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Mumbai, India  मुंबई, भारत

A GLOBAL CONFERENCE ON NOVEL RSV PREVENTIVE AND THERAPEUTIC INTERVENTIONS

ABSTRACT BOOKLET

ReSViNET
RESPIRATORY SyncytIAL VIRUS FOUNDATION

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CLINICAL STUDIES
BACTERIAL CO-DETECTION IN CHILDREN WITH RESPIRATORY SYNCYTIAL VIRUS

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Background: Respiratory Syncytial Virus (RSV) is a significant cause of pediatric morbidity. Though bacterial co-detection in RSV-positive children is recognized, detailed insights into its frequency and implicated organisms are crucial for refining clinical practices. Therefore, we sought to investigate bacterial co-detection in RSV-positive children.

Methods: Using Epic Clarity, we extracted clinical data for children 14 days after a preceding encounter was considered a new case. For each encounter, we retrieved unadjudicated culture results for respiratory, blood, urine, and cerebrospinal fluid specimens collected up to 72 hours after presentation.

Results: Of children who underwent RPP testing, 2,830/27,670 (10.2%) were RSV-positive (Table 1). Of 1,038 children who had at least one culture performed, 129 (12.4%) were positive for one or more co-detected bacteria. Bacterial growth was observed in 54.1% of respiratory (n=59/109), 5.6% of urine (n=34/603), 3.7% of blood (n=39/836), and 1.3% of cerebrospinal fluid cultures (n=2/159; Table 2). Escherichia coli was the predominant isolate from urine (n=21/34), Staphylococcus epidermidis from blood (n=16/39), and Haemophilus influenzae from respiratory specimens (n=13/59). Streptococcus pneumoniae was isolated from both positive cerebrospinal fluid specimens. Of 109 RSV-positive children for whom a respiratory culture was performed, 94 were intubated, and over half of these (n=52/94) had bacterial co-detection.

Conclusion: Respiratory bacterial co-detection is strikingly prominent in children with severe RSV-associated illness. Future research should focus on delineating the clinical implications and effective management strategies for these co-detections.

Abstract category: Clinical Studies

Keywords: Respiratory Syncytial Virus Infections; Bacteria; Antibiotics

Conflict of Interest: None declared
INPATIENT BURDEN OF RESPIRATORY SYNCTIAL VIRUS INFECTION IN NEONATES AND INFANTS IN JAPAN, 2011-2022: A DATABASE STUDY

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Background: Comprehensive evidence on inpatient burden of respiratory syncytial virus (RSV) infection among children is scarce in Japan.

Methods: A large-scale electronic health records database covering 445 hospitals (approximately 25% of acute care hospitals) in Japan were used. The study population comprised of infants (<1 year of age) with a confirmed RSV diagnosis in outpatients or inpatients using ICD-10 diagnostic codes between April 2011 and July 2022. Hospitalization rate, inpatient characteristics, various inpatient outcomes, and healthcare resource utilization (HCRU) were described.

Results: A total of 109,332 RSV-confirmed outpatients and 54,100 RSV-confirmed inpatients were identified. Among infants diagnosed outpatient, 23.3% required hospitalization in the same hospital within 6 days post-diagnosis. Among all hospitalized infants, 50,648/54,100 (93.6%) had no record of comorbidities or prematurity eligible for palivizumab. As in-hospital outcomes/HCRU, 51,012/54,100 (94.3%) used intravenous fluid, 25,419/54,100 (47.0%) required oxygen use, 1,472/54,100 (2.7%) required mechanical ventilation, and 20/54,100 (0.04%) resulted in death. As in-hospital complications, 13,074/54,100 (24.2%) had pneumonia, 2,923/54,100 (5.4%) had otitis media, 197/54,100 (0.4%) had febrile seizure, 26/54,100 (0.05%) had encephalitis or encephalopathy, and 2/54,100 (0.0%) had myocarditis. Antibiotics were prescribed in 21,785/54,100 (40.3%). The mean inpatient stay was 6.1 days at a direct medical cost of 435,743 JPY/patient.

Conclusions: Large number of RSV cases were diagnosed in both outpatient and inpatient settings with substantial HCRU and in-hospital outcomes/complications. Approximately one in four RSV infection resulted in hospitalizations with most hospitalizations occurring among healthy term infants, emphasizing the need for RSV prevention measures in all infants.

Abstract category: Clinical Studies

Conflict of Interest: Takeshi Arashiro, Rolf Kramer, Jing Jin, and Munehide Kano are Sanofi employees. Fangyuan Wang is a Syneos Health employee. The study is funded by Sanofi and AstraZeneca.

POST-MORTEM INVESTIGATIONS ON THE ROLE OF RESPIRATORY SYNCTIAL VIRUS IN CHILDHOOD DEATHS IN SOUTH AFRICA

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Presenting author: Vicky Baillie

Respiratory syncytial virus (RSV) is estimated to cause 101,400 childhood deaths in 2019; however, there is limited post-mortem studies which have been undertaken to quantify the role of RSV in childhood deaths.

We analysed deaths occurring between December 2016-December 2022 to determine the contribution of RSV to under-5 childhood deaths using minimally invasive tissue sampling (MITS). A panel of experts determined the cause of death (CoD) by reviewing the antemortem medical and laboratory records, together with postmortem results generated from the MITS. Postmortem testing included lung tissue histology, immunohistochemistry, and molecular tests.

Of the 1393 decedents, 3%(n=38) had RSV detected in their postmortem specimens; while, RSV attributed to the CoD in 2%(n=22) of the deaths, including in <1%(n=1/899) among those <28days age, 4%(n=13/332) in the 28-365 days age-group and 5%(n=8/162) in the 12-59 months age-group. Amongst those >28 days of age in whom RSV was included in the CoD, it was the underlying, immediate, and antecedent cause in 24%(n=5/21), 48%(n=10/21) and 29%(n=6/21), respectively. Of the decedents where RSV was attributed as an immediate CoD, 60%(n=6/10) were hospital-acquired infections. Further, of decedents with pneumonia as the underlying (8.5%, n=42/494) or immediate (23%, n=115/494) CoD, RSV was the causal pathogen in 12%(n=5/42) and 9%(n=10/115) of the underlying and immediate pneumonia related deaths, respectively.

RSV is responsible for a substantial portion of childhood pneumonia related mortality. These data highlight the need for better and more cost-effective treatment options and more importantly the need for preventative options to protect young children against RSV.

Abstract category: Clinical Studies

Keywords: Childhood Deaths; Minimally Invasive Tissue Sampling; Pneumonia

Conflict of Interest: None declared

A COMPREHENSIVE ASSESSMENT OF DOUBLE-BLIND RANDOMIZED HUMAN CHALLENGE CLINICAL STUDIES FOR RESPIRATORY SYNCTIAL VIRUS: SYSTEMATIC REVIEW AND META-ANALYSIS

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Respiratory Syncytial Virus (RSV) remains a major global health concern among infants, elderly, and individuals with underlying comorbidities. RSV infections can lead to severe respiratory illnesses, often requiring hospitalization and posing a significant burden on healthcare systems. In response to this challenge, numerous trials have been conducted to assess the early signal of efficacy of various anti-viral treatments. However, the landscape of RSV treatment remains complex, with a variety of interventions and outcomes across studies. Our work provides the first comprehensive assessment of the meta-analytic placebo and treatment effects reported in several human challenge studies The key endpoints are mean time from inoculation to peak viral load (VL) and peak symptom score, mean VL Area
under the curve (AUC) and mean peak VL for placebo and treatment groups. A systematic search is performed from PubMed, ClinicalTrials.gov and EudraCT from data inception to August 2023. Four to seven studies are included in meta-analysis depending on endpoints. The primary findings for placebo are the mean time from inoculation to peak VL and peak symptom score are respectively 4.9 days (95% CI: 4.05-5.71) and 4.3 days (95% CI: 3.2-5.3). Comparing with influenza (1.7 and 2.9 days for peak VL and symptom score, respectively) and SARS-nCoV-2 (7 and 7.9 days for peak VL and symptom score, respectively). These results suggests that the clinical profile for RSV lies between SARS-nCoV-2 and influenza. Our systematic review will allow clinicians, researchers, and policymakers to inform decision for designing RSV treatment studies and their implications in clinical practice.

Figure 1: Imputed Mean Time (days) to Peak Viral Load for Placebo – Human Viral Challenge Model

Figure 2: Imputed Mean Time (days) to Peak Symptom Score for Placebo – Human Viral Challenge Model

Abstract category: Clinical Studies

Keywords: Human Challenge Studies, Randomized, Placebo-Controlled, Meta-Analysis, Viral Load, RSV Treatment, Peak Symptom Score.

Conflict of Interest: Authors hold shares and stocks of Pfizer Inc.

RESPIRATORY SYNCYTIAL VIRUS INFECTION BURDEN IN FEBRILE CHILDREN AND ADULTS IN LAOS, MALAWI, MOZAMBIQUE AND ZIMBABWE.

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After the introduction of the pneumococcal and Haemophilus influenzae conjugate vaccines, Respiratory Syncytial Virus (RSV) has stood out as one of the main causes of acute respiratory infections in children, particularly among infants. In Low and Middle-Income Countries (LMIC), its real burden among febrile patients, particularly beyond childhood, remains poorly characterized. We aimed to describe the prevalence of RSV infections among febrile adults and children recruited in Laos, Malawi, Mozambique and Zimbabwe as part of the “Febrile Illness Evaluation in a Broad Range of Endemicities” (FIEBRE) study whose overall objective was to investigate the detailed etiologies of fever in LMIC.

After providing written informed consent, a physical examination was performed on those aged 2 months and older residing at one of four sites who presented with documented fever. Nasal and oropharyngeal swabs were tested. Controls are recruited two times per month at each site and enrolled if they or their parents/guardians provide informed consent.

A total of 10,252 children and adults were recruited between November 2018 to March 2021. Of those, 142 (1.3%) tested positive for RSV type A were 116 children (48 outpatients, 49 inpatients and 19 controls) and 26 were adults (19 outpatients and 7 inpatients), 80 (0.7%) tested positive for RSV type B were 65 children (32 outpatients, 29 inpatients and 4 controls) and 15 adults (9 outpatients, 3 inpatients and 3 controls). We will present detailed stratified data related to age group, gender and country, as well as clinical characterization, co-infections and outcome.

Abstract category: Clinical Studies

Keywords: RSV Infection, Pediatrics, Adults, Fever

Conflict of Interest: None declared
**EFFECTIVENESS OF HIGH-DOSE VITAMIN D SUPPLEMENTATION TO REDUCE THE INCIDENCE RATE OF REPEAT EPISODES OF PNEUMONIA IN CHILDREN: A SYSTEMATIC REVIEW**

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Introduction: 125(OH)2D3 is a key component of response in immune cells in response to pathogens. However, there is no consensus among the different clinical practice guidelines in recommending Vitamin D supplementation to reduce the recurrence of pneumonia.

Methods: Searches of computerized databases (MEDLINE, EMBASE, CENTRAL, and Lilacs) and references cited in published literature identified potentially applicable studies from January 2020 to January 2023. We included studies that have evaluated vitamin D as a supplementary treatment to antibiotic management in patients under 18 years of age hospitalized with a diagnosis of pneumonia, and that report the incidence of recurrent episodes of pneumonia after hospitalization and mortality.

