION, POST-FUSION, AND P27 EPITOPES THAT TOGETHER CONTRIBUTE TO BROADLY NEUTRALIZING ANTIBODIES AND PROTECTION AGAINST LIVE VIRUS CHALLENGE

Nita Patel (1)*, Jing-Hui Tian (1), Bin Zhou (1), Youri Lee (1), Kelsey Jacobson (1), Mimi Guebre-Xabier (1), Vivek Shinde (1), Gale Smith (1), Gregory Glenn (1)

1Novavax, Inc. Gaithersburg, Maryland, USA

The Novavax Pre-fusion RSVF Cav1 nanoparticle vaccine is a stabilized near full-length F protein expressed in insect cells. Prefusogenic F was used as a backbone to assess the immunogenicity and protective efficacy upon introducing Cav1 prefusion-stabilizing mutations. Octet kinetic analysis of antigenic site-specific monoclonal antibodies confirmed all pre-and post-fusion antigenic sites and neutralizing epitopes were intact. Cotton rats were immunized with pre-fusion RSVF at suboptimal doses adjuvanted with Matrix-M® adjuvant on Day 0 and 21, then challenged intranasally with RSVA Long on Day 42. Immune responses were evaluated by ELISA to RSV F protein, an RSV Neutralization assay, and prefusion F specificity of antibodies was determined by competitive ELISA and Octet competition binding assays using antigenic site-specific antibodies to pre- and post-fusion epitopes. Prefusogenic F with Cav1 mutations was significantly more immunogenic than Prefusion F with DS-Cav1 mutations. Functional RSVA and RSVB Neutralization responses were higher with RSVF Vaccine-Cav1 nanoparticles. Antibody responses to pre-fusion specific antigenic sites increased after the second vaccine dose. Pre-fusion RSVF nanoparticle vaccine provided sterilizing immunity in the lungs and reduced viral load in upper airways post RSV live virus challenge in cotton rats. Together, these data show that Novavax’ Pre-fusion RSVF nanoparticle vaccine is a potent immunogen eliciting a robust RSV F-specific immune response to pre- and post-fusion F epitopes.

**Keywords:** RSV, F Protein, RSV F, Vaccine, Cotton Rat, Neutralizing Antibody, Cav1, Immunogenicity, Protection, Challenge, Efficacy

**Conflict of Interest**

Authors are employees of Novavax, Inc.; compensation includes salary and stock ownership. This compensation does not compromise the integrity of the scientific findings presented herein.
INTRODUCTION: New long-acting antibodies for the single dose prevention of respiratory syncytial virus (RSV) lung infection are in development to be administered to all infants before or during their first RSV season. For infants born during the season, administration as soon as feasible after birth is expected to provide optimal protection.

OBJECTIVE: This study examined the timing of a first outpatient visit after birth hospitalization for US infants with commercial and Medicaid insurance.

METHODS: Outcome: time to the first outpatient visit following birth-hospitalization discharge (FOV). This study used the Merative® MarketScan® Commercial and Multi-state Medicaid Databases. Timeframe: April 2015 – September 2021. Population: US infants with a birth hospitalization of up to 5 days.

RESULTS: Since April 2020 (COVID era), 87.0% of commercially insured infants had an FOV within 5 days as compared to 77.7% of Medicaid infants (Table 1). 93.5% of commercially insured infants had an FOV within 14 days as compared to 86.6% of Medicaid infants (Table 1). There were no differences between infants born during the RSV season (November-March) and out-of-season (April-October).

CONCLUSION: While the percent of infants with FOV within 5 days increased in the COVID era, Medicaid infants still lag commercially insured infants. Approximately 1 in 7 commercially insured and 1 in 4 Medicaid infants do not have an outpatient visit within 5 days of birth hospitalization discharge. For US infants born during the RSV season, administration of long-acting RSV antibodies prior to birth hospitalization discharge could ensure optimal uptake.

Keywords: monoclonal antibody

Conflict of Interest: CBN, WLV, MG, and CPR are employees of Sanofi. BLB, MR, and CRL are employees of Merative whose work was supported by Sanofi.

Table 1. Time to the first outpatient visit following birth hospitalization discharge, in the pre-COVID (April 2015 – January 2020) and COVID (April 2020 – September 2021) eras, for commercially insured infants and Medicaid infants. (Merative® MarketScan® Commercial and Multi-state Medicaid Databases; among infants with a birth hospitalization discharge up to 5 days of age.)
from severe RSV disease, an extended half-life monoclonal antibody (i.e. nirsevimab) was developed as a the basis for a universal immunoprophylaxis strategy. Modelling was utilized to assess the health and economic burden of RSV disease, comparing nirsevimab to the standard of care in Canada.

Methods: Utilizing a static decision tree model, various health outcomes (inpatient hospitalization, ICU, mechanical ventilation, ER, primary care, mortality) and associated direct healthcare costs were calculated over one RSV season for three infant categories (palivizumab-eligible, preterm, term). Scenario analysis explored four costing matrices ranging from conservative to liberal. All health-related parameters and costs were tailored to the Canadian environment with appropriate CPI adjustments.

Results: Implementing an immunization strategy with nirsevimab across all three infant categories (i.e. all-infant) during an infant’s first RSV season may reduce healthcare-related outcomes in Canada by approximately 24,600 hospital-related admissions. Among the various scenarios, direct healthcare savings reached a maximum net amount of $37.5M.

Conclusions: All possible scenarios for an all-infant immunization strategy with nirsevimab (relative to the standard of care) resulted in reductions in RSV-related health and economic burden across Canada. Additional considerations pertaining to societal impact and downstream sequelae may optimize this model’s final results.

Keywords: economics, model, lower respiratory tract illness, nirsevimab, RSV, burden, cost, infants, Canada

Conflict of Interest: TS, JKL, GL, and AK are employees of Sanofi

157. PHARMACOKINETICS, SERUM-NEUTRALIZING ACTIVITY, AND EFFICACY AGAINST RSV MALRI FROM A PHASE 1B/2A STUDY OF MONOCLONAL ANTIBODY CLESROVIMAB (MK-1654) IN INFANTS

1. Merck & Co., Inc., Rahway, NJ, USA
2. Certara, Princeton, NJ, USA

Background: Clesrovimab (MK-1654), an investigational RSV-neutralizing monoclonal antibody that targets site IV of the RSV F protein, is in phase 3 development for the prevention of RSV medically attended lower respiratory tract infection (MALRI) in infants.

Methods: This phase 1b/2a study was conducted to evaluate safety, tolerability, pharmacokinetics (PK), and serum neutralizing antibody (SNA) titers of MK-1654 in preterm (29-35 weeks’ gestational age) and full-term infants. Participants (age, 2 weeks-8 months) were randomized in a 4:1 ratio within 5 panels (preterm: 20, 50, 75, or 100 mg; full-term: 100 mg) to receive a single dose of MK-1654 or placebo. MK-1654 serum concentrations and SNA titers were quantified. A preliminary population pharmacometrics (popPK) model was developed. Efficacy of MK-1654 was predicted using clinical trial simulations based on this model. Exploratory efficacy analysis of observed RSV MALRI through day 150 was conducted.

Results: Data from 111 preterm infants and 32 full-term infants were available. The PK of MK-1654 was best characterized by a linear 2-compartment popPK model. The half-life of MK-1654 was ~42 days. Increasing concentrations of MK-1654 were associated with increasing SNA. A single dose of MK-1654 100 mg was predicted to provide >76% efficacy against RSV MALRI for 5 months. Exploratory analysis yielded an observed efficacy of 74.2% (20-100 mg groups) and 80.6% (100-mg group) versus placebo.

Conclusions: Model-based efficacy predictions aligned with observed MK-1654 efficacy in prevention of RSV MALRI in this phase 1b/2a study. The data support continued evaluation of MK-1654 in phase 3 studies.

Keywords: respiratory syncytial virus, monoclonal antibody, drug therapy, lower respiratory tract infection, infants, pharmacokinetics, population pharmacometrics model

Conflict of Interest: BM, RR, XC, AK, IC, JC, BR, JS, KV, AA and AL are employees of Merck Sharpe & Dohme, Corp., a subsidiary of Merck & Co., Inc., Rahway, NJ, USA and may own and/or hold stock options in Merck & Co, Inc., Rahway, NJ, USA. The remaining authors declare no conflict of interest.

158. FUNCTIONAL ANTIBODIES IN DRIED BLOOD TO MEASURE PROTECTION AGAINST RSV.

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2. Center for Translational Immunology, University Medical Centre Utrecht, Utrecht, the Netherlands
3. Bill and Melinda Gates Medical Research Institute, Cambridge, Massachusetts, United States of America
4. Respiratory Syncytial Virus Network (ReSViNET) Foundation, Zest, Netherlands.