Results: The searches yielded 115 citations and a total of 12 studies were examined in full. No publication bias was found (Egger’s: intercept = -1.41, p = .20; Begg’s: z = 0.62, p = .71). The analysis found that Vitamin D does not reduce the risk of recurrent episodes of pneumonia (RR 0.70 CI 0.47–1.14, I2: 79%) neither was observed effect when were compared single dose regarding no single dose, Figure 1. Also, Vitamin D does not reduce mortality in children with pneumonia (RR 0.78 CI 0.54–1.13, I2: 0%).

Conclusion: High-Dose Vitamin D Supplementation does not reduce the incidence rate of repeat episodes of pneumonia or mortality from pneumonia. Our study provides evidence that should be used by decision-makers to improve clinical practice guidelines.

**Abstract category:** Clinical Studies

**Keywords:** Vitamin D Supplementation, Pneumonia, Mortality

**Conflict of Interest:** None

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**RSV BURDEN IN INFANTS ATTENDING HOSPITAL EMERGENCY DEPARTMENTS IN IBERIA FROM 2022 TO 2023: THE RHEDI STUDY.**

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After the SARS-CoV-2 pandemic, evolving patterns of epidemiology have been observed. The aim of this study is to describe the burden of RSV and other respiratory infections in children ≤2-years-old presenting to the emergency department (ED).

A prospective, hospital-based surveillance in EDs of eight pediatric hospitals in Spain and Portugal was carried out. Patients were recruited in two seasons: between January–April 2022, and between September 2022–April 2023. During the ED visit, clinical, demographic data and nasopharyngeal sample for PCR-based microbiological analysis were collected from each participant.

914 children were recruited, of whom 87.0% were diagnosed with lower respiratory tract infections (LRTI), and 13.0% with upper respiratory tract infections (URTI). 91.2% were diagnosed with viral infection and 38.9% had viral coinfection. The most frequently isolated organisms were rhinovirus (37.9%), followed by RSV (24.8%). Microorganisms were not detected in 8.6% of patients. Patients with RSV viral infection accounted for 8.1% and 40.0% of all infections in seasons 2021–2022 and 2022–2023 respectively. Compared to patients with non-RSV infection, patients with RSV viral infection showed a higher frequency of LRTI diagnosis (94.7% vs 85.4%; P = 1.12 × 10-4) and hospital admission (39.2% vs 12.1%; P = 10^-15). No difference was observed between RSV-infected/non-RSV-infected patients regarding intensive care unit admission (5.6% for RSV vs 7.2% for no-RSV; P = 0.761).

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**Figure 1.** Percentage of Patients by Microorganism in Total and By the Different Seasons (A), and the Difference Between Clinical Presentation (URTI vs. LRTI) (B). HRV: Human Rhinovirus, RSV: Respiratory Syncytial Virus, HEV: Human Enterovirus, MPV: Metapneumovirus, AdV: Adenovirus, PIV: Parainfluenza, HboV: Human Bocavirus, CoV: Coronavirus (non SARS-CoV-2), BPP: Bordetella Parapertussis, MP: Mycoplasma pneumoniae
During the COVID-19 pandemic period, children ≤ 2 years attending ED with RSV were less frequently detected than expected; however it has re-emerged as one of the main pathogens in ED since COVID-19 restrictions were removed. Infections by RSV were associated with more severe outcomes compared to other viral pathogens.

**Abstract category:** Clinical Studies

**Keywords:** Pediatric Emergency Medicine, Bronchiolitis, Respiratory Syncytial Virus Human, Respiratory Syncytial Virus Infections

**Conflict of Interest:** The study was funded by Sanofi and AstraZeneca. Mathieu Bangert, Rolf Kramer, Leticia Platero and Catrina Gomes are employees of and may own shares / have stock options in Sanofi.

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**CHILDREN UNDER FIVE YEARS OF AGE IN SENEGAL: A GROUP HIGHLY EXPOSED TO RESPIRATORY VIRUS INFECTIONS**

**Presenting author:** Jean Baptiste Niokhor Diouf

**Background:** Acute respiratory infections (ARI) continue to be the leading cause of pediatric morbidity and mortality worldwide. The present study is a prospective analysis of the prevalence and diversity of respiratory viruses associated with acute RTIs in children under 5 years of age in Senegal, and their association with disease severity.

**Patients/Methods:** An active surveillance of ARI was conducted from March 2021 to December 2022 in three pediatric referral Healthcare departments of Dakar. 288 children with ARI were enrolled and respiratory specimens collected. A two-step multiplex real-time RT-PCR for the simultaneous testing of 16 different respiratory viruses was performed.

**Results:** 93 children required hospitalization. Viral etiologies were identified in 224 patients while 64 were negative for all tested viruses. Single viral infections accounted for 30.5% and co-infections for 46.9%. A total of 439 respiratory viruses were identified in all children. Among these, 154 (35.3%) were detected in hospitalized children. Adenoviruses with 44.4%, influenza viruses 36.5%, rhinoviruses (HRV) 28.5%, enteroviruses 19.8% and respiratory syncytial virus (RSV) with 10.1% were the most detected. RSV infections were significantly more frequent in the first 6 months of life (p-value = 0.00213). RSV and HRV are mostly associated with bronchiolitis and bronchitis. Influenza detection is also the most related with pneumonia disease (47.6%).

**Conclusion:** This study investigated the role of 16 different respiratory viruses in children with ARI in this Senegal. Data clearly suggest that respiratory viruses are major contributors to childhood acute respiratory infections in Senegal.

**Abstract category:** Clinical Studies

**Keywords:** ARI, Child, Virus, Senegal

**Conflict of Interest:** No

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**VITAMIN D DEFICIENCY – A TRIGGER FACTOR FOR BRONCHIOLITIS**

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**Presenting author:** Narendra Gemawat

Bronchiolitis caused by mostly respiratory syncytial virus. For more than half cases in younger than 1 year age. There is paucity of RSV vaccination studies. RSV is mild infection but at times require hospitalization. Cross-sectional studies in 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 an immune modulator and appears to influence host defenses. We present our observation of vitamin D deficiency and bronchiolitis in otherwise healthy infants.

Total 7 infants of 8-13 months, who presented with bronchiolitis were 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.

Our result showed that all infants were deficient in vitamin D, none of them were on vitamin D supplements. They all improved well with general management and vitamin supplementation of 1000 iu per day for six months.

The present study though small, shows that vitamin D, deficiency in infants, even in well nourish, well immunized, is may be trigger factor in occurrence of bronchiolitis. Vitamin D is a important immunomedulation factor in infants, advocating early supplementation to trigger immune complex system. Further bigger studies may be done for further evaluation.

**Abstract category:** Clinical Studies

**Keywords:** Bronchiolitis; Vitamin D

**Conflict of Interest:** None declared

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**VITAMIN D SUPPLEMENTATION TO PREVENT ACUTE RESPIRATORY INFECTIONS IN CHILDREN**

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**Presenting author:** Diana Guerrero

Introduction: Increasing evidence has demonstrated the effectiveness and safety of vitamin D supplementation to prevent acute respiratory infections in children. More economic evaluations incorporating the new evidence and in the pediatric population are needed to know the efficiency of this treatment. This study aimed to determine the cost-utility of vitamin D supplementation to prevent acute respiratory infections in pediatric patients.

**Methods:** A decision tree model was used to estimate the cost and quality-adjusted life-years (QALYs) of vitamin D supplementation in healthy school children between 1 and 16 years. Multiple sensitivity analyses were conducted. Cost-effectiveness was evaluated at a willingness-to-pay (WTP) value of $19,000.

**Results:** The base-case analysis showed that vitamin D supplementation was associated with lower costs and higher QALYS than strategy without this supplementation. The QALYs per person estimated in the model for those treatments were 0.99 with vitamin D supplementation and 0.98 without vitamin D
supplementation. The total costs per person were US$ 1354 for vitamin D supplementation and US$ 1948 without vitamin D supplementation. This position of absolute dominance of vitamin D supplementation makes it unnecessary to estimate the incremental cost-effectiveness ratio.

Conclusion: In conclusion, our study shows that Vitamin D supplementation is a cost-effective strategy to prevent ARI in pediatric patients, from a societal perspective.

Abstract category: Clinical Studies

Keywords: Vitamin D, Cost, Colombia, Infection

Conflict of Interest: None

RSV-RELATED PEDIATRIC IN-HOSPITAL MORTALITY IN GAVI-ELIGIBLE COUNTRIES

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Presenting author: Nynke C J van Haastregt

Background: There are key gaps in our knowledge and understanding of pediatric RSV-mortality in Gavi-eligible countries. The RSV GOLD III – ICU Network Study aimed to describe clinical and socio-economic characteristics of children <2 years admitted with life-threatening RSV infection to the pediatric intensive care unit (PICU) in Gavi-eligible countries. Here we present the characteristics of RSV-related mortality cases included in this study.

Methods: Children <2 years admitted to the PICU with severe acute respiratory infection were tested for RSV with a point-of-care diagnostic device during 2 local respiratory disease seasons. Patients were followed until death or discharge.

Results: Between April 2021 – September 2023, 608 RSV-positive children were included at referral hospitals in 10 Gavi-eligible countries. In total 30 deaths (4.9%) occurred at 7/10 study sites. Mortality ranged between 0-26.9%. Children who died were younger than survivors (1.8 vs 3.1 months, p=0.03) and had more often comorbidities (44.8% vs 14.5%, p<0.001) of which congenital heart disease was the most common (N=6, 20%). Five children (17%) were born prematurely. Twenty-three mothers (77%) had received a tetanus vaccine during pregnancy and antenatal care coverage (at least 4 visits) was 63.3%.

Conclusion: RSV-related in-hospital mortality was 4.9% (range 0-26.9%). Young age and presence of comorbidities were risk factors for mortality in RSV-positive children. Considering the median age of RSV-related deaths, we expect that maternal vaccination and extended half-life monoclonal antibodies will have a high impact on infant survival in Gavi-eligible countries.

Funded by the Bill & Melinda Gates Foundation

Abstract category: Clinical Studies

Conflict of Interest: None declared
ANTIBIOTIC USE DURING RSV INFECTIONS IN INFANCY - AN INTERNATIONAL PROSPECTIVE BIRTH COHORT STUDY

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Presenting author: Sarah Hak

Introduction: Antibiotic use during infancy impacts microbiome diversity and composition, and contributes to the emergence of antimicrobial resistance. Estimates of antibiotic use during respiratory syncytial virus (RSV) infections range widely. Therefore, we determined antibiotic use among infants with RSV acute respiratory infections (ARI) in the ambulatory and hospital care setting.

Methods: RESCEU is a prospective observational birth cohort study that enrolled healthy term infants between 2017 and 2019 in five European countries. Antibiotic use during RSV-associated hospitalization in the first year of life was identified through hospital chart review in the total cohort (n=9154), while ambulatory care data were collected by parental questionnaires in a nested cohort (n=993).

Results: Based on preliminary data, 251 RSV infections were identified, of which 113 (45.0%) required outpatient care. The antibiotic prescription rate was 8.8% (10/113; 95% confidence interval [CI]: 4.3-15.7). We identified 145 RSV-associated hospital admissions, of which 8 (5.6%) required intensive care unit (ICU) admission. Antibiotics were prescribed in 20.4% (28/137; 95% CI: 14.0-28.2) of infants admitted to general paediatric wards and 62.5% (5/8; 95% CI 24.5-91.5) of ICU-admitted infants.

Conclusions: This birth cohort study confirms that RSV infection is associated with antibiotic use, and that the rate of antibiotic use is associated with disease severity. In further analyses we plan to determine the attributable fraction of ARI-associated antibiotic use due to RSV infection. Our findings suggest that RSV immunization could decrease antibiotic use in healthy term infants’ first year of life.

Abstract category: Clinical Studies

Keywords: RSV, Antibiotics, Burden

Conflict of Interest: SH: None declared. RVP: None declared. CV: None declared. MB: None declared. MVH has received honoraria for participation in advisory boards from Sanofi and Moderna and acted as PI in randomized clinical trials for Pfizer. AJP is part of the RESCEU consortium and his University received grant funding from the European Commission IMI programme for this work. Oxford University has also received grant funding from Medical Research Council, Wellcome Trust, Bill & Melinda Gates Foundation, Serum Institute of India and AstraZeneca. AJP is a contributor to intellectual property licensed by Oxford University Innovation to AstraZeneca. AIP is chair of the UK Joint Committee of Vaccination and Immunisation and was a member of WHO SAGE till 2022. TH has received honoraria for lectures or participation in advisory boards or data monitoring committees from Janssen, Sanofi, and MSD. SC had provided clinical study advice or acted as PI for GSK, Pfizer, MedImmune, Abylnx, Gilead, Ark Biosciences, Shionogi, Janssen/Alios with fees paid to the University of Edinburgh. FMT has received honoraria from GSK group of companies, Biofabri, Pfizer Inc, Sanofi Pasteur, MSD, Seirgus and Janssen for taking part in advisory boards and expert meetings and for acting as a speaker in congresses outside the scope of the submitted work. F. Martín-Torres has also acted as principal investigator in randomized controlled trials of the above-mentioned companies as well as Abylnx, Gilead, Regeneron, Roche, Abbott, Novavax and MedImmune, with honoraria paid to his institution.

LUB has regular interaction with pharmaceutical and other industrial partners. He has not received personal fees or other personal benefits. UMCU has received major funding (>€100000 per industrial partner) for investigator-initiated studies from AbbVie, MedImmune, AstraZeneca, Sanofi, Janssen, Pfizer, MSD, and MeMed Diagnostics. UMCU has received major funding for the RSV GOLD study from the Bill & Melinda Gates Foundation. UMCU has received major funding as part of the European research IMI-funded RESCEU and PROMISE projects with partners GSK, Novavax, Janssen, AstraZeneca, Pfizer, and Sanofi. UMCU has received major funding from Julius Clinical for participating in clinical studies sponsored by MedImmune and Pfizer. UMCU received minor funding (€1000–25000 per industrial partner) for consultation and invited lectures by AbbVie, MedImmune, Abylnx, Bavaria Nordic, MabXience, GSK, Novavax, Pfizer, Moderna, AstraZeneca, MSD, Sanofi, Genzyme, and Janssen. LUB is the founding chairman of the ReSVINET Foundation. JGW has an interest in clinical trials sponsored by pharmaceutical companies including AstraZeneca, Merck, Pfizer, Sanofi, and Janssen. All funds have been paid to UMCU. JGW participated in the advisory board of Janssen and Sanofi with fees paid to UMCU.

THE BURDEN OF RSV INFECTIONS IN OLDER ADULTS IN PRIMARY CARE

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Presenting author: Sarah Hak

Introduction: Respiratory Syncytial Virus (RSV) is increasingly recognized as important cause of acute respiratory infections (ARI) in elderly. However, data on RSV infections managed in the outpatient setting are scarce. We therefore aim to determine the burden of RSV infections among older adults in primary care.

Methods: We are conducting a prospective, observational study during two winter seasons ('22-'23 and '23-'24). Older adults (≥60 years) seeking primary care with symptoms of an ARI were tested for RSV using point-of-care PCR in the Netherlands, and multiplex PCR in Italy. In RSV-positive patients, the disease burden is assessed using three questionnaires (baseline, 14 and 30 days, respectively).

Results: During the '22-'23 winter season, 312 nasal swabs (NL: 160, Italy: 152) were collected, of which 53 (17.0%) tested RSV-positive. RSV-positive patients had a mean age of 74 years (SD: 8) in the Netherlands, and 79 years (SD: 8) in Italy. The majority (78.8%) had at least one chronic disease and 49.0% reported polypharmacy. RSV illness lasted a median of 14 days (IQR: 10-21), and most (66.7%; Dutch data only) reported moderate to severe limitation of daily activities.
Mean number of primary care visits was 1.7 (SD: 1.0) and antibiotic use was reported in 49%. During 30 days of follow-up, two patients (4.1%) were hospitalized.

Conclusions: Our preliminary results suggest a considerable burden of RSV infections among older adults in primary care. The final results will support decision-making regarding the potential implementation of an RSV vaccine in public immunization programs.

Abstract category: Clinical Studies
Keywords: RSV, Burden, Older Adults, Elderly, Primary Care, Outpatient

Conflict of Interest: Funding: The Dutch part of this investigator-initiated study is funded by Janssen Pharmaceutica. The Italian part of this study did not receive external funding.

Potential conflict of interest: SH, SB, MS, EE, TC, EB, RP, Jv report no potential conflict of interest. LB has regular interaction with pharmaceutical and other industrial partners. He has not received personal fees or other personal benefits. UMCU has received major funding (>€100000 per industrial partner) for investigator-initiated studies from AbbVie, MedImmune, AstraZeneca, Sanofi, Janssen, Pfizer, MSD, and MeMed Diagnostics. UMCU has received major funding for the RSV GOLD study from the Bill & Melinda Gates Foundation. UMCU has received major funding as part of the public private partnership IMI-funded RESCEU and PROMISE projects with partners GSK, Novavax, Janssen, AstraZeneca, Pfizer, and Sanofi. UMCU has received major funding from Julius Clinical for participating in clinical studies sponsored by MedImmune and Pfizer. UMCU received minor funding (€1000–25000 per industrial partner) for consultation and invited lectures by AbbVie, MedImmune, Ablynx, Bavaria Nordic, MalXience, GSK, Novavax, Pfizer, Moderna, AstraZeneca, MSD, Sanofi, Genzyme, and Janssen. JB is the founding chairman of the ReSViNET Foundation. CR participated in Advisory Board and Expert scientific discussion for Seqirus, MDS, GSK, Sanofi, and AstraZeneca. JW has been an investigator for clinical trials sponsored by pharmaceutical companies including AstraZeneca, Merck, Pfizer, Sanofi, and Janssen. All funds have been paid to UMCU. JW participated in the advisory board of Janssen and Sanofi with fees paid to UMCU.

A NOVEL DE NOVO LIKELY PATHOGENIC VARIANT OF WFS-1 GENE IN A PAKISTANI CHILD WITH NON CLASSIC WFS-1 SPECTRUM DISORDER

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Respiratory Distress (RD) is a common issue during the neonatal phase and significantly contributes to neonatal morbidity and mortality. It often arises from various factors such as hyaline membrane disease (HMD), also known as respiratory distress syndrome (RDS), transient tachypnea of the newborns (TTN), and infections, particularly in premature babies. To prevent irreversible harm or brain injury to these vulnerable infants, prompt and accurate diagnosis of respiratory distress is crucial.

This study aimed to determine the frequency of respiratory distress, identify contributing factors, and evaluate the outcomes of infants treated at the neonatal intensive care unit (NICU) in the Sindh Institute of Child Health and Neonatology. This facility is located in the comparatively underprivileged area of Korangi, Karachi. The observational study was conducted from September 2022 to February 2023, during which all neonates diagnosed with respiratory distress were enrolled and closely monitored for their subsequent progress.

Out of 680 neonates referred for evaluation, 587 (86.32%) were diagnosed with respiratory distress. Among them, 312 (61.17%) were male and 198 (38.8%) were female. The study found that premature births accounted for a significant portion, with 321 (63%) of the total newborns experiencing respiratory distress.

The etiologies of respiratory distress were investigated, with the following success rates reported: 197 (94.7%) had hyaline membrane disease, 187 (80%) had sepsis, 58 (95%) had pneumonia, 32 (100%) had Transient tachypnea of the newborns (TTN), 20 (74%) had meconium aspiration syndrome (MAS), 11 (2.15%) had bronchiolitis, and 5 (0.98%) had congenital heart abnormalities. Notably, the study did not screen for respiratory syncytial virus (RSV) as a potential cause of sepsis, which could have been a contributing factor in some cases.

Unfortunately, sepsis was identified as the most frequent cause of death among neonates with respiratory distress, accounting for 47 out of 77 cases (61.03%). This highlights the urgency of early diagnosis and effective management of respiratory distress, including screening for potential viral infections such as RSV, to improve patient outcomes and reduce mortality rates.

Abstract category: Clinical Studies
Keywords: Wolfram Syndrome, WFS-1 Spectrum Disorder, Optic Atrophy, Autosomal Dominant

SEASONALITY AND OUTCOMES OF RESPIRATORY VIRUSES AMONG HOSPITALIZED CHILDREN IN AMMAN, JORDAN, OVER MULTIPLE RESPIRATORY SEASONS (2007–2023)

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Presenting author: Haya Hayek

Background: Acute Respiratory Infections (ARIs) are a significant cause of pediatric hospitalizations; however, there is a paucity of data from the Middle East. We examined the seasonality and outcomes of respiratory syncytial virus (RSV) and other respiratory viruses across multiple seasons in Jordan.

Methods: We analyzed data from four viral surveillance studies, conducted at Amman’s largest public hospital in 2007, 2010–2013, 2020, and 2023. The study population included children <2 years old hospitalized with fever and/or respiratory symptoms. Nasal and/or throat swabs were tested for common respiratory viruses using RT-qPCR. We collected demographic and clinical data, including ICU admission and supplemental oxygen use, through parental interviews and chart abstractions.
Results: Among 4,766 children included, 4,046 (84.9%) had at least one virus detected, and 2,233 (46.9%) were RSV-positive. The median age was 3.5 months (IQR, 1.6–8.2), and 59.3% (n=2,826) were male. RSV circulation peaked during winter months before the COVID-19 pandemic (Figure 1). However, RSV circulation was lower in January–March 2023 compared with historical trends. Other respiratory viruses except for hMPV, which circulated more frequently during January–April 2023, showed relatively consistent seasonality across study years (Figure 2). Among children with RSV-only detection, 47.3% received supplemental oxygen (significantly higher than all other groups), and 8.7% required intensive care (significantly higher than hMPV and influenza; Table).

Conclusion: RSV seasonality remains disrupted in Jordan compared with historical patterns. Moreover, RSV infections are associated with poor clinical outcomes compared to other respiratory viruses. Vigilant tracking of seasonal RSV circulation is imperative to optimize healthcare preparedness.

Abstract category: Clinical Studies
Keywords: Respiratory Syncytial Virus, Virus Seasonality, Clinical Outcomes, COVID-19 Pandemic, Viral Surveillance Study
Conflict of Interest: Natasha Halasa, MD, MPH, receives grant support from Sanofi Pasteur, Quidel, and Merck.

EMPOWERING MOTHERS IN RURAL RESOURCE-POOR COMMUNITIES: A CRITICAL INTERVENTION TOOL IN PREVENTING RSV-LIKE INFECTIONS.

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Background: Rural and resource-poor communities are faced with the challenges of access to health care; even where there is access, laboratory confirmation of RSV is nonexistent. So, the management emphasis shifts from confirmation to the identification and prevention of RSV like symptoms, signs and complications. This study aimed to assess the knowledge, attitudes, and practices of mothers in rural communities regarding RSV-like infections in Nigeria.

Methods: A mixed-method cross-sectional design was employed. It included an initial focal group discussion with 15 women from rural communities in Imo State, Nigeria. This was followed by an interviewer-administered questionnaire on 399 postpartum women attending child immunization services. Chi-square and logistic regression analyses were done at a level of significance set at p = 0.05.