Introduction: The respiratory syncytial virus (RSV) prevention landscape has rapidly expanded with 33 candidates currently in clinical development. The monoclonal antibody (mAb) RSM01 is in development for lower respiratory tract illness (MALRI) in infants. Virus neutralization is considered the key correlate of protection of RSV vaccines and currently measured through venipuncture. Dried blood samples obtained with a simple finger prick can simplify acquisition, processing, storage, and transport in vaccine trials, especially in remote areas.

Methods: We aim to determine if antibodies retain their function in dried blood using Mitra® (Trajan Scientific) volumetric absorptive microsampling (VAMS®, Neoteryx). We validate an RSV neutralization assay for dried blood compared to serum. Hep2 cells were infected with a serial dilution of sample-virus mixture using RSV-A2-mKate to measure fluorescence endpoints.

Results: The functional antibodies in dried blood correlated strongly with serum (R² = 0.98, p < 0.00001). The neutralization assay had a wide range of linearity with limits of detection between 0.1 µg/mL and 10 mg/mL of RSM01. The intra-assay, inter-assay and inter-operator precision of dried blood was non-inferior to serum. Dried blood samples were stable at room temperature up to 6 months storage for 100 µg/mL RSM01 but not for the lower concentration of 10 µg/mL.

Conclusion: We demonstrated RSV neutralization on dried blood as an alternative for serum. Functional antibodies in dried blood is a patient-centered solution that may replace serology testing in vaccine trials in LMICs and potentially be used as a tool to monitor protection against RSV globally.

Keywords: dried blood; serum; neutralization; mAb; vaccine; trials; LMIC; functional assay

Conflict of Interest: UMCC has received major funding (>€100 000 per industrial partner) for investigator-initiated studies from AbbVie, MedImmune, Janssen, Pfizer, the Bill & Melinda Gates Foundation, and MeMed Diagnostics. LB is the founding chairman of ResVINET.
159. QUANTIFICATION OF CLESROVIMAB (MK-1654), AN INVESTIGATIONAL, HALF-LIFE-EXTENDED, ANTI-RESPIRATORY SYNCYTIAL VIRUS PROTEIN F HUMAN MONOCLONAL ANTIBODY IN THE NASAL COMPARTMENT OF HEALTHY ADULTS

Jia Yao Phuah (1) Brian M. Maas (1) Luzelena Caro (1) Radha Rallikar (1) Qinlei Huang (1) Brad Roadcap (1) Andrew P. Catchpole (2) Jeffrey R. Sachs (1) Antonios O. Aliprantis (1) Kalp A. Vora (1)* 1. Merck & Co., Inc., Rahway, NJ, USA 2. GSK, Wavre, Belgium

Background: Respiratory syncytial virus (RSV) is a respiratory pathogen with a high mortality risk for infants and the elderly. Antibodies that bind to prefusion F protein have demonstrated potent neutralizing activity against RSV and have therefore been used prophylactically in clinical settings to prevent RSV infection. Clesrovimab (MK-1654) is an investigational, fully human, extended half-life monoclonal antibody (mAb) against RSV F glycoprotein in clinical trials as a prophylactic agent for prevention of RSV infection in infants.

Methods: Establishing MK-1654 levels at the site of RSV infection, such as the nasal compartment, is essential to correlating serum PK levels and exposure in target tissue for RSV neutralization. This study measures MK-1654 concentrations in serum and the nasal compartment to establish partitioning of the mAb, enabling assessment of the relationship.

Results: For mAbs with YTE mutations, ~1-2% of serum antibodies were detected in nasal mucosa. Urea concentrations were used to normalize the MK-1654 concentrations from nasal samples of adults in 2 clinical trials and find ratios of 1:30-1:68 (nasal:serum), which translates to 1.5-3.3% of serum concentrations. The PK in the nasal compartment correlated with that of serum. In a small phase 1b/2a dose-escalating study (P002), upper respiratory tract infections were observed in a lower proportion of infants with RSV who received MK-1654 compared with placebo.

Conclusions: These ratios for an FcRn-mediated extended half-life mAbs would signal greater tissue penetration, which could be an added advantage along with extended half-life in protecting infants against RSV using passive approaches to prophylaxis.

Keywords: respiratory syncytial virus, monoclonal antibody, drug therapy, adults, pharmacokinetics

Conflict of Interest: JYP, BM, LC, RR, QH, BR, JS, AA and KV are employees of Merck Sharpe & Dohme, Corp., a subsidiary of Merck & Co., Inc., Rahway, NJ, USA and may own and/or hold stock options in Merck & Co., Inc., Rahway, NJ, USA. The remaining authors declare no conflict of interest.

160. BROAD NEUTRALIZATION AGAINST CONTEMPORARY AND ANTIGENICALLY DISTANT RESPIRATORY SYNCYTIAL VIRUS (RSV) STRAINS ELICITED BY THE VACCINE CANDIDATE RSVPREF3-AS01

Lionel Sacconay (1), Vera Rocha-Perugini (1), Jonathan De Smedt (1), Edison Ong (1,a), Romuald Mascolo (1), Anne Atas (1), Carlene Vanden Abeele (2), Magali de Heusch (2), Nathalie De Schrevel (1), Marie-Pierre David (2), Badiaa Bouzya (2), Kim Stobbaelaar (3), Yannick Vannloubbeeck (1), Peter L. Delputte (3), Corey P. Mallett (4), Nancy Dezutter (2), Lucile Warter (1)*
1. GSK, Rixensart, Belgium 2. GSK, Wavre, Belgium 3. Department of Biomedical Sciences, University of Antwerp, Antwerp, Belgium 4. GSK, Rockville, Maryland, United States

a. Current affiliation: Moderna, Cambridge, Massachusetts, United States

Contact details for presenting author: Lucile Warter
Email address: lucile.x.warter@gsk.com

Background: RSVPref3-AS01 containing the RSV pre-fusion F protein and AS01 adjuvant demonstrated high and consistent efficacy against RSV disease in older adults (OAs). RSV F is highly conserved across RSV-A/RSV-B subtypes, but variations in major viral antigenic sites are reported. Here we characterized the breadth of RSVPref3-AS01 elicited neutralizing activity against contemporary RSV strains (RSVs) containing variations representative of the currently dominant RSV strains.

Methods: We retrieved all human RSV F sequences from NCBI and GISAID databases and analyzed the amino acid (aa) variations and may own and/or hold stock options in Merck & Co., Inc., Rahway, NJ, USA. The remaining authors declare no conflict of interest.

Results: Twenty-nine aa variations were identified among contemporary RSV sequences. Six RSVs, including representatives of the currently dominant sequences, were further tested: 4 contemporary RSVs with combinations of major aa variations and 2 laboratory-adapted RSVs. Two strains recapitulating the globally dominant RSV-B sequences were not neutralized by 1 of the tested RSVPref3-specific mAbs. In mice, cows and OAs, RSVPref3-AS01 elicited broad RSV-neutralizing antibody responses against the 4 tested contemporary RSVs, irrespective of the antigenic distance to RSVPref3. In OAs, non-adjuvanted RSVPref3 was less potent at neutralizing antigenically-distant strains/contemporary RSV-B strains (Figure).

Conclusion: The breadth of RSVPref3-AS01 elicited neutralizing antibody response may contribute to vaccine efficacy against contemporary and emergent RSVs.

Keywords: prefusion F protein, neutralizing antibody, RSV-A, RSV-B, contemporary RSV strains, older adults

Funding: GlaxoSmithKline Biologicals SA

Conflict of Interest: AA, BB, CPM, CVA, EO, JDS, LS, LW, MdH, M-PD, ND, NDS, RM, VRF, and YY are, or were (for EO), GSK employees at the time the studies were designed, initiated, and/or conducted. EO is currently an employee of Moderna and holds stocks from Moderna as part of his employee remuneration.
Objective: Respiratory syncytial virus (RSV) is a leading cause of hospitalization for all infants in their first RSV season and is responsible for a significant burden on healthcare systems and families. A first-single-dose long-acting monoclonal antibody (mAb) has been recently approved in Europe for prevention of RSV lower respiratory tract infection in infants during their first RSV season. Implementation of a RSV immunisation program with a prophylactic mAb may raise specific questions, in terms of when, where and by whom it should be administered, which are critical to anticipate to secure acceptability and uptake.

Methods: These findings are based on views and insights gathered from 9 global experts (EU, Japan, China, UK) during an advisory board held in July 2022 to discuss RSV prevention strategies.