Results: Qualitative analysis revealed that the mothers had a basic understanding of RSV-like signs and symptoms but observed certain traditions and beliefs. They identified a dirty environment as a common cause of infection and engaged in traditional practices, including herbal medications and unconventional practices, such as using a razor blade. The participants had mixed views on seeking hospital care, with some relying on traditional remedies and others recognizing the need for medical attention in severe cases. Quantitative analysis showed that only 26% of mothers had a good level of knowledge about RSV, but a majority (51%) recognized the importance of vaccination. Positive attitudes towards prevention and control of RSV-like infections were prevalent (58%), although some mothers (26%) believed in spiritual causes of respiratory tract infections. The use of herbal medicines and razor blades were reported in 12% of mothers. Factors such as education, occupation, income, knowledge, attitude, and immunization status were associated with the level of preventive practices (p<0.05).

Conclusion: The findings highlight the need to empower mothers in rural communities through education and culturally sensitive interventions.

Abstract category: Clinical Studies
Keywords: Knowledge, Attitude, Practice, RSV-Like Infections, Rural, Nigeria
Conflict of Interest: None declared
CLINICAL ANALYSIS OF RESPIRATORY Syncytial Virus REINFECTION IN HOSPITALIZED CHILDREN

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Background: Respiratory Syncytial Virus (RSV) is the most important cause of severe acute respiratory infections (ARTI) in children. Almost all children have been infected at least once before 24 months, and about half have been infected twice. Therefore, it is particularly important to study whether reinfection of RSV leads to more severe conditions.

Methods: Clinical data of hospitalized children with recurrent RSV infection in Shenzhen Children’s Hospital from January 2020 to December 2022 were collected. A pre- and post matched design was performed, and Wilcoxon rank sum test and Pearson chi square test were used to compare and analyze the severity of primary infection and reinfection.

Results: From 2020 to 2022, there were 17 cases of reinfection among RSV positive children in Shenzhen, including 12 male children (70.6%), and a total of 14 cases (82.4%) with onset time between July and October. Paired design showed that there was no statistically significant difference in hospitalization time, fever peak, fever duration, Wheezing, rales, triple concave sign, chest X-ray manifestations, antibiotic use, antiviral drug use, glucocorticoid use, oxygen therapy etc between primary infection and reinfection in RSV positive children.

Conclusions: RSV reinfection is not less severe than primary infection, so we should pay more attention to the prevention of RSV.

Abstract category: Clinical Studies
Keywords: Respiratory Syncytial Virus, Primary Infection, Reinfection, Severity
Conflict of Interest: None declared

SAFETY AND IMMUNOGENICITY OF A RESPIRATORY Syncytial Virus AND HUMAN METAPNEUMOVIRUS BIVALENT VIRUS-LIKE PARTICLE PROTEIN SUBUNIT VACCINE (IVX-A12) IN OLDER ADULTS

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Respiratory Syncytial Virus (RSV) and human metapneumovirus (hMPV) cause a significant proportion of serious lower respiratory tract infections in older adults. In this ongoing first-in-human phase 1 clinical trial, we evaluated the safety and immunogenicity of IVX-A12, a bivalent RSV/hMPV virus-like particle subunit vaccine in healthy 60–75 year-old adults (NCT05664334). Five single-dose formulations were tested (low dose: 75µg RSV/75µg hMPV and medium dose: 75µg RSV/150µg hMPV, ± MF59® (CSL Seqirus) oil-in-water adjuvant, or high dose: 75µg RSV/225µg hMPV, unadjuvanted). 117 subjects received IVX-A12 and 23 received placebo.

No serious adverse events, Grade 4 adverse events (AEs), clinical events of special interest, related medically-attended AEs, or AEs leading to death/study discontinuation were reported up to Day 28. Local AEs were mild to moderate and higher with adjuvanted formulations. Rates of systemic AEs were similar to placebo. Neutralizing antibody geometric mean titers (GMTs) on Day 28 were up to 16,110 International Units (IU)/mL for RSV and 23,946 assay units/mL for hMPV, with 5x overall and up to 7-11x in subjects with low baseline titers. Overall, IVX-A12 was well tolerated and immunogenic against RSV and hMPV in healthy older adults, without immune interference. This trial is the first demonstration of hMPV vaccine immunogenicity in this at-risk population.

Abstract category: Clinical Studies
Keywords: RSV, hMPV, VLP, Bivalent Vaccine, Clinical Trial, Older Adults
Conflict of Interest: None declared

MANAGEMENT OF BRONCHIOLITIS INFECTION IN MONKOLE HOSPITAL (D.R CONGO)

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Introduction: Bronchiolitis is an infection of the respiratory tract, common in children under 5 years old. We carried out a retrospective study in children aged 6 months to 17 years hospitalized in the pediatric department of the Monkole hospital center during the period from January 2020 to December 2022. The aim of the study was to compare the frequency of bronchiolitis to pneumonia.

Results: 586 children were hospitalized during the period, 171 (29,1%) for bronchiolitis and 415 (80,9%) for pneumonia. We recorded for bronchiolitis 24 in 2020, 30 in 2021 and 61 in 2022 and for pneumonia we had 160, 159 and 96 respectively for the years 2020, 2021 and 2022.

Conclusion: The authors discuss the intervention of COVID infection on the circulation of viruses causing bronchiolitis.

Abstract category: Clinical Studies
Keywords: Bronchiolitis, Pneumonia, Children, D.R. Congo
Conflict of Interest: No conflict interest
CLINICAL CHARACTERISTICS AND OUTCOMES OF CHILDREN HOSPITALIZED WITH RESPIRATORY SYNCYTIAL VIRUS, HUMAN METAPNEUMOVIRUS, OR BOTH IN AMMAN, JORDAN

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Presenting author: Ahmad Khader

Background: Respiratory Syncytial Virus (RSV) and human metapneumovirus (hMPV), both belonging to the Pneumoviridae family, cause acute respiratory infections with similar presentations. This study compares clinical characteristics and outcomes in hospitalized children with RSV, hMPV, or both.

Methods: Data from four viral surveillance studies conducted at Al-Bashir Hospital in 2007, 2010–2013, 2020, and 2023 were analyzed. Hospitalized children <2 years old with research detection of RSV, hMPV, or both were included in this analysis. Clinical and demographic data were obtained from parent/guardian interviews and chart abstractions. Nasal or throat swabs were collected and tested for RSV and hMPV by RT-qPCR.

Results: Of the 1,529 children included, RSV was detected in 83.9%, hMPV in 13.3%, and RSV/hMPV in 2.8%. Children with hMPV-only detection were older and more likely to be born prematurely, have underlying conditions, and present with fever than those with RSV-only detection. They were also less likely to present with congestion or runny nose and require supplemental oxygen or intensive care (Table 1). Children with RSV/hMPV co-detection were less likely to present with cough or congestion or runny nose but more likely to require intensive care than those with RSV. After 2020, the seasonal patterns of RSV and hMPV were disrupted during the period of January-March 2023 in contrast to prior seasons (Figure 1).

Conclusion: Despite the genetic similarities between RSV and hMPV, we observed significant differences in clinical characteristics and outcomes. Additional studies with larger sample sizes are needed to assess the clinical features of RSV/hMPV co-detection.

Abstract category: Clinical Studies

Keywords: Respiratory Syncytial Virus Infections, Metapneumovirus, Jordan

Conflict of Interest: Data collected during 2023 are from an ongoing study supported by the Merck Investigator Studies Program.


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Presenting author: Tala Khraise

Background: Smoking rates and involuntary secondhand smoke (SHS) exposure in Jordan are among the highest in the world. SHS leads to heightened risk and severity of respiratory illnesses, notably among children hospitalized with bronchiolitis. We explored the evolving trends of smoking exposure among RSV-hospitalized children in Amman, Jordan.

Methods: We analyzed data from four prospective viral surveillance studies conducted in 2007, 2010–2013, 2020, and 2023 at Amman’s largest public hospital. Our study population included children <2 years old who presented with fever and/or respiratory symptoms, tested positive for RSV via RT-qPCR, and had available smoking exposure history. Demographic data were obtained through parental interviews.

Results: Of the 2,233 children included, 1,679 (75.1%) were exposed to SHS. The median age was 3.3 months (IQR, 1.6–6.9). Across the study years, most children experienced some form of smoke exposure, with proportions fluctuating between 66.0% (2007) and 79.6% (2020), and a minimum proportion of 68.2% in 2023 (Figure 1). Cigarette smoke was the predominant source of exposure, whereas exposure to waterpipe smoke was less frequent. The proportion of vape smoke exposure rose sharply from 0.5% in 2020 to 11.5% in 2023. Maternal smoking during pregnancy increased until 2020, declining in 2023 (Table 1 – next page).
Conclusion: Smoking exposure remains high among RSV-hospitalized children in Jordan. These findings highlight the importance of continued research into the incidence and effects of SHS in RSV-infected children, which will inform understanding of disease risk and severity, and guide interventions to reduce this modifiable risk factor for pediatric respiratory infections.

Abstract category: Clinical Studies

Keywords: Respiratory Syncytial Virus Infections; Smoking; Jordan

Conflict of Interest: Data collected during 2023 are from an ongoing study supported by the Merck Investigator Studies Program.

SEVERE RSV INFECTION AMONG CHILDREN YOUNGER THAN 2 YEARS REQUIRING INTENSIVE CARE: A PROSPECTIVE OBSERVATIONAL STUDY IN 10 GAVI-ELIGIBLE COUNTRIES

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Presenting author: Yvette Löwensteyn

Background: Lack of country-level RSV disease burden data may limit demand for RSV interventions in low- and middle-income countries (LMICs) who rely on support from Gavi, the Vaccine Alliance. We conducted the RSV GOLD III – ICU Network study to collect country-specific clinical and demographic data from paediatric patients with life-threatening RSV infection from 10 Gavi-eligible countries.

Methods: Children <2 years admitted to the paediatric intensive care unit (PICU) with respiratory symptoms fulfilling the World Health Organization (WHO) "extended severe acute respiratory infection (eSARI)" case definition were tested for RSV using molecular point-of-care diagnostics during 2 predefined respiratory seasons.

Results: Between April 2021 – September 2023, a total of 2118 children with eSARI have been tested in 10 Gavi-eligible countries (Bolivia, Cameroon, The Gambia, Ghana, Haiti, Mozambique, Nepal, Nigeria, Sudan, Tanzania). RSV-positivity (N=614) was 29% (range 23-38.2%). Median age at testing was 3 months and 415 (68.3%) children were younger than 6 months. Eighty (13.4%) children were born prematurely and 99 (16.3%) had one or more comorbidities. RSV-mortality was 4.9% (range O-26.9%).

Conclusion: Smoking exposure remains high among RSV-hospitalized children in Gavi-eligible countries. As PICU access is lacking for most children from these countries, RSV interventions are urgently needed. Based on the median age of 3 months, extended half-life monoclonal antibodies and maternal vaccination will have high impact on infant survival in Gavi-eligible countries.

Abstract category: Clinical Studies

Keywords: Respiratory Syncytial Virus; Gavi; PICU; Mortality; Disease Burden; Global Health

Conflict of Interest: Funded by the Bill & Melinda Gates Foundation.

SEVERE RESPIRATORY SYNCYTIAL INFECTION IN CHILDREN LESS THAN TWO YEARS ADMITTED TO THE HIGH-DEPENDENCY UNIT IN THE GAMBIA

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Presenting author: Lamin Makalo

Background: Patient-level clinical data on instances of life-threatening RSV infection in LMICs are required to raise country-level awareness about RSV burden of disease. We describe clinical, demographic, and socioeconomic characteristics of children younger than 2 years admitted with life-threatening RSV infection to the high-dependency unit (HDU) of Edward Francis Small Teaching Hospital.

Methods: As part of the RSV GOLD-III network study, prospective observational study was conducted at the HDU during local respiratory seasons for 2 years between October to May 2021 to 2023. Children younger than 2 years of age with respiratory symptoms fulfilling the World Health Organization (WHO) "extended severe acute respiratory infection (eSARI)" case definition were tested for RSV using a molecular point-of-care diagnostic device. Patient characteristics were collected through a questionnaire.

Result: A total of 106 patients were included in the study. Of these, 27 (25.5%) were RSV-positive. The median (IQR) age was 8.0 months (IQR 2.0 – 12.0) and there were more boys (16; 59.3%). There were 3 (11.1%) patients with at least 1 comorbidity and 1 (3.7%) patient was born preterm. Median length of admission was 3.0 days (IQR 2-5). None of the patients died. Twenty-six (96.3%) of the mothers had been vaccinated against tetanus during pregnancy.

Conclusion: Respiratory Syncytial Virus is associated with one quarter of respiratory admissions in young children in The Gambia. The RSV-positivity rate was highest (70%) between October-December. The majority of the patients were born healthy term. Our data contribute to country-level awareness of RSV disease burden.

Abstract category: Clinical Studies

Keywords: Comorbidity; Demographic; Extended severe acute respiratory infection (eSARI); High Dependence Unit; Life-threatening; Socioeconomic; The Gambia

Conflict of Interest: None declared

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Presenting author: Michael Melgar

Respiratory syncytial virus (RSV) is a major cause of hospitalizations in children, older adults, and adults with chronic conditions. Infrequent RSV testing in certain age groups makes surveillance challenging. RSV testing practices may have changed during the COVID-19 pandemic.

RSV-Net, an active surveillance system, relies on clinician-driven testing to detect laboratory-confirmed RSV-associated hospitalizations in 12 U.S. states. RSV-Net also collects RSV testing data from a convenience sample of hospitalizations with acute respiratory illness (ARI) diagnosis codes; these data are used to adjust per-population RSV-associated hospitalization rates for under-ascertainment. We analyzed RSV testing data among 10,889 sampled ARI hospitalizations from two states, Tennessee and Connecticut, comparing percentage tested for RSV during three pre-COVID-19 seasons (2017–2020) and the 2022–2023 season. Statistical significance in differences was assessed using the chi-squared test (p<0.05).

RSV testing practices changed over the two periods with differences by age and site. In Tennessee, the percentage of hospitalized adults (≥18 years) tested for RSV decreased in 2022–2023 compared with pre-COVID-19 but did not change significantly among hospitalized children (<18 years) (Figure 1). In Connecticut, the percentage of hospitalized children tested for RSV increased in 2022–2023 but did not change significantly among hospitalized adults (Figure 2). In 2022–2023, there were no significant differences in RSV testing by race and ethnicity within each age group (Figure 3).

RSV testing practices among hospitalized patients changed during the COVID-19 pandemic with geographic and age-based variation, likely impacting disease burden estimation and, among recorded hospitalizations, demographic characteristics and indicators of clinical severity.

Abstract category: Clinical Studies
Keywords: Testing Practices, Hospitalizations, COVID-19 Pandemic, Surveillance
Conflict of Interest: None declared
VACCINE EFFICACY AND VANING VALUES FROM THE ADJUVANTED RSV PREFUSION F PROTEIN-BASED VACCINE (AREXVY) CLINICAL TRIAL

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Presenting author: Daniel Molnar

BACKGROUND: The adjuvanted respiratory syncytial virus preFusion F protein-based vaccine (RSVPref3 OA) demonstrated efficacy in preventing RSV-related lower respiratory tract disease (RSV-LRTD) among individuals aged ≥60 years across two complete RSV seasons. Data from the AReSVi-006 phase 3 pivotal efficacy trial, until end of season 2 of the Northern Hemisphere, are displayed in Table 1. Vaccine efficacy and waning values were estimated from the trial data and used to project values beyond the trial follow-up period.

METHODS: Monthly RSV-related acute respiratory illnesses (RSV-ARI) and RSV-LRTD incidence data from both the placebo and the RSVPref3 OA arms of the AReSVi-006 trial were aggregated by vaccine group ensuring robust estimates (i.e., ≥8 cases observed in the placebo arm). Weighted linear regression model was fitted on the efficacy data points to estimate the intercept (peak efficacy) and slope (monthly waning rate). To estimate uncertainty around the regression coefficients, a bootstrap procedure with 1,000 bootstrap samples was performed.

RESULTS: Peak efficacy was 88.0% for RSV-LRTD and 74.2% for RSV-ARI (Figure 1). Efficacy waned monthly by 2.1% for RSV-LRTD and by 2.3% for RSV-ARI.

CONCLUSION: Our model suggests that one dose of RSVPref3 OA vaccine could provide protection for older adults against RSV-LRTD and RSV-ARI over three RSV seasons. The analysis should be updated as new clinical data becomes available.

FUNDING: GlaxoSmithKline Biologicals SA (VEO-000319)

Abstract category: Clinical Studies

Keywords: RSV, Vaccine Efficacy, Pref3, Older Adults, Arexvy, Clinical Trial

Conflict of Interest: Desmond Curran, Marie-Pierre David, Daniel Molnar, Aurélie Olivier and Frederik Verelst are employed by and hold shares in GSK. Marie-Pierre David is co-applicant on a pending patent filed by GSK. The authors declare no other financial and non-financial relationships and activities.

SEX DIFFERENCES IN OUTCOMES OF CHILDREN

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Presenting author: Quasai Odeh

Background: Respiratory syncytial virus (RSV) is a leading cause of hospitalization in young children, with male predominance in frequency. However, potential sex differences in RSV outcomes within this age group are not well-understood. This study aimed to compare the outcomes of RSV infection between male and female children <2 years old admitted to Al-Bashir Hospital in Amman, Jordan.

Methods: Data from four prospective viral surveillance studies, conducted in 2007, 2010–2013, 2020, and 2023, were analyzed. Hospitalized children <2 years old presenting with fever or respiratory symptoms and who were RSV-positive by RT-qPCR were included. Outcomes assessed were supplemental oxygen use and intensive care unit (ICU) admission. Logistic regression models were fit for both outcomes, adjusting for age, underlying medical conditions, prematurity, and viral co-detection.

Results: The study cohort consisted of 2,233 RSV-positive children, including 1,300 males (58.2%) and 933 females (41.8%). The median age was 3.3 months (IQR, 1.6–6.9), with females being younger on average (Table 1; p=0.025). A higher observed proportion of females required supplemental oxygen (46.5% vs. 43.3%) and ICU admission (10.1% vs. 7.5%; Table 1). However, after adjusting for potential confounders, there was insufficient evidence of sex differences in either outcome (p=0.32 for supplemental oxygen use and p=0.13 for ICU admission).

Conclusion: Despite more males presenting with RSV than females, we did not identify significant sex differences in measured outcomes of illness severity among young RSV-positive children with similar risk factor profiles. Further investigations are warranted to explore sex-based disparities in the incidence of RSV in more diverse cohorts.

Abstract category: Clinical Studies

Keywords: Respiratory Syncytial Virus Infections; Sex Differences; Jordan

Conflict of Interest: Data collected during 2023 are from an ongoing study supported by the Merck Investigator Studies Program.

Table 1. Clinical characteristics and outcomes of children <2 years old hospitalized at Al-Bashir Hospital (2007, 2010–2013, 2020, and 2023) with respiratory syncytial virus, stratified by sex assigned at birth (n=2,233)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Female, n=933</th>
<th>Male, n=1,300</th>
<th>p-valuea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at admission (months)</td>
<td>2.9 (1.4–6.5)</td>
<td>3.1 (1.7–7.9)</td>
<td>0.025</td>
</tr>
<tr>
<td>Born premature (%)</td>
<td>123 (13.6)</td>
<td>155 (11.9)</td>
<td>0.31</td>
</tr>
<tr>
<td>History of severe illness (%)</td>
<td>716 (75.7)</td>
<td>963 (74.1)</td>
<td>0.15</td>
</tr>
<tr>
<td>Family history of asthma (%)</td>
<td>216/751 (29.0)</td>
<td>293/973 (27.0)</td>
<td>0.42</td>
</tr>
<tr>
<td>Ever breastfeeding (%)</td>
<td>605 (66.3)</td>
<td>1,126 (88.4)</td>
<td>0.74</td>
</tr>
<tr>
<td>Birth weight (kg)</td>
<td>2.5 (1.7–3.9)</td>
<td>2.7 (2.2–4.3)</td>
<td>0.29</td>
</tr>
<tr>
<td>At least one co-morbid condition (%)</td>
<td>61 (8.7)</td>
<td>132 (10.2)</td>
<td>0.24</td>
</tr>
<tr>
<td>Viral co-detection (%)</td>
<td>360 (41.3)</td>
<td>569 (43.1)</td>
<td>0.55</td>
</tr>
<tr>
<td>Supplemental oxygen use (%)</td>
<td>432/1,000 (43.2)</td>
<td>555/1,973 (53.2)</td>
<td>0.34</td>
</tr>
<tr>
<td>ICU admission (%)</td>
<td>0/4/930 (0.1%)</td>
<td>70/1,280 (5.1%)</td>
<td>0.034</td>
</tr>
</tbody>
</table>

Abbreviations: ICU, Intensive care unit

|x-values were calculated using Pearson’s x2 test for categorical variables and the independent-samples t-test for continuous variables. The testing panel included respiratory syncytial virus (all years), influenza (all years), human metapneumovirus (all years), human rhinovirus/enterovirus (all years), and parainfluenza viruses 1–4 (all years except 2007), adenovirus (all years except 2007), common cold coronaviruses (all years except 2017), and SAR-CoV-2 (2020 and 2023).
BACTERIAL CO-DETECTION IN ADULTS WITH RESPIRATORY SYNCYTIAL VIRUS

Yasmeen Z. Qwaider (1), Justin Z. Amarin (1), Haya Hayek (1), Tess Stopczynski (1), Olla Hamdan (1), James D. Chappell (1), Andrew J. Spieker (1), Jesse O. Wrenn (1), Natasha B. Halasa (1)

1. Vanderbilt University Medical Center, Nashville, TN.

Presenting author: Yasmeen Qwaider

Introduction: Respiratory syncytial virus (RSV) is an important cause of respiratory morbidity and mortality in adults. Data on bacterial co-detection in adults with RSV are scarce. We aimed to examine the frequency of bacterial co-detection in this demographic.

Methods: We included all adults (≥18 years old) who tested positive for RSV at Vanderbilt University Medical Center (1/2018 – 6/2023) via respiratory pathogen panel testing (RPP), a provider-ordered multiplex PCR assay for common respiratory pathogens. Any patient who had a positive respiratory, urine, blood, or cerebrospinal fluid (CSF) culture up to 72 hours post-presentation was considered to have bacterial co-detection. Any adult who presented >14 days following a previous presentation was considered a distinct case.

Results: Of the 29,589 adults with RPP testing performed, 411 (1.4%) were RSV-positive. Table 1 includes demographics, clinical characteristics, and outcomes. Of those, 255 (62.0%) had at least one culture performed and 47 (18.4%) had at least one positive result Table 2). Respiratory cultures were most frequently positive (20/112 [17.9%]), followed by urinary (13/74 [17.6%]), blood (17/205 [8.3%]), and CSF (0/2 [0.0%]). The most commonly detected bacteria were Pseudomonas aeruginosa in the respiratory tract (n=9), Escherichia coli in urine (n=8), and Staphylococcus epidermidis in blood (n=4). Approximately 2/3 of adults with RSV were given an antibiotic.