Results: RSV mAb has the potential to protect all infants through administration at birth for infants born during the RSV season. Key implementation criteria identified were: 1/ coordination between inpatient and primary care settings, 2/ RSV seasonality and immunisation timing, 3/ education and communication to healthcare professionals and parents. Potential solutions suggested were the need for an overarching program management body encompassing hospital and outpatient settings, expansion of immunisation actors, robust surveillance system, and scientific societies implementation guidelines.

Conclusion: Each country should anticipate and define clear implementation modalities and ensure a strong coordination across all actors to facilitate access, and ultimately reach a high uptake to protect all infants and alleviate hospital burden.

Keywords: Immunization programme, implementation, RSV, prophylactic monoclonal antibody

Conflict of Interest: The abstract is based on insights from an expert meeting supported by Sanofi and AstraZeneca, for which the authors receive research grants from Pfizer and Merck on work unrelated to this manuscript. ZZ is expected to receive consulting fees from Pfizer and Merck for work unrelated to this manuscript. All authors have no other financial and non-financial interests to declare.

162. ESTIMATED EFFECTIVENESS OF VACCINES AND EXTENDED HALF-LIFE MONOCLONAL ANTIBODIES AGAINST RESPIRATORY SYNCYTIAL VIRUS (RSV) HOSPITALIZATIONS IN YOUNG CHILDREN

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1. Department of Epidemiology of Microbial Diseases and the Public Health Modeling Unit, Yale School of Public Health, New Haven, CT, USA.

Several vaccines and extended half-life monoclonal antibodies (mAbs) against respiratory syncytial virus (RSV) have shown promise in clinical trials. We used age-structured transmission models to evaluate the possible impact of various RSV prevention strategies including maternal immunization, live-attenuated vaccines, and long-lasting mAbs. Our results suggest that maternal immunization and long-lasting mAbs are likely to be highly effective in preventing RSV hospitalizations in infants under 6 months of age, averted more than half of RSV hospitalizations in neonates. Live-attenuated vaccines could reduce RSV hospitalizations in vaccinated age groups and are also predicted to have a modest effect in unvaccinated age groups because of disruptions to transmission.

Compared to year-round vaccination, a seasonal vaccination program at the country level provides at most a minor advantage regarding efficiency. Our findings highlight the substantial public health impact that upcoming RSV prevention strategies may provide.

Keywords: maternal immunization; extended-half-life monoclonal antibodies; live-attenuated vaccines; public health impact; transmission models; effectiveness

Conflict of Interest: VEP has received reimbursement from Merck and Pfizer for travel expenses to Scientific Input Engagements on respiratory syncytial virus. DMW has received consulting fees from Pfizer, Merck, GSK, Affinivax, and Matrivax for work unrelated to this manuscript and is the principal investigator on research grants from Pfizer and Merck on work unrelated to this manuscript. ZZ is expected to receive consulting fees from Pfizer for work unrelated to this manuscript.
Virology & Immunology
163. PEDIATRIC RSV-RELATED ILLNESS FREQUENCY, GENOTYPING, MORTALITY AND SEASONALITY AT INTENSIVE CARE UNITS IN JAFAR IBN AUF SPECIALIZED HOSPITAL FOR CHILDREN, KHARTOUM_SUDAN

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1. Central Laboratory – Ministry of Higher Education and Scientific Research

Background: Respiratory Syncytial Virus (RSV) infection causes a substantial disease burden in the infant, with nearly all children infected with RSV by age two. RSV has been prioritized for vaccine development by the Global Alliance for Vaccines and Immunizations (GAVI). Many of the countries eligible for GAVI support lack individual patient data which required to specify target populations for near future RSV interventions. This study aims to provide pediatric RSV illness data among Jafar Ibn Auf hospital care units.

Materials and methods: 130 nasal swabs collected from <2 year children admitted to Jafar Ibn Auf hospital intensive care units and meeting the WHO “extended SARI” case definition. Samples were tested for RSV through real time PCR and RSV genotypes were screened. RSV seasonality, clinical presentation, admission length and outcome have been studied.

Results: Among the included cases, 16.2% were positive for RSV. Among the infected cases, 71.4% of cases were male and children less than 6 months are the most infected age group (71.4%). Bronchiolitis is the common presentation of the disease (57.1%) followed by pneumonia (33.3%) with median hospital stay for 1 day. RSV-A was the dominant circulating genotype (57.1%), 14.2% of circulating RSV have mix genotypes (A&B) while un-typable strains seen in 28.5%. RSV found to be circulate in both high and low temperatures with nearly similar percentages.

Conclusion: This study helps to clarify the RSV situation in Sudan among children under 2 years old through providing epidemiologic and clinical data.

Keywords: RSV, Children, Mortality, Seasonality, RSV Genotypes, Sudan

Conflict of Interest: None declared

164. A FINELY TUNED INTERPLAY BETWEEN CALCIUM BINDING, IONIC STRENGTH AND PH MODULATES CONFORMATIONAL AND OLIGOMERIZATION EQUILIBRIA IN THE RESPIRATORY SYNCYTIAL VIRUS MATRIX (M) PROTEIN

Damian Alvarez Paggi (1)*, Sebastián Esperante (1), Mariano Salgueiro (2), Martín Desimone (3), Guilherme A. P. de Oliveira (4), Martin Arán (2), Javier García Pardo (5), Ariel Aptekman (6), Salvador Ventura (5), Gonzalo Prat Gay (2)

1. Fundacion INFANT
2. Fundacion Instituto Leloir
3. IQIUMEA, CONICET-UBA
4. Programa de Biología Estrutural, Instituto de Bioquímica Médica Leopoldo de Meis
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As in most enveloped RNA viruses, the Respiratory Syncytial Virus Matrix (RSV-M) protein plays key roles in viral assembly and uncoating. It also plays non-structural roles related to transcription modulation through nucleo-cytoplasmic shuttling and nucleic acid binding ability. We dissected the structural and conformational changes underlying the switch between multiple functionalities, identifying Ca2+ binding as a key factor. To this end, we tackled the analysis of M’s conformational stability and equilibria. While in silico calculations predict two potential calcium binding sites per protomer, purified RSV-M dimer contains only one strongly bound calcium ion per protomer. We experimentally evaluated the presence of additional Ca2+ binding sites, that elicit changes in thermal stability, oligomerization and aggregations routes. This prompted us to determine the dissociation constants for the low- and high affinity calcium binding sites, assessing values of 13 μM and 58 nM, respectively, suggesting an intracellular calcium sensing mechanism of RSV-M upon infection.

We uncover a finely tuned interplay between calcium binding, ionic strength, and pH changes compatible with the different cellular compartments where M plays key roles, uncovering diverse conformational equilibria, oligomerization, and high order structures, required to stabilize the virion particle by a layer of molecules positioned between the membrane and the nucleocapsid.

Keywords: RSV, Matrix Protein, Calcium Binding, Conformational Equilibrium

Conflict of Interest: None declared

165. PEDIATRIC RESPIRATORY SYNCYTIAL VIRUS DIAGNOSTIC TESTING PERFORMANCE: A SYSTEMATIC REVIEW AND META-ANALYSIS

Chukwuekeoma Onwuchekwa (1), Jessica Atwell (2), Laura Mora Moreo (1), Sonia Menon (1), Belen Machado (1), Mariana Siapka (1), Neha Agarwal (1), Michelle Rubbrecht (1), Zuleika Aponte-Torres (1), Mark Rozenbaum (4), Daniel Curcio (2), Harish Nair (3), Warren K Kalina (2), Bradford Gessner (2), Hilde Vroling (1), Elizabeth Begier (2)*

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Background: Among adults adding additional specimen types (e.g., serology and sputum RT-PCR) to nasopharyngeal swab (NPS) RT-PCR increases RSV detection substantially. We sought to determine if a similar effect occurs in children and to quantify under-ascertainment associated with pediatric diagnostic testing.

Methods: We systematically searched indexed and non-indexed sources (01 Jan 2000 – 27 Dec 2021) for studies reporting RSV detection in persons <18 years, using 22 specimen types or diagnostic tests. Study quality was assessed using the QUADAS-2 tool. We pooled RSV detection rates by specimen and diagnostic test and quantified diagnostic test performance against RT-PCR.

Results: Among 157 included studies (of 8066 reviewed), nasopharyngeal aspirates (NPA) and NPS were the most common specimens (54.8% and 35.7%, respectively). Adding RT-PCR testing of additional specimen types to NPA, NPS and/or nasal swab (NS) RT-PCR resulted in statistically non-significant increases in RSV detection: paired acute/convalescent serology +10% (versus NPS alone), NS +8% (versus NPS/NPA alone), oropharyngeal swabs +5% (versus NPS/NS alone),
and NPS +1% (versus NPA alone) (Figure 1). Compared to RT-PCR, direct fluorescent antibody’s sensitivity was 87%, rapid antigen detection tests 74%, and viral culture 76% (pooled specificities all ≥98%). Pooled sensitivity of multiplex versus singleplex RT-PCR was 96%.