Conclusion: Our data suggest that bacterial co-detection in adults with RSV should be considered in the differential diagnosis of clinical presentation. However, antibiotics might be over-prescribed in the management of RSV-associated illness, warranting further research to promote their appropriate use in the setting of RSV detection.

LATIN AMERICAN VALIDATION OF THE INTERNATIONAL RISK SCORING TOOL FOR IDENTIFYING MODERATE-TO-LATE PRETERM INFANTS AT GREATEST RISK OF SEVERE RESPIRATORY SYNCYTIAL VIRUS INFECTION

Carlos E. Rodriguez-Martinez (1), Bosco Paes (2), Xavier Carbonell-Estrany (3), Barry Rodgers-Gray (4), John Fullarton (4), Ian Keary (4), Paulo Andre Ribeiro (5,6)

1. Universidad Nacional de Colombia, Bogota, Colombia
2. McMaster University, Hamilton, Ontario, Canada
3. Hospital Clinic, Barcelona, Spain
4. Violicom Medical Limited, Aldermaston, United Kingdom
5. Centro Hospitalar Unimed - Unimed Joinville, Brazil
6. Hospital Infantil Dr Jeser Amarante Farias, Joinville, Brazil

Presenting author: Barry Rodgers-Gray

Objective: To support adoption of the International Risk Scoring Tool (IRST) in Latin America (LATAM) it was validated against data from Colombia and Brazil.

Methods: Data covering the IRST risk factors (birth 3 months before to two months after the respiratory syncytial virus (RSV) season start date; smoking in the household and/or maternal smoking; siblings and/or daycare) together with two others considered important in LATAM; breast feeding and maternal education to primary level, were collected from two hospitals in Colombia and three hospitals in Brazil. Premature infants born 32-35 weeks’ gestational age (wGA) without...
comorbidities (e.g. bronchopulmonary dysplasia/congenital heart disease) who had RSV hospitalisation (RSVH) at ≤6 months old (cases) were matched with gestationally and chronologically age-matched controls without RSVH. Predictive accuracy was assessed by calculating the area under the receiver operating characteristic curve (AUROC).

**Results:** Using the Colombian data, the IRST risk factors (substituting chronological age for wGA as RSV endemic) plus mixed breast feeding and maternal education to primary level produced an AUROC of 0.823 (Table). For Brazil, utilising siblings and daycare attendance as individual variables and adding exclusive breast feeding to the other IRST risk factors resulted in an AUROC of 0.737.

**Conclusions:** The IRST appears predictive of RSVH in LATAM countries and (mixed) breast feeding and maternal education to primary level are worthwhile country-specific additions. Where RSV is endemic, wGA appears a suitable substitute for chronological age. The IRST provides a mechanism to target prophylaxis to LATAM infants born 32–35wGA who are most likely to benefit.

**Abstract category:** Clinical Studies

**Keywords:** Risk factors, risk scoring tools, prophylaxis, moderate-to-late preterm infants

**Conflict of Interest:** BRG, IK and JF employers have received payment from AstraZeneca for work on various projects. XCE, BP, CERM and PAR have received research funding and/or compensation as advisor/lecturer from AstraZeneca and/or Sanofi and/or Pfizer outside the scope of this study. Financial support for this study was provided by AstraZeneca. All authors contributed to the development of the publication and maintained control over the final content.

**DIFFERENCES IN CLINICAL CHARACTERISTICS AND OUTCOMES AMONG CHILDREN <2 YEARS OLD WITH RESPIRATORY ILLNESS ADMITTED TO AL-BASHIR HOSPITAL: IMPACT OF PREHOSPITALIZATION ANTIBIOTICS**

Rami Salim (1), Haya Hayek (1), Justin Z. Amarin (1), Olla Hamdan (1), Yasmeen Z. Qwaider (1), Ahmad Khader (1), Qusai Odeh (1), Tala Khraise (1), Ahmad Alhajajra (2), Basim Al-Zoubi (2), Leigh M. Howard (1), Andrew J. Spieker (1), James D. Chappell (1), Najwa Khuri-Bulos (3), Natasha B. Halasa (1)

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2. Al-Bashir Hospital, Amman, Jordan
3. The University of Jordan, Amman, Jordan

**Presenting author:** Rami Salim

**Background:** Acute respiratory infections (ARIs) in young children represent a substantial healthcare burden. Antibiotics are commonly prescribed or used over the counter for ARIs, especially in Jordan. Yet, their impact on illness course is poorly understood. We aimed to compare the clinical characteristics and outcomes of hospitalized children who did or did not receive prehospitalization antibiotics.

**Methods:** We analyzed data from four prospective viral surveillance studies conducted at Al-Bashir Hospital (Amman, Jordan) in 2007, 2010-2013, 2020, and 2023. We included children <2 years old, hospitalized with fever and/or respiratory symptoms, who had nasal and/or throat swabs research tested for respiratory viruses using RT-qPCR, and had available antibiotic history. Antibiotic usage and clinical data were collected through parental/legal guardian interviews and chart reviews.

**Results:** Of 4,106 children included, 1,658 (40.3%) received antibiotics for the presenting illness prior to hospitalization. Children who received prehospitalization antibiotics were older and more likely to have an underlying medical condition; present with cough, fever, shortness of breath, and wheezing; and test positive for at least one respiratory virus, particularly RSV. However, they were less likely to be born prematurely, receive supplemental oxygen, or be admitted to the intensive care unit. Fewer cultures were obtained on children who received antibiotics, and a smaller proportion of those cultures yielded positive results (Table).

**Conclusion:** Children who received antibiotics prior to hospitalization exhibited distinct demographic and clinical characteristics, potentially indicating selective use of antibiotics. Additional research is required to define factors influencing outpatient antibiotic use and its impact on recovery in children with ARIs.

**Abstract category:** Clinical Studies

**Keywords:** Jordan, Acute Respiratory Infections, Pediatrics, Anti-Bacterial Agents

**Conflict of Interest:** Data collected during 2023 are from an ongoing study supported by the Merck Investigator Studies Program.

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**Table: Risk factors and predictive accuracy of RST and LATAM validations**

<table>
<thead>
<tr>
<th>IRST</th>
<th>RSVH (&lt;1y)</th>
<th>Control (&lt;1y)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colombia (cases: n=81) controls: n=68</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brazil (cases: n=49) controls: n=48</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Risk Factors (a)</strong></td>
<td><strong>3</strong></td>
<td><strong>5</strong></td>
</tr>
<tr>
<td>1. Birth between 3 months before and 2 months after RSV season start date</td>
<td>1. Gestational age</td>
<td></td>
</tr>
<tr>
<td>2. Smokers in the household and/or maternal smoking</td>
<td>2. Smokers in the household and/or maternal smoking</td>
<td></td>
</tr>
<tr>
<td>3. Siblings and/or daycare attendance</td>
<td>4. Mixed breast feeding</td>
<td></td>
</tr>
<tr>
<td>4. Maternal education to primary level</td>
<td>5. Siblings and/or daycare attendance</td>
<td></td>
</tr>
<tr>
<td>5. Breast feeding</td>
<td>5. Siblings and/or daycare attendance</td>
<td></td>
</tr>
</tbody>
</table>

**Predictive accuracy (AUROC)**

- **Colombia:** 0.773
- **Brazil:** 0.823

**Table: Clinical characteristics and outcomes of children <2 years old hospitalized at Al-Bashir Hospital (2007-2010, 2013-2020, 2023), stratified by prehospitalization receipt of antibiotic (n=1,406)**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. n=1,406</th>
<th>Yes. n=668</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at admission (months)-median (IQR)</td>
<td>2.1 (1.9)</td>
<td>2.3 (2.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male (%)</td>
<td>509/1,406</td>
<td>294/668</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prematurely born (%)</td>
<td>388/1,406</td>
<td>188/668</td>
<td>0.017</td>
</tr>
<tr>
<td>At least one co-morbid condition (%)</td>
<td>397/1,406</td>
<td>206/668</td>
<td>0.15</td>
</tr>
<tr>
<td>Congestion or rainy nose (%)</td>
<td>408/1,406</td>
<td>214/668</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Wheezing (%)</td>
<td>360/1,406</td>
<td>196/668</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Admitted to the intensive care unit (%)</td>
<td>357/1,406</td>
<td>175/668</td>
<td>0.034</td>
</tr>
<tr>
<td>Culture obtained (%)</td>
<td>190/1,406</td>
<td>131/668</td>
<td>&lt;0.13</td>
</tr>
<tr>
<td>Culture positive (%)</td>
<td>1,406/1,406</td>
<td>668/668</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>SARS-CoV-2</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>1,451/1,406</strong></td>
<td>701/668</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

**p-values were calculated using Pearson’s χ² test for categorical variables and the independent samples t-test with unequal variances for continuous variables.**

**Abbreviations:** ICU, intensive care unit; RSV, respiratory syncytial virus; H1RV/E, human rhinovirus/enterovirus; IMPV, human metapneumovirus; PIU, influenza; PIV, parainfluenza virus; cCoV, common cold coronaviruses; AdV, adenovirus; SARS-COV-2, severe acute respiratory syndrome coronavirus 2.
RSV BURDEN IN INDIA

Ashish Satav (1), Vibhawari Dani (1), Rowena Crow (1), Varsha Potdar (3), Shilpa Satav(1), Manddeep Chadha (3), Sameer Palaskar (1), Danielle Hessong(2), Phyllis Carosone-Link (2), Eric A. F. Simões, MB BS DCH MD. (2)

1. MAHAN trust, Mahatma Gandhi Tribal Hospital, Karmagram, Utavali, Tamhini, Amaravati, India.
2. Department of Pediatric Infectious Diseases, University of Colorado School of Medicine and Children’s Hospital Colorado Aurora, CO; USA
3. National Institute of Virology, Indian Counsel of Medical Research, Pune, India.

Presenting author: Ashish Satav

Background: Globally, respiratory syncytial virus (RSV) is an important cause of acute lower tract infection (LRTI) and deaths in children < 2 years age, but studies in rural communities are rare.

Methods: Active surveillance of LRTI was performed in the community and hospital setting for the population of 93 tribal villages in Melghat, Central India, over 4 respiratory seasons. A nasopharyngeal swab was obtained from severe LRTI cases for molecular analysis of respiratory viruses.

Results: In the 12134 subjects, there were 2064 episodes of severe LRTIs and 1732 of very severe LRTIs, of which 271 and 195, respectively, had RSV. Out of 16 RSV deaths, 94% children died of LRTIs, 14 in community and 1 in hospital. Community severe RSV LRTI rates for 0–6 months of age was 15.9 (11.8–21.4)/1000 child-years (CY) and the hospital-associated rate was 12.9 (9.3–18.0)/1000 CY. The case fatality ratios for severe RSV LRTIs in the first 6 months of life were 7.1% and 2.8% in the community and hospital, respectively. Of those with very severe LRTIs in the community, 17.6% died and no hospital deaths. The adjusted RSV LRTI mortality rates in infants ranged from 1.0 to 3.0/1000 CY, accounting for 20% of the LRTI deaths and 10% of the post-neonatal infant mortality.

Conclusions: Hospital studies significantly underestimate the burden of RSV LRTI and deaths. Community deaths from RSV account for the majority of RSV LRTI deaths, and efforts at prevention should be preferentially directed at difficult to access populations.