Conclusions: RT-PCR was the most sensitive pediatric RSV diagnostic test. Adding multiple specimens did not substantially increase RSV detection in children in pairwise comparisons, but even small proportional increases could result in meaningful changes in burden estimates. The synergistic effect of adding multiple specimens should be evaluated.

Keywords: RSV diagnosis, serology, incidence, epidemiology, diagnostic sampling

Conflict of Interest: P95 was funded by Pfizer to conduct this study. Persons with Pfizer affiliations are Pfizer employees and may hold Pfizer stock.

### Table 1. Increase in RSV detection rate due to the addition of another specimen testing to reference RT-PCR of Nasopharyngeal (NP) swab or Nasal swab.

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Age group</th>
<th>Clinical setting</th>
<th>Clinical presentation</th>
<th>Specimen (reference)</th>
<th>Diagnostic testing</th>
<th>N</th>
<th>Detection Rate [95% CI]</th>
<th>Detection Rate [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wu et al. (2016)</td>
<td>&lt;18 years</td>
<td>Hospitalised or admitted</td>
<td>Community-acquired pneumonia</td>
<td>Nasopharyngeal swab</td>
<td>RT-PCR</td>
<td>1087</td>
<td>1.10 [0.65, 1.77]</td>
<td>1.07 [0.59, 1.61]</td>
</tr>
</tbody>
</table>

**Figure 1.** Increase in RSV detection rate due to the addition of another specimen testing to reference RT-PCR of Nasopharyngeal (NP) swab or Nasal swab. Detection ratios >1.0 indicates an increase in RSV detection associated with additional specimen testing.

### 166. A RETROSPECTIVE ANALYSIS OF RESPIRATORY VIRUS TRANSMISSION BEFORE AND DURING THE COVID-19 PANDEMIC IN PUNE, THE WESTERN REGION OF INDIA

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In December 2019, SARS-CoV-2 reported from China. We used India’s National Influenza Center monitoring system from 2017 to 2021 to demonstrate that the NPI limited the transmission of other viral infections. At the National Influenza Center of the Indian Council of Medical Research-National Institute of Virology, Pune, influenza and other respiratory viruses are monitored. We investigated respiratory virus and/or SARS-CoV-2 testing data from 2017 to 2021. Respiratory viruses were detected using multiplex real-time PCR. Over an epi-year, weekly data showed each virus’s % positivity. Pre-pandemic (January 2017 to March 2020) and post-pandemic (April 2020 to December 2021) were separated into P1: early pandemic (April 2020 to December 2020) and P2: late pandemic (January 2021 to December 2021). Results: The study evaluated 9,617 individuals for respiratory viruses. Demographics show more men (56.4% vs. 61.7%) and a higher median age (19.3 years vs. 41 years). During the pandemic, influenza A pdm09 (H1N1), A (H3N2), B, HMPV, PIV1-4, RSV A & B, AdV, and rhinovirus test positives declined. Children were more viral positive before and throughout the epidemic. Before the pandemic, influenza virus activity peaked in February and March. Flu A and B were active from August to December 2021. Influenza A and B, metapneumovirus, parainfluenza virus, respiratory syncytial virus, and human coronavirus decreased throughout the pandemic. In 2020 and 21, no influenza, RSV, or other respiratory virus occurrences were observed. This information may help public health experts plan for future pandemics.

Keywords: COVID-19, Influenza, RSV, Other respiratory viruses, pandemic

Conflict of Interest: None declared
UNRAVELING THE LOCAL AND SYSTEMIC TRANSCRIPTOMIC PROFILE OF MONOCYTES IN CHILDREN EXPERIENCING SEVERE RSV INFECTION

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Respiratory syncytial virus (RSV) is a major cause of childhood lower respiratory tract infection (LRTI) and of infant hospitalizations in the developed world. Several risks factors are known that predispose individuals for severe disease, such as prematurity and congenital heart disease. However, there is still an incomplete understanding of the antiviral immune response in the lungs of critically ill infants. Monocytes and alveolar macrophages are amongst the first cells to encounter viral particles and previous studies have shown their important role in viral clearance and COVID-19 pathology. In this study we aim to get a better understanding of the functional biology of monocytes during severe RSV infection. Therefore, we performed RNA sequencing on isolated monocytes (CD14+) from tracheobronchial aspirates (sputum) and whole blood samples obtained from infants admitted to the intensive care unit experiencing severe RSV disease and from control patients. Using transcriptomic analysis, we found that the inflammatory profile in monocytes associated with RSV infection extended from the lungs into the periphery, which was not observed previously in neutrophils. Furthermore, RSV transcripts were found in both monocytes and neutrophils isolated from sputum samples, confirming the presence of this viral pathogen within these cell types. Insights in the host transcriptomic immune response could increase our understanding of the (dys)regulation of the immune response leading to severe disease and could help the development of future therapeutics and vaccine development.

Keywords: Transcriptomics, monocytes, neutrophils, immune response, sputum, blood, viral transcripts, severe, RSV infection, inflammation

Conflict of Interest: None declared

MECHANISMS RESULTING IN IMPAIRED MUCOSAL IGA AGAINST RESPIRATORY SYNCYTIAL VIRUS IN INFANTS

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Respiratory syncytial virus (RSV) specific IgA responses correlate significantly with protection; and compared with adults, human infants and neonatal mice fail to mount IgA responses upon infection. We have previously shown that supplementation with IFNα increased the proliferation of total IgA-producing B cells as well as levels of RSV-specific IgA in the nasal mucosa of neonatal mice. Antibody isotypes such as IgA are formed by class switch recombination (CSR). T cell-independent CSR relies on type I interferon conditioning of pDCs and their secretion of BAFF and/or APRIL. It is unclear if BAFF and/or APRIL signal through TACI to produce IgA and no data on this exists for RSV infection during infancy. To understand why infants fail to produce IgA in response to RSV infection, we first evaluated the expression of APRIL and BAFF in the lungs of neonatal mice infected with RSV. We observed increased BAFF and APRIL mRNA expression in the nasal associated lymphoid tissue of RSV-infected adult mice and neonatal mice receiving IFNα compared with RSV-infected mice receiving placebo. TACI expression across these groups was unchanged. Longitudinal RNASeq revealed that BAFF levels in the neonatal mice increased rapidly upon infection; however, APRIL induction in neonates infected with RSV was significantly attenuated suggesting a distinct role for BAFF and APRIL in IgA induction and that decreased signaling by APRIL through TACI leads to decreased IgA production against RSV in infants.

Keywords: IgA, infant, mucosal, respiratory syncytial virus, neonatal mouse model

Conflict of Interest: None declared
169. KINETIC ANALYSIS REVEALS DECREASED MUCOSAL CONCENTRATIONS OF INNATE CYTOKINES AND INTERFERONS IN CRITICALLY ILL CHILDREN WITH RSV DISEASE

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4. The Ohio State University College of Medicine (Columbus, OH); Department of Pediatrics

Background: RSV is the most common cause of acute lower respiratory tract infections (LRTI) in young children. Innate mucosal cytokines play a dual role in both controlling viral replication but also contributing to critical disease severity.

Methods: From 2015-2017, children <2 yo hospitalized for RSV LRTI were enrolled within 16-93 hours of admission, and nasopharyngeal swabs and clinical data collected daily until discharge. Viral loads (VLs) were quantified using RT-qPCR targeting the F-gene. Sequential mucosal cytokine concentrations were measured using an immunoassay and compared between children critically ill requiring PICU care vs those with severe disease hospitalized in the inpatient ward.

Results: Of the 116 children enrolled, 33 required ICU care (age: 2.3 [1.6-4.5] mo) and 83 were hospitalized in the ward (2.1 [1.1-5.9] mo; p >0.05). Duration of illness at enrollment was 4 [3, 5] days in both groups. RSV-A (61%) was more common than RSV B (39%), with no differences between ICU and ward patients. Overall VLs were slightly lower in ICU vs ward patients (6.3 [5.3-7.0] vs 6.9 [5.7-7.5] log10 copies/ml, respectively; p=0.049). In addition, critically ill children had lower concentrations of IFN-α on day (D)1; IL-6, IL-8, and TNFα on D3; IFNα2, IFNγ, and IFNα2/3 on D4, and IFNγ and IL-10 on D5, vs non-severe patients.