Abstract category: Clinical Studies

Keywords: RSV, Mortality, Morbidity, Community, Rural.

Conflict of Interest:

ECONOMIC BURDEN OF INFANT RSV INFECTION IN NEPAL

Arun K Sharma(1,3), Rupesh Shrestha(1,3), Ram H Chapagain(2,3), Prakash Joshi(2,3), Uttam Poudel(3), Krishna P Bista(3), Farina Shaaban(4), Neele Rave(4), An Nguyen(5), Clint Pecenka(6), Louis Bont(4,7)

1. Tribhuvan University, Institute of Medicine, Tribhuvan University Teaching Hospital, Kathmandu, Nepal
2. Kanti Children’s Hospital, Kathmandu, Nepal
3. Nepal Paediatric Society, Kathmandu, Nepal
4. Wilhelmmina Children’s Hospital, LMC Utrecht, the Netherlands
5. PATH, Hanoi, Vietnam
6. Center for Vaccine Innovation and Access, PATH, Seattle, WA, United States
7. Respiratory Syncytial Virus Network (ReSViNET) Foundation, Zeist, the Netherlands

Presenting author: Arun K Sharma

Background: Low- and lower-middle-income countries (LMICs) bear the greatest burden of global RSV morbidity and mortality. Cost data from LMICs are needed to evaluate the financial impact of the RSV burden on families, the healthcare system and society as a whole. This study estimates the cost associated with RSV illness.

Methods: We collected resource utilization data from children under 2 years of age who fulfilled the WHO (S)ARI case definition and were evaluated at the emergency room/outpatient department or were admitted to the general ward or intensive care. Direct medical, direct non-medical and indirect cost data were gathered from hospital records and caregiver interviews. A bottom-up data collection approach was employed to generate total per-patient costs. Costs in RSV positive children were compared with all-cause acute respiratory infections and stratified by location of care received. Data was collected during the local RSV season from July - November 2023.

Preliminary Results: A preliminary analysis of cost of illness of 75 RSV positive children admitted to hospital revealed that families incurred a median total cost of US$145 (IQR: 35-297) over the course of 4 weeks. Indirect costs contributed 73.7% [US$ 107 (IQR: 30.9-298.5)] of that cost. Further data analysis is ongoing.

Conclusion: This study represents cost estimates of economic burden of RSV care for the Nepali society. Preliminary data suggest a significant cost burden of RSV illness. Cost burden evidence will be critical for cost effectiveness analysis to inform policy decisions for future RSV interventions in Nepal.

Abstract category: Clinical Studies

Keywords: Cost of Illness, RSV, LMIC, Nepal

Conflict of Interest: None declared

PREVALENCE OF RSV DISEASE AMONG CHILDREN UNDER TWO WITH SEVERE ACUTE RESPIRATORY ILLNESS REQUIRING INTENSIVE CARE IN TWO TERTIARY PEDIATRIC HOSPITALS IN NEPAL

Rupesh Shrestha (1), Arun Kumar Sharma (1), Ram Hari Chapagain (2), Prakash Joshi (2), Krishna Prasad Bista (3), Prabina Shrestha (1)

1. Tribhuvan University Teaching Hospital, Kathmandu, Nepal
2. Kanti Children Hospital, Kathmandu, Nepal
3. Nepal Paediatric Society, Kathmandu, Nepal

Presenting author: Rupesh Shrestha

Background: Respiratory Syncytial Virus (RSV) is a major cause of acute lower respiratory infection in young children requiring hospital admission worldwide. While the burden of RSV-associated morbidity and mortality is already high especially in low- and lower-middle-income countries, it is likely to increase as vaccines...
against bacterial pneumonia become more accessible. Currently, individual patient level data to identify the target population for RSV intervention is lacking due to unavailability of RSV testing facilities.

Methods: in this prospective observational study conducted in High Dependency Units (HDUs) and Pediatric Intensive Care Units (PICUs) of two Pediatric Hospitals in Nepal, clinical data of severely ill children with RSV infection were collected during two RSV seasons. This study was a part of a larger, multi-center, the RSV GOLD III – ICU Network study, participating 10 LMICs. All children <2 years of age admitted to HDUs and PICUs fulfilling SARI case definition of World Health Organization were tested for RSV using point-of-care molecular diagnostic test.

Results: Between July 2021 – February 2023, out of 1556 eligible children, 1328 (85.3%) were tested. Of these, 390 (29.4%) were RSV positive. Median age at testing was 3 months. The peak incidence of RSV positive cases occurred during September–October. Most RSV-positive cases occurred in the 0–6-month age group constituting about two third of total positive cases. Overall case fatality ratio was 3%.

Conclusion: These results underscore the significant impact of RSV on young children with severe respiratory illness requiring intensive care in Nepal. This study provides important data that can aid in the development and implementation of effective prevention and treatment strategies to mitigate the burden of RSV.

Abstract category: Clinical Studies

Keywords: Respiratory syncytial virus, Severe acute respiratory illness, Children under two

Conflict of Interest: None declared

A PHASE 1B/2A SINGLE ASCENDING DOSE STUDY TO EVALUATE THE SAFETY, TOLERABILITY, AND PHARMACOKINETICS OF AN RSV-NEUTRALIZING ANTIBODY, CLESROVIMAB, IN PRETERM AND FULL-TERM INFANTS

Shabir A. Madhi MB BCH, FCPaedS, PhD (1), Eric A.F. Simões, MD (2), Armando Acevedo, MD (3), Jose M. Novoa Pizarro, MD (4), Julie S. Shepard, MD, MPH (5), Radha A. Raiikar, PhD (6), Xin Cao, PhD (6), Brian M. Maas, PharmD (6), Xiaowei Zang, PhD (6), Andrea Krick, PhD (6), Brad Roadcap, MS (6), Kalpita A. Vora, PhD (6), Antonios O. Aliprantis, MD, PhD (6), Andrew W. Lee, MD, MD (6), Anushua Sinha, MD, MPH (6)

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2. Children’s Hospital Colorado, University of Colorado School of Medicine, Aurora, Colorado, USA; and Colorado School of Public Health, Aurora, Colorado, USA
3. Acevedo Clinical Research Associates, Miami, Florida, USA
4. Hospital Padre Hurtado, Faculty of Medicine. Universidad del Desarrollo Santiago, Chile
5. Ohio Pediatric Research Association, Dayton, OH, USA
6. Merck & Co., Inc., Rahway, NJ, USA

Presenting author: Anushua Sinha

Background: Clesrovimab is an investigational RSV-neutralizing monoclonal antibody for the prevention of RSV lower respiratory tract infection in infants.

Methods: This phase 1b/2a, double-blind, randomized, placebo-controlled study enrolled healthy preterm and full-term infants 2 weeks to 8 months of age. Participants were randomized 4:1 within 5 panels (pre-term: 20, 50, 75 or 100 mg, full-term: 100 mg) to receive 1 dose of clesrovimab or placebo. Safety was evaluated by the proportion of participants with adverse events (AEs). Pharmacokinetics, serum neutralizing antibodies, and anti-drug antibodies were analyzed through 1 year. RSV-associated endpoints, as determined by RT-PCR and the presence of symptoms, were evaluated through Day 150 postdose.

Results: Overall, 183 participants were randomized; 181 received treatment. The proportions of participants with solicited injection-site adverse events (AEs), solicited systemic AEs, and serious AEs were generally comparable across all clesrovimab groups and placebo (Table 1). Clesrovimab serum concentrations increased proportionally with dose and displayed a geometric mean apparent half-life of 44.9 days. Of the participants receiving clesrovimab, 13.1% and 22.8% were positive for ADA concentrations increased proportionally with dose and displayed a geometric mean apparent half-life of 44.9 days. Of the participants receiving clesrovimab, 13.1% and 22.8%, were positive for ADA

Conclusion: Single doses of clesrovimab were generally well tolerated in infants, the antibody displayed an extended half-life, and the incidence of RSV-associated disease endpoints were lower in clesrovimab group compared to placebo.

Abstract category: Clinical Studies

Keywords: clesrovimab, monoclonal antibody

Conflict of Interest: S. A. Madhi received funding from Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA (MSD); grants from BMGF, GSK, Pfizer, Minervax, Novavax, Providence, Gritstone, and ImmunityBio; honoraria from GSK; and participated on the Merck Data Safety Monitoring Board (DSMB) for PATH and CAPRISA. E. A. F. Simões received funding from MSD: grants from Astra Zeneca, MSD, Pfizer, Roche, and Johnson & Johnson; consulting fees from MSD, Pfizer, Sanofi Pasteur, Cidera, Adiagio, Nuance, Icosavax, Johnson & Johnson and Sobi; honoraria from Pfizer and Astra Zeneca; meeting support from Astra Zeneca; and participated on DSMB or Advisory Board for Abbvie, GSK, and Bill & Melinda Gates Foundation. A. Acevedo has no potential conflicts of interest to report. J. M. Novoa Pizarro and J. S. Shepard were principal investigators for the study. R. A. Raiikar, X. Cao, B. M. Maas, X. Zang, A. Krick, B. Roadcap, K. A. Vora, A. O. Aliprantis, A. W. Lee, A. Sinha are employees of Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA and may hold stock or stock options in Merck & Co., Inc., Rahway, NJ, USA. K. A. Vora also holds a patent for R6B1 antibody, the parent of Clesrovimab, with Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

Table 1. Safety Summary by Treated Population

<table>
<thead>
<tr>
<th>Dose Group</th>
<th>Participants</th>
<th>Positive for ADA</th>
<th>Safety Events</th>
<th>Cardiovascular</th>
<th>Gastrointestinal</th>
<th>Neuropsychiatric</th>
<th>All-cause</th>
<th>Total AEs</th>
<th>Severe AEs</th>
<th>Life-threatening</th>
<th>75 mg</th>
<th>100 mg</th>
<th>Placebo</th>
<th>Total AEs</th>
<th>Severe AEs</th>
<th>Life-threatening</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 mg</td>
<td>29</td>
<td>5</td>
<td>8</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>13</td>
<td>11</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>10</td>
<td>1</td>
<td>0</td>
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<tr>
<td>50 mg</td>
<td>29</td>
<td>5</td>
<td>8</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>13</td>
<td>11</td>
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<td>1</td>
<td>2</td>
<td>10</td>
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</tr>
<tr>
<td>75 mg</td>
<td>29</td>
<td>5</td>
<td>8</td>
<td>2</td>
<td>0</td>
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<td>2</td>
<td>13</td>
<td>11</td>
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<td>2</td>
<td>1</td>
<td>2</td>
<td>10</td>
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<td>0</td>
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<tr>
<td>100 mg</td>
<td>29</td>
<td>5</td>
<td>8</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>13</td>
<td>11</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>10</td>
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</table>

Table 2. Efficacy by Day 150, IV Analysis Set

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<th>50 mg</th>
<th>75 mg</th>
<th>100 mg</th>
<th>Placebo</th>
<th>Total AEs</th>
<th>Severe AEs</th>
<th>Life-threatening</th>
<th>Total AEs</th>
<th>Severe AEs</th>
<th>Life-threatening</th>
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<td>10</td>
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</tbody>
</table>

All adverse events, 100% serious adverse events.

Conflict of Interest: None declared
RSV NEUTRALIZING ANTIBODIES IN DRIED BLOOD

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4. Vaccine Research Center, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD, United States of America
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Presenting author: Jonne Terstappen

Introduction: The key correlate of protection of respiratory syncytial virus (RSV) vaccines and monoclonal antibodies (mAb) is virus neutralization, measured using sera obtained through venipuncture. Dried blood obtained with a finger prick can simplify acquisition, processing, storage, and transport in trials, and thereby reduce costs. In this study we aim to validate a low-tech assay to measure RSV neutralization in dried capillary blood.