Conclusions: Critically ill children with RSV LRTI had less robust inflammatory and IFN responses than those with severe disease, suggesting disease severity is associated with less effective innate mucosal responses. These observations are important for developing mucosal RSV vaccines.

170. GENOTYPIC AND PHENOTYPIC FEATURES OF RSV INFECTIONS DURING MEDLEY, A RANDOMIZED DOUBLE-BLIND PHASE III STUDY OF NIRSIVIMAB IN CHILDREN AT HIGH RISK OF SEVERE DISEASE

Deide Wilkins (1)+ Kevin M. Tuffy (1)+ Anastasia A. Aksyuk (1) Bahar Ahani (1) Joseph Domachowske (2) Kenji Furuno (3) Hong Ji (1) Anna Kushnir (1) Amanda Leach (1) Shabir Madhi (4) Vaishali S. Mankad (5) Ann Marie Stanley (1) Ulrika Wåhlby Hamrén (6) Tonya Villafana (1) Elizabeth J. Kelly (1)*

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* Contributed equally

Background: Nirsevimab, a recombinant monoclonal antibody authorized for the prevention of RSV lower respiratory tract disease in infants, is being assessed in the Phase 2/3 MEDLEY trial in infants with congenital heart disease (CHD), chronic lung disease of prematurity (CLD), or born preterm entering their first RSV season and in children with CHD/CLD entering their second season. Features of RSV isolates from all breakthrough infections were assessed for all breakthrough infections.

Methods: Eligible children (n=925) were randomized 2:1 to nirsevimab or palivizumab prior to their first RSV season; 262 children with CHD/CLD received a first or second dose of nirsevimab or palivizumab prior to the second season. RSV isolates from breakthrough infections were subtyped and the RSV fusion protein gene was sequenced; phenotypic analyses of binding site substitutions were performed.

Results: Twelve nirsevimab and ten palivizumab recipients had RSV isolates sequenced in the first season. One palivizumab recipient with RSV A in Season 1 had one major variant palivizumab binding site substitution (≥25% molecular allele frequency; MAF) and two minor variant palivizumab binding site substitutions (<25% MAF) in the same residue; both minor variants decreased susceptibility to palivizumab, but retained susceptibility to nirsevimab. Nirsevimab binding site substitutions (I206M, Q209R, S210F) in the same residue; both minor variants decreased susceptibility to palivizumab, but retained susceptibility to nirsevimab.

Conclusions: No nirsevimab binding site substitutions identified in breakthrough RSV infections during MEDLEY affected susceptibility to nirsevimab.

Keywords: nirsevimab, palivizumab

Conflict of Interest: J Domachowske has received grant/research support from AstraZeneca; consulting fees for Sanofi. D Wilkins, KM Tuffy, AA Aksyuk, B Ahani, Hong Ji, Anna Kushnir, A Leach, VS Mankad, A Stanley, U Wåhlby Hamrén, T Villafana, and EJ Kelly are employees and shareholders of AstraZeneca. K Furuno and S Madhi have no conflicts of interest to disclose.

171. EVALUATION OF THE RESPIRATORY SYNCTYIAL VIRUS G-DIRECTED NEUTRALIZING ANTIBODY RESPONSE IN THE HUMAN AIRWAY EPIDERMAL CELL MODEL

Michael Kishko (1)*, John Catalan (1), Kurt Swanson (1) (2), Josh DiNapoli (1), Chih-Jen Wei (1) (3), Simon Delagreve (1), (2), Sudha Chivukula (1), Linong Zhang (1)

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Human respiratory syncytial virus (RSV) is a major cause of serious respiratory tract infections in infants and the elderly. A safe and effective vaccine against RSV remains an important unmet public health need. RSV vaccine development relies heavily on the determination of neutralizing antibody (NAb) titers on immortalized cell lines. However, these cell lines are not suitable for detecting the NAbs against the RSV attachment (G) glycoprotein, as RSV infects them via the fusion (F) glycoprotein interactions with heparin sulfate, obviating the necessity for G in viral entry. It was shown that RSV uses CX3CR1 as a receptor for G to attach to human airway epithelial cells (HAE) and that G-specific NAbs can be detected on HAE. To investigate the contributions of G-specific antibodies to RSV neutralization, we performed HAE based neutralization assays on sera from RSV G immunized mice or RSV exposed humans. Substantial neutralizing activity on HAE of mice immunized with RSV G was detected on HAE but not Vero cells. When mice were immunized with F together with G, both contributed to neutralization activity on HAE. We next examined sera from human infants who were likely exposed to RSV infection only once and showed that RSV G-specific antibodies in these infants were either subgroup specific or cross-neutralizing. Altogether, our results suggest that G is an important target for generating NAbs and would be beneficial to include in an RSV vaccine. Further, inclusion of G antigens from both RSV subgroups may enhance the vaccine cross protection potency.

Keywords: HAE G NEUTRALIZING ANTIBODY

Conflict of Interest: The study funded by Sanofi. All authors were employees of Sanofi at the time this work was performed and may hold stock in the company.
172. GENETIC CHARACTERIZATION OF RSV CIRCULATING IN PORTUGAL DURING 2021/2022 SEASON

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1. National Reference Laboratory for Influenza and other Respiratory Viruses
2. National Network of RSV Sentinel Surveillance

Background: Human respiratory syncytial virus (RSV) is associated with substantial morbidity and mortality in infants, young children and the elderly since it is the leading cause of acute lower respiratory infections in these groups. In Portugal, a National Network of RSV Sentinel Surveillance (VigiRSV) in children hospitalized under 2 years old was created in 2021. The aim of this study was to characterize at genomic level the RSV circulating in Portugal during the 2021/2022 season.

Methods: Epidemiological data and RSV-positive samples from patients with a respiratory infection were collected through the VigiRSV during the 2021/2022 period. RSV detection, subtyping A and B, and sequencing of the ectodomain region of the G gene were performed by molecular methods.

Results: 85 RSV positive samples (43 RSV-A and 42 RSV-B) of the 253 clinical samples from the VigiRSV, with Cts<25, were selected for genomic characterization. Based on newly RSV classification proposed by Goya et al., phylogenetic analysis revealed that the RSV-A genotype GA2 (formerly named as ON1 strains), subgenotype GA2.3, and RSV-B genotype GB5 (formerly named as BA strains), subgenotype GB5.0 were predominant in Portugal during the 2021/2022 season. Although, GA2.3 subgenotype is characterized with the amino acid substitutions V122A and P156Q, MB5.0 subgenotype is characterized with T143N and L237P/S.

Conclusion: The phylogenetic analysis reflected the high diversity of Portuguese RSV strains. GA2.3 and GB5.0 subgenotypes, which have been circulating in Portugal in previously seasons, predominated during the whole study period, and are consistent with the currently circulating genotypes worldwide.

Keywords: RSV, clinical data, epidemiological data, surveillance, Portugal

Conflict of Interest: None declared

175. TEMPORAL CHANGES IN RESPIRATORY MICROBIOME, VIROME AND INNATE INFLAMMATORY RESPONSE IN RSV INFECTION IN INFANCY REVEALED THROUGH DEEP SHOTGUN METAGENOMIC SEQUENCING

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1. Kemri-Wellcome Trust Research Centre, Kilifi, Kenya

Introduction: RSV infection triggers changes in the composition of airway microbiome. Few studies have examined long-term dynamic changes in the relationship between the host and the microbiota in the upper airway during a primary RSV infection. We present preliminary observations of incidental changes in these parameters using nasal swab samples from longitudinally sampled RSV-naïve infants.

Methods: Sixteen infants from Kilifi, Kenya, were recruited and followed up for approximately 6 months, spanning the local RSV epidemic wave. Approximately 5 samples per child were collected each month. A multiplex real-time PCR panel was used for diagnosis of 16 respiratory pathogens including RSV. Total DNA was extracted and sequenced on the Illumina next-seq platform resulting in an average 0.5 billion reads per child. Analysis of shotgun metagenomics data was conducted using the metaphor3 and humann3 pipelines in python. Innate immune response data was collected during RSV infections using the MSD mesoscale platform, where the airway concentrations of 21 soluble mediators were measured.

Results: M. cattarrhalis, M. nonliquefaciens were dominant with intermittent colonisation by S. pneumoniae. Frequent spikes in virus infection, including CMV, EBV was noted. RSV infection was marked by incidental increases in S. pneumoniae, H. influenzae colonisation. Temporal changes in RSV viral load were also positively correlated with the concentration of IL-6, IL-1b and TNF-a.

Conclusion: S. pneumoniae and H. influenzae present a rich platform for an RSV infection.

Keywords: RSV, Microbiome, Virome, Metagenomic Sequencing

Conflict of Interest: None declared

174. HIGH SEROPREVALENCE OF ANTIBODIES AGAINST HUMAN RESPIRATORY SYNCYTIAL VIRUS AND EVIDENCE OF RSV REINFECTION IN YOUNG CHILDREN IN THAILAND

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3. Center for Vaccines and Immunity, Abigail Wexner Research Institute at Nationwide Children’s Hospital, Columbus, Ohio, USA

Objective: To investigate the seroprevalence of RSV infections in young children, the correlation between RSV antibody levels in maternal and cord blood, and to provide evidence of RSV reinfection in Thai children after primary infections.

Methods: Serum samples were collected from 302 mothers and 291 children between 2015 and 2020. Maternal and cord blood were collected at birth. Serial serum samples of children were collected at the ages of 2, 7, 18, 24, 36, 48, and 60 months and the presence of anti-RSV IgG was tested using an enzyme-linked immunosorbent assay.

Results: The cord: maternal serum antibody ratio was 1.09 (95% CI 1.08–1.11). Although >90% of babies at birth were seropositive through transplacental transfer, antibody levels gradually declined, with the highest seronegative rate (91.9%) at 7 months of age. Subsequently, anti-RSV IgG levels increased with age, most likely due to natural infection. One third of the children showed evidence of reinfection as determined by seroconversion of anti-RSV IgG or increased titers of at least 50 RU/mL.

Conclusions: Waning of RSV antibodies in infants is rapid, and RSV infection subsequently increases anti-RSV IgG titers. RSV vaccination in children before age 7 months should be recommended.

Keywords: Seroprevalence, RSV, reinfection, infants, young children

Conflict of Interest: None declared

Respiratory syncytial virus (RSV) IgG seroprevalence among mothers and children stratified by age. The age groups of mothers and children are shown on the X-axis. The proportion of the rate of RSV IgG seropositivity (%) is presented on the left Y-axis. The GMT in each age group indicated as red dots are represented on the right y-axis (log10 scale). Anti-RSV IgG antibody levels are indicated as follows: <16 RU/mL (grey), 16 to <22 RU/mL (light blue), 22 to <100 RU/mL (blue), and >100 RU/mL (dark blue).
175. CD14 AND RELATED GENES IN RESPIRATORY MORBIDITY AFTER RESPIRATORY SYNCYTIAL VIRUS INFECTION


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4 Unidade de Xenética, Instituto de Ciencias Forenses, Facultad de Medicina, Universidade de Santiago de Compostela, and GenPoB Research Group, Instituto de Investigación Sanitaria (IDIS), Hospital Clínico Universitario de Santiago (SERGAS), Galicia, Spain.

Recent findings indicated an autosomal recessive CD14 deficiency in a patient developing recurrent respiratory syncytial virus (RSV). We have analyzed transcriptomic and epigenomic data from blood samples collected in hospitalized RSV infected children during the acute phase of infection. After three years of follow-up, the patients were classified as complete recovered, recurrent wheezing, and asthmatic. We observed evidence in our data pointing to a reduced expression of the CD14 gene and nine of its most closely interacting protein genes in children with respiratory sequelae, being this reduction more remarkable in those children developing asthma.

Keywords: Respiratory syncytial virus; asthma; epigenomics; host; transcriptomics.

Conflict of Interest: None declared

176. SEQUENTIAL INTERACTIONS BETWEEN RSV AND PNEUMOCOCCUS IN THE NASOPHARYNX OF ZAMBIAN INFANTS AND THEIR MOTHERS

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A number of epidemiologic studies have reported important interactions between respiratory syncytial virus (RSV) and Streptococcus pneumoniae (SP), which may lead to more severe infections. However, the vast majority of these studies are either performed in mice or consist of cross-sectional measurements from children with acute lower respiratory infections. To understand the impact of RSV and SP in a population, we analyzed nasopharyngeal samples from healthy mother-infant pairs in Lusaka, Zambia. The mothers were followed from ~1 week postpartum until the infants reached 14 weeks of age, and the sampling was done at 2-week intervals with cataloging of respiratory symptoms. Surprisingly, unlike existing reports, we found that prior RSV infection resulted in an overall higher bacterial cycle threshold value compared to SP-only infections in infants, whereas no difference was found in the mothers. In addition, SP carriage, as a binary event, was more common post- than comparator groups (simultaneous infection or prior-RSV). Bacterial carriage density showed a bimodal distribution with density being lower at first visit post RSV detection and significantly higher when detected at visits 2 or more after RSV. Moreover, our data suggests that RSV was not significantly affected by prior SP infection in infants or mothers. Finally, when screening for interactions between Moraxella catarrhalis (MC) and RSV, no longitudinal interaction was observed in either mothers or infants. However, we found RSV increased carriage densities when MC was present in infants.

Keywords: Longitudinal study, Streptococcus pneumoniae, Cycle threshold, Virus-Bacteria sequential interactions

Conflict of Interest: None declared

177. THE EFFICIENCY OF P27 PEPTIDE CLEAVAGE DURING IN VITRO RESPIRATORY SYNCYTIAL VIRUS (RSV) INFECTION IS CELL LINE AND RSV SUBTYPE DEPENDENT

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Respiratory Syncytial Virus (RSV) Fusion protein (F) is conserved between subtypes. Enzymatic cleavage of the F precursor yields subunits F1 and F2 and releases the p27 peptide, whereas partial cleavage retains p27 in the mature F. Virus-cell fusion occurs when the F undergoes conformational change from pre-F to post-F, and p27 is cleaved entirely. Our objective is to determine the amounts of p27 on RSV/A and RSV/B strains and if its detection depends on the F protein conformation.

Monoclonal antibodies were used against p27, Site Ø, and Site II to monitor the F protein conformation in sucrose purified (sp)RSV/A and spRSV/B, and on the surface of RSV/A and RSV/B infected Hep-2 or A549 cells. ELISA and flow cytometry were used to quantitate the antigenic sites on pre-F. Temperature-stress test was used to evaluate the stability of pre-F.

spRSV/A showed 1.6x and 2.9x more p27 and Site Ø than spRSV/B, respectively, and its pre-F could withstand higher temperatures than spRSV/B before converting to post-F. Hep-2 cells infected with RSV/A retained more pre-F:p27 than RSV/B; levels of Site Ø were comparable between subtypes. On either cell line, RSV/A had more pre-F:p27 and could withstand higher temperatures than pre-F of RSV/B.

The efficiency of p27 cleavage was lower on RSV/A than RSV/B strains and cell-line dependent. RSVs with higher levels of pre-F:p27 could better sustain the pre-F conformation during temperature-stress challenge. Therefore, the incomplete cleavage of p27 may confer higher stability to the pre-F and provide a fitness advantage.

Keywords: Fusion Protein; p27; pep27; Cleavage; RSV subtypes; Pre-Fusion; protein stability; conformation; flow cytometry; ELISA;

Conflict of Interest: None declared
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The respiratory syncytial virus (RSV) matrix (M) protein interacts with the actin cytoskeleton in viral assembly and budding. The M-actin interaction may facilitate the transportation of the ribonucleoprotein complexes (RNP)s of RSV to viral assembly and budding sites. Previously, we have shown that RSV M interacts with actin microfilaments in cell culture and that destabilization of the cytoskeleton leads to the nuclear localization of M. As the dimerization of M has been shown to be important for RSV infection, in this study we have identified a role for M dimerization in the M-actin interaction.

The dimerization mutants used in this study were constructed based on previously described dimerization interface and mutation sites (S63A, S63E, N93A, N93E, Y229A). The M-actin interaction was investigated in cells transfected to express full length (1-256) wildtype M and M dimerization mutants as GFP-tagged proteins. Transfected cells were treated with the cytoskeleton destabilizing drug, cytochalasin D, and subcellular localization was visualized by live cell confocal microscopy.

In this current study, we show that the actin microfilament network is important for the movement of M and that the M-actin interaction can be influenced by its dimerization. This, ultimately, has implications for viral assembly. As the dimerization and oligomerization of M is dependent on its phosphorylation, further investigations are focused on determining whether phosphorylation can also play a role in this interaction. Moreover, further studies will elucidate the role of the M-actin interaction in the transportation of RNP to assembly sites.

Keywords: actin cytoskeleton; virus transport; respiratory syncytial virus; matrix protein

Conflict of Interest: None declared

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Background: Gut microbiota-derived short-chain fatty acid (SCFA) acetate protects mice against RSV A2 strain infection by increasing interferon-β production and expression of interferon-stimulated genes (ISGs). Methods: We used RSV clinical strains isolated from infants hospitalized with RSV bronchiolitis to further investigate the effects of in vitro SCFA-acetate treatment of human pulmonary epithelial cells. We also examined whether SCFA-acetate treatment is beneficial in a mouse model of RSV infection using clinical isolates. We investigate the relationship of gut microbiota and fecal acetate with disease severity among infants hospitalized with RSV bronchiolitis, and whether treating their respiratory epithelial cells with SCFA-acetate ex-vivo impacts viral load and ISG expression. We treated epithelial cells from SARS-CoV-2 infected patients with SCFA-acetate. Findings: In vitro pre-treatment of A549 cells with SCFA-acetate reduced RSV infection with clinical isolates and increased the expression of RIG-I and ISG15. Experiments in RIG-I knockout A549 cells demonstrated that the protection relies on RIG-I presence. Animals treated with SCFA-acetate intranasally recovered significantly faster, with reduction in the RSV clinical isolates viral load, and increased lung expression of IFNβ and the RIG-I. Gut microbial profile was associated with bronchiolitis severity and with acetate in stool. Increased SCFA-acetate levels were associated with increasing oxygen saturation at admission, and shorter duration of fever. Ex-vivo treatment of patients' respiratory cells with SCFA-acetate reduced RSV load and increased expression of ISGs OAS1 and ISG15, and virus recognition receptors MAVS and RIG-I, but not IFNB1. These SCFA-acetate effects were not found on cells from SARS-CoV-2 infected patients.

Keywords: Acetate; Clinical isolates; RIG-I; Respiratory syncytial virus, microbiota, INF, short-chain fatty acids.

Conflict of Interest: none declared

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Preclinical models that accurately mimic the consequences of respiratory syncytial virus (RSV) infections are crucial for studying RSV pathogenesis and predicting responsiveness to novel immunotherapies. Immortalized cell lines such as AS49, Hep-2 and VeroE6 cells, currently often used in RSV studies, poorly represent the morphological and functional complexity of respiratory epithelium. Here, we report a well-differentiated submerged human nasal epithelial cell (HNEC) culture platform that recapitulates the complex interactions between RSV-A strains or RSV-B strains and primary patient-derived epithelial cells. HNECs were differentiated on conventional 96-wells plastic plates, allowing a significant increase in throughput and ease of handling in comparison to conventional air-liquid-interface cultured cells. Optimization of indirect enzyme-linked immunosorbent assay (ELISAs) allows investigation of multiplicity of infection (MOI) range dependency and monoclonal antibodies (mAb) resistance in a high-throughput manner. Preliminary results based on such experiments allow the comparison of infectivity of strains, and characterization of for example Palivizumab. Additionally, we performed immunofluorescent (IF) stainings to characterize which cell type is most prone to infection. First confocal images of immunofluorescent stainings seem to confirm the conventional thought that RSV infection mainly propagates in ciliated cells. We also investigate the applicability of our submerged virus model to study viral fitness in a viral competition assay set-up. Our pipeline allows for elaborate characterization in primary cells of viral (competitive) fitness of a large panel of RSV strains, with the potential of characterization of the efficacy and potency of newly discovered mAbs in preventing infection.

Keywords: Primary model system, high-throughput system, RSV infectivity, monoclonal antibodies, competition assay

Conflict of Interest: The study was funded by a grant from Astrazeneca; KT is partially employed by Astrazeneca; the other authors have no competing financial interest in relation to the presented work.
**181. RISK FACTORS ASSOCIATED WITH SEVERE RSV INFECTION IN INFANTS: WHAT IS THE ROLE OF VIRAL CO-INFECTIONS?**

Kim Stobbelaar (1,2,3,4), Thomas C. Mangodt (1,4), Winke Van der Gucht (2), Cyril Barbezange (5), Annemieke Smet (3,6), Benedicte Y. De Winter (1,3,6,7), Stijn Verhulst (1,3,4,6), Peter L. Delputte (2,6).

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**Background:** The respiratory syncytial virus (RSV) represents the leading cause of viral bronchiolitis and pneumonia in children worldwide and is associated with significant morbidity and mortality rates. The clinical picture of an RSV infection differs substantially between patients and the role of viral co-infections is poorly investigated.

**Methods:** During two consecutive winter seasons from October 2018 until February 2020, we included previously healthy children up to 2 years of age presenting with an acute lower respiratory tract infection, both ambulatory and hospitalized, at a tertiary hospital. We collected clinical data and tested nasopharyngeal secretions for a panel of 16 different respiratory viruses with multiplex RT-qPCR. Disease severity was assessed with both traditional clinical parameters and scoring systems.

**Results:** 120 patients were included, of which 91.7% were RSV positive. Within the RSV positive group, 42.5% of patients (47/110) had a co-infection with at least one other respiratory virus. We found that patients suffering from a single RSV infection had higher paediatric intensive care unit (PICU) admission rates (OR = 5.9, 95% CI 1.53-22.74), longer length of hospital stay (IRR= 1.25, 95% CI 1.03-1.52), and a higher Bronchiolitis Risk of Admission Score (BRAS) (IRR= 1.31, 95% CI 1.02-1.70) compared to patients with RSV co-infections.

**Conclusion:** In our cohort, patients with a single RSV infection had increased disease severity compared to patients with RSV co-infections, suggesting that the absence or presence of viral co-infections might influence the course of RSV bronchiolitis.

**Keywords:** RSV, Viral co-infections, Risk factors, Disease severity, Paediatrics

**Conflict of Interest:** None declared

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**182. CLINICAL RSV ISOLATES: OUT WITH THE OLD, IN WITH THE NEW.**

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**Background:** The Respiratory Syncytial Virus (RSV) continues to pose a great burden on health care systems worldwide. Current knowledge about RSV is largely based on historical and laboratory-adapted strains. To allow for a better understanding of the biological features of RSV related to host specificity, pathogenicity, immune escape and vaccine efficacy, there is a clear need to acquire and characterize recent RSV isolates.

**Aim:** Isolation of low-passage clinical RSV isolates from children suffering from a lower respiratory tract infection (LRTI) and evaluation of phenotypic and genetic differences between them and historical reference strains.

**Methods:** We included paediatric patients between 1 month and 2 years old presenting with LRTI. Nasopharyngeal aspirates were inoculated on HEp-2 cells to obtain RSV isolates. These were then phenotypically characterized for growth in cell culture, fusogenicity, and sensitivity to palivizumab neutralization. Genotyping and sequencing of the G and F gene was also performed.

**Results:** 101 clinical RSV isolates were obtained, of which 52 RSV-A and 49 RSV-B. Although ON-1 and BA-IX genotypes predominate, phylogenetic analysis suggests that recent RSV-A isolates form a new subclade. In general, RSV-B isolates were more sensitive to palivizumab, and RSV-A isolates showed larger mean syncytium sizes. Notably, although RSV-A isolates grew to higher titers compared to most RSV-B isolates, some RSV-B isolates reached similar levels.

**Conclusions:** Recent clinical RSV isolates show clear differences, both genetically and phenotypically, in between them and compared to historical strains, emphasizing the need for continued surveillance and live virus isolation for use in research and development.

**Keywords:** Clinical isolates, RSV, Paediatrics, Viral infections, Virology

**Conflict of Interest:** None declared

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**183. THE ROLE OF A20 IN THE IMMUNOPATHOGENESIS OF RESPIRATORY SYNCYTIAL VIRUS (RSV) AND ITS THERAPEUTIC APPLICATION**

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**Background:** The complex and unknown immunopathology of respiratory syncytial virus (RSV) infection is the main obstacle to developing an effective vaccine or therapy. A20 protein is a key player in the termination of inflammation and has been shown to regulate innate immune signaling pathways. Despite the intense research on A20 and the knowledge about RSV is largely based on historical and laboratory-adapted strains. To allow for a better understanding of the biological features of RSV related to host specificity, pathogenicity, immune escape and vaccine efficacy, there is a clear need to acquire and characterize recent RSV isolates.

**Aim:** Isolation of low-passage clinical RSV isolates from children suffering from a lower respiratory tract infection (LRTI) and evaluation of phenotypic and genetic differences between them and historical reference strains.

**Methods:** We included paediatric patients between 1 month and 2 years old presenting with LRTI. Nasopharyngeal aspirates were inoculated on HEp-2 cells to obtain RSV isolates. These were then phenotypically characterized for growth in cell culture, fusogenicity, and sensitivity to palivizumab neutralization. Genotyping and sequencing of the G and F gene was also performed.

**Results:** 101 clinical RSV isolates were obtained, of which 52 RSV-A and 49 RSV-B. Although ON-1 and BA-IX genotypes predominate, phylogenetic analysis suggests that recent RSV-A isolates form a new subclade. In general, RSV-B isolates were more sensitive to palivizumab, and RSV-A isolates showed larger mean syncytium sizes. Notably, although RSV-A isolates grew to higher titers compared to most RSV-B isolates, some RSV-B isolates reached similar levels.

**Conclusions:** Recent clinical RSV isolates show clear differences, both genetically and phenotypically, in between them and compared to historical strains, emphasizing the need for continued surveillance and live virus isolation for use in research and development.

**Keywords:** Clinical isolates, RSV, Paediatrics, Viral infections, Virology

**Conflict of Interest:** None declared
Conclusions: These findings indicated that A20 regulates the inflammatory response to RSV infection and is a potential therapeutic candidate for alleviating RSV-associated immunopathology.

Keywords: RSV, A20, immunopathology, mice model

Conflict of Interest: None declared

184. FC MEDIATED FUNCTION OF NIRSEVIMAB COMPLEMENTS DIRECT RSV NEUTRALIZATION BUT IS NOT REQUIRED FOR OPTIMAL THERAPEUTIC PROTECTION IN PRECLINICAL MODELS

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Background: Nirsevimab, an extended half-life (YTE modification) monoclonal antibody that binds the pre-fusion (pre-F) protein of RSV, is approved for the prevention of RSV disease in infants entering their first RSV season. Nirsevimab has demonstrated protection from lower respiratory tract infection, and provides high levels of neutralizing antibodies, without evidence of antibody-mediated enhancement of disease. Here we investigate the preclinical and ex vivo mechanism of action of nirsevimab.

Methods: Binding of nirsevimab, MEDI8897* (nirsevimab without YTE modification), and MEDI8897*-TM (MEDI8897* with substitutions that reduce Fc-mediated effector functions) to Rfcs was evaluated by surface plasmon resonance. A cotton-rat challenge study was performed with MEDI8897* and MEDI8897-TM to evaluate the contribution of Fc-mediated activity to the protection from RSV infection. Antibody-dependent cellular cytotoxicity (ADCC), antibody-dependent complement deposition (ADCD), and antibody-dependent cellular phagocytosis (ADCP) were assessed through in vitro and ex vivo serological analyses.

Results: Nirsevimab and MEDI8897* exhibited binding to all FcγRs tested, with KD values ranging from 8.94 x 10-9 M (FcγRIIa) to 5.30 x 10-4 M (FcγRIIB). Nirsevimab demonstrated ADCP activity in a macrophage cell line, ADCD upon engagement of pre-F and purified complement C3, and mediated ADC. MEDI8897* and MEDI8897*-TM exhibited similar dose-dependent reduction in RSV replication in the lungs and nasal turbinatea in the cotton rat model.

Conclusions: Nirsevimab demonstrated binding to FcγRs and Fc-mediated activity in vitro and ex vivo models. However, the equivalent reductions in viral titers with MEDI8897*, and MEDI8897*-TM, strongly suggest that protection from RSV infection is primarily dependent on neutralization activity.

Keywords: nirsevimab, respiratory syncytial virus

Conflict of Interest: KM Tuffy, T Brady, C Cayatte, LA Machiesky, D Wilkins, T Zhang, Y-M Loo, W Blair and EJ Kelly are employees and shareholders at AstraZeneca. S Speer is a former employee and shareholder of AstraZeneca.

185. EVALUATING THE SHELF LIFE OF THE ID NOW RSV POINT-OF-CARE TEST: A PILOT STUDY

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Background: Respiratory syncytial virus (RSV) infection can be diagnosed with the ID NOW RSV point-of-care (POC) test manufactured by Abbott™. The test components expire by one year after production according to Abbott™. The POC test uses isothermal nucleic acid amplification as the basis for the molecular diagnostics. Because of this sensitive molecular underlying mechanism, we hypothesized that the tests will be useful for infant RSV studies when it is able to measure RSV concentrations of 100 times the limit of detection (LOD) after their expiration date.

Methods: We defined the LOD as the lowest concentration RSV by the Abbott™ ID NOW RSV test device before the expiration date. The LOD was determined by testing different concentrations of RSV. We then determined the diagnostic capacity of the Abbott™ ID NOW RSV test in duplicate using a pragmatic concentration of 100 times the LOD at t=1, t=6, t=8, t=12, t=16, t=18, t=24 and t=36 months after the expiration date.

Results: A single RSV A lab strain was used. The LOD was determined at 1x103 TCID50/mL. RSV A was detected in both duplicates for t=1, t=6, t=8, t=12, t=16, t=18, t=24 and t=36 months.

Conclusion: This pilot study shows that the Abbott™ ID NOW RSV POC test may give valid RSV test results for RSV A at least 36 months after the expiration date. We cannot exclude minor decrease in sensitivity over time.

Keywords: RSV, Point of care, ID NOW, Diagnostic testing, Antibody tests, Shelf life

Conflict of Interest: Louis Bont has regular interaction with pharmaceutical and other industrial partners. He has not received personal fees or other personal benefits. UMCU has received major funding (>$100,000 per industrial partner) for investigator-initiated studies from AbbVie, MedImmune, Janssen, the Bill and Melinda Gates Foundation, Nutricia (Danone) and MeMed Diagnostics. UMCU has received major cash or in-kind funding as part of the public private partnership IMI-funded RESCEU project from GSK, Novavax, Janssen, AstraZeneca, Pfizer and Sanofi. UMCU has received major funding by Julius Clinical for participating in the INFORM study sponsored by MedImmune. UMCU has received minor funding for participation in trials by Regeneron and Janssen from 2015-2017 (total annual estimate less than €20,000). UMCU received minor funding for consultation and invited lectures by AbbVie, MedImmune, Ablynx, Bavaria Nordic, MabXience, Novavax, Pfizer, Janssen (total annual estimate less than €20,000). UMCU received minor funding for participation in trials by Regeneron and Janssen from 2015-2017 (total annual estimate less than €20,000). UMCU received minor funding for consultation and invited lectures by AbbVie, MedImmune, Ablynx, Bavaria Nordic, MabXience, Novavax, Pfizer, Janssen (total annual estimate less than €20,000). UMCU received minor funding for consultation and invited lectures by AbbVie, MedImmune, Ablynx, Bavaria Nordic, MabXience, Novavax, Pfizer, Janssen (total annual estimate less than €20,000). UMCU received minor funding for consultation and invited lectures by AbbVie, MedImmune, Ablynx, Bavaria Nordic, MabXience, Novavax, Pfizer, Janssen (total annual estimate less than €20,000). UMCU received minor funding for consultation and invited lectures by AbbVie, MedImmune, Ablynx, Bavaria Nordic, MabXience, Novavax, Pfizer, Janssen (total annual estimate less than €20,000). UMCU received minor funding for consultation and invited lectures by AbbVie, MedImmune, Ablynx, Bavaria Nordic, MabXience, Novavax, Pfizer, Janssen (total annual estimate less than €20,000).

186. RESPIRATORY SYNCTYIAL VIRUS CAN INFECT APICAL CILIATED CELLS BY THE BASOLATERAL ROUTE OF INFECTION; DIFFERENCES IN INFECTION PHENOTYPES BETWEEN RSV SUBTYPES

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Background: Respiratory Syncytial Virus (RSV) causes 30 million lower respiratory tract infections (LRTIs) in children <5 years old annually. To date, the mechanism behind progression from a self-limiting RSV upper respiratory tract infection to an LRTI remains unknown. We hypothesize that during viremic conditions, RSV can infect the basal cell layer of the airway epithelium with subsequent spread to the target apical ciliated cells. Our goal was to determine if RSV could infect the apical ciliated cells through the basolateral route of virus exposure using an RSV/A and RSV/B strain.

Methods: Utilizing transwell air-liquid interface (ALI) cultures of fully differentiated human nasal organoids (HNOs), we inoculated the basolateral side of 4 donor-derived HNO lines with either RSV/A or RSV/B to simulate RSV infection.
Results: We observed consistent differences between RSV/A and RSV/B kinetics. For RSV/B, at five days post inoculation, infectious virus was detected in the apical lumen across all HNO lines. For RSV/A, this phenomenon was observed sporadically. Additionally, immunohistochemistry revealed epithelial damage and viral antigens at the apical surface in HNOs infected via the basolateral route.

Conclusion: From this data we theorize that RSV in the bloodstream can infect basal cells and spread intracellularly to apical ciliated cells where viral shedding occurs. This data demonstrates for the first-time, differences in infection pattern between RSV strains when using the basolateral route of inoculation. Through these studies we will continue to investigate mechanisms of RSV infection and how differences in RSV strains and infection pathway contribute to the development of LRTIs in children.

Keywords: Nasal Organoids, Pathogenesis, LRTI, Infection Route, Differences in RSV Subtypes

Conflict of Interest: None declared