Methods: Recovery of mAb from dried blood (volumetric absorptive microsampling) was used to validate the elution method using indirect ELISA. Functional antibodies measured by a neutralization assay were compared between matched serum and dried blood samples from a phase I trial with RSM01, a novel investigational anti-RSV Prefusion F mAb. Hep-2 cells were infected with a serial dilution of sample-virus mixture using RSV-A2-mKate to determine half-maximal inhibitory concentration. Stability of dried blood was evaluated over time and during temperature stress.

Results: Functional antibodies in dried blood were highly correlated with serum (R2=0.98, p<0.0001). The intra-assay, inter-assay, and inter-operator precision of the assay for dried blood was similar to serum. Functional antibodies in dried blood remained stable for 6 months at room temperature and frozen samples showed no instability at 9 months. Dried blood samples resisted 48 hours of temperature stress.

Conclusion: We demonstrated the feasibility of measuring RSV neutralization using dried blood as an alternative to serum. Measuring antibody function using dried blood is a patient-centered solution that may replace serology testing in trials against RSV or other viruses, such as influenza and SARS-CoV-2.

Abstract category: Clinical Studies

Keywords: Respiratory Syncytial Virus, Vaccine, Neutralization, Dried Blood, Immunization, Antibodies, Serology, Clinical Trials

Conflict of Interest: UMCU has received major funding (>€100,000 per industrial partner) for investigator initiated studies from AbbVie, MedImmune, AstraZeneca, Sanofi, Janssen, Pfizer, MSD and MeMed Diagnostics, the Bill and Melinda Gates Foundation, Bill & Melinda Gates Medical Research Institute and the Dutch Lung Foundation. UMCU has received major funding as part of the public private partnership IMI-funded RESCEU and PROMISE projects with partners GSK, Novavax, Janssen, AstraZeneca, Pfizer and Sanofi. UMCU has received major funding by Julius Clinical for participating in clinical studies sponsored by MedImmune and Pfizer. UMCU received minor funding (€1,000-25,000 per industrial partner) for consultation and invited lectures by AbbVie, MedImmune, Abylna, Bavaria Nordic, MabXience, GSK, Novavax, Pfizer, Moderna, AstraZeneca, MSD, Sanofi, Janssen. LIB and NIM have regular interaction with pharmaceutical and other industrial partners. They have not received personal fees or other personal benefits. LJB is the founding chairman of the ReSViNET Foundation. JTW is an employee at the Bill & Melinda Gates Medical Research Institute. ADC and TR are supported by funding from intramural NIAID.

ALL-CAUSE HOSPITALIZATION AFTER POSITIVE RSV LABORATORY TEST IN THE OUTPATIENT SETTING IN CHILDREN UNDER 5 YEARS IN THE UNITED STATES

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1. Pfizer, Inc.
2. Truveta

Presenting author: Sima Toussi

Infants and children with high-risk conditions are at increased risk for severe RSV infection and hospitalization. Most patients are managed at home, yet data are sparse on the course of RSV infection in non-hospitalized populations. To address this gap, we examined the hospitalization risk associated with RSV infection in children initially managed in the outpatient setting.

In US-based Truveta electronic health record database, infection episodes among children (<5 years) with a positive RSV laboratory test in the outpatient setting were identified from October 2017 through September 2023. Episodes were excluded if hospitalized within 24 hours of positive test, and repeat infections were allowed if >28 days apart. Occurrence of all-cause hospitalization was assessed 28 days after test result, stratified by age and presence of comorbidity (prematurity, congenital heart disease [CHD], neuromuscular disorders [ND], and chronic lung disease [CLD]) captured using ICD-10-CM diagnostic codes.

From the six included health systems, 68,162 RSV infection episodes were identified in children. CLD was the most common comorbidity (11.6%), followed by prematurity (9.5%) and CHD (2.8%, Table 1). The risk of hospitalization decreased with advancing age (<6 months: 5.9%, 6-<24 months: 2.2%, 2-<5 years: 0.9%), and was higher when restricted to children with any comorbidity (Table 2). Infants with CHD, prematurity, CLD, or ND who were <6 months of age were most likely to be hospitalized.

A considerable portion of children with RSV diagnosed in the outpatient setting were ultimately hospitalized. Future work is needed to examine the risk of RSV-specific hospitalizations.

Abstract category: Clinical Studies

Conflict of Interest: This study was funded by Pfizer, Inc. D. Garofalo, S. Toussi, S. Landi, A. Banerjee, N. Alami, and S. Kelly are full-time employees and stock shareholders of Pfizer, Inc.
Prolonged Recovery Among Critically Ill Infants Hospitalized During the U.S. 2022 RSV Seasonal Peak—Application of the Modified Clinical Progression Scale for Pediatric Patients (CPS-Ped)

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Presenting author: Laura Zambrano

Background: The modified Clinical Progression Scale for Pediatric Patients (CPS-Ped) is used to assess respiratory disease severity based upon hospitalization status, degree of respiratory support received, and level of hypoxia (Figure 1A). We used CPS-Ped to describe the recovery of infants with respiratory syncytial virus (RSV) critical illness during the U.S. 2022 RSV seasonal peak, and to identify factors associated with prolonged recovery.

Methods: We established a prospective surveillance registry of 600 infants admitted for RSV in 39 pediatric intensive care units (PICUs) across 27 states from 10/17/2022–12/16/2022, and collected data on patient characteristics, laboratory values, clinical support, and outcomes. We assigned a CPS-Ped score on hospital days 1–7, 10, and 14, and defined recovery as having a score ≤2 by day 7. We used multivariable log-binomial models to calculate relative prevalence of day 7 nonrecovery by patient characteristics.

Results: Of 600 infants, 217 (36%) had not clinically recovered by day 7 (Figure 1B), of which 174 (80%) were previously healthy and 135 (62%) were born at term. There were 79 (13%) and 28 (5%) whose CPS-Ped increased by 2 and ≥3 points respectively after admission (Figure 1C). Factors associated with prolonged recovery included younger age on admission, prematurity, any underlying respiratory condition, invasive mechanical ventilation on admission, and apnea/bradycardia on admission (Table 1 and Figure 2).

Conclusion: Infants born prematurely and those with underlying respiratory conditions are at higher risk of a prolonged clinical course. However, most infants not recovering within a week of hospitalization were previously healthy.

Abstract category: Clinical Studies

Keywords: RSV; clinical progression; hospital course; severity; prolonged recovery; clinical endpoints; 2022 RSV season

Conflict of Interest: Margaret M. Newhams, Amber O. Orzel-Lockwood, and Adrienne G. Randolph report research funding to their institution from CDC. Natasha B. Halasa reports past grant support from Quidel and Sanofi, and current grant support from Merck. Neither Laura Zambrano, Shannon Leland, Justin Amarin, Laura Stewart, Elizabeth McNamara, nor Angela Campbell report any conflicts.
EVOLUTION & EPIDEMIOLOGY
ANALYSIS OF RESPIRATORY MICROBIOME IN RSV INFECTIONS WITH DIFFERENT CLINICAL SEVERITIES IN PEDIATRIC HOSPITALS IN BUENOS AIRES, ARGENTINA

Acuña, Dolores (1,2); Nabaes Jodar, Mercedes S.(1,2); Montoto, Luciana(3); Wenk, Gretel(4); Miño, Laura(4); Valeri, Clara(4); Reyden, Silvina(4); Domínguez Figueredo, Lourdes(4); Bokser, Vivian(4); Lucion, M. Eugenia(5); Miño, Laura(4); Valeri, Clara(4); Reyden, Silvina(4); Domínguez Figueredo, Lourdes(4); Bokser, Vivian(4); Lucion, M. Eugenia(5); Miño, Laura(4); Valeri, Clara(4); Reyden, Silvina(4); Domínguez Figueredo, Lourdes(4); Bokser, Vivian(4); Lucion, M. Eugenia(5); Miño, Laura(4); Valeri, Clara(4); Reyden, Silvina(4); Domínguez Figueredo, Lourdes(4); Bokser, Vivian(4); Lucion, M. Eugenia(5); Miño, Laura(4); Valeri, Clara(4).

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Presenting author: Dolores Acuña

The analysis of microbiome is a factor that should be studied to understand the severity of respiratory diseases. The studied population comprised 19 outpatients and 53 hospitalized patients with a positive diagnosis of respiratory syncytial virus (RSV) and 22 healthy children serving as control patients, from pediatric hospitals in Buenos Aires.

RSV complete genomes and V4 region of the 16S rRNA were sequenced by Illumina-NGS. All patients were under 12 months of age, without viral coinfections and comorbidities. The average age of the infected patients was 5 months. Bronchiolitis was diagnosed in 85.2% of cases, while 14.8% had pneumonia. The average TAL score was 6.7 in hospitalized patients and 4.46 in outpatients. In hospitalized cases, 41.4% received high-flow nasal cannula support and average duration of hospitalization was 9 days (from 1 to 55).

The RSV genetic lineages identified were GA2.3.5, GA2.3.6b, and GB5.0.5a, accounting for 47.3%, 10.5%, and 42.1% respectively.

The Partitioning Around Medoids algorithm showed five different clusters that characterize the different patient populations. The microbiomes from hospitalized patients revealed two bacterial profiles, one dominated by Moraxella and Dolosigranulum pigrum, while the other showed greater diversity and a slight dominance of Haemophilus. The population of outpatient cases showed a dominance of Moraxella, followed by Dolosigranulum pigrum and Corninebacterium. Finally, the microbiome of control cases without RSV exhibited a higher prevalence of Dolosigranulum pigrum over Moraxella and Corninebacterium.

In conclusion, each patient population exhibited differences in their predominant bacteria and their relative abundance.

Abstract category: Evolution & Epidemiology
Keywords: RSV, Infection; Microbiome; Clinical Severities; Bioinformatics
Conflict of Interest: None declared

RESPIRATORY SYNCYTIAL VIRUS (RSV) GENOME SURVEILLANCE TO ASSESS THE ANTIGENIC SITE VARIATIONS (2014-2023)

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National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, USA

Presenting author: Megha Aggarwal

Background: Respiratory syncytial virus (RSV) is the primary cause of respiratory infections in young children. Nirsevimab and palivizumab are the only approved monoclonal antibodies for the prevention of RSV infection in infants. In the last decade, several amino acids within the antigenic sites drifted in RSV F (fusion) protein. There is a need for genomic surveillance and assessment of antigenic site variations in RSV F protein to characterize the effect of mutations on current prophylactics.

Methods: We assessed >5,000 sequences of RSV submitted to GenBank and EpiRSV between 2014-2023. The structures of RSV F in both pre- as well as post-fusion forms were analyzed to functionally characterize the antigenic site mutations.

Results: Sequencing data indicate no changes in the palivizumab binding site (antigenic site II) except S276N in RSV B F protein which has persisted at low levels over the past ten years. However, we observe mutations to the nirsevimab binding site (antigenic site Ø) in RSV B F protein, specifically the three substitutions I206M, Q209R and S211N. In RSV A, there are also a few mutations (N63S and K65R) observed in the nirsevimab binding site, at very low levels.

Conclusion: It is crucial that we closely monitor the antigenic site variations for any potential escape mutants to inform policy decisions on RSV prevention and therapeutics. This analysis has limitations because many available sequences are linked to outbreaks, and not baseline surveillance, and therefore evolution rates are hard to assess.

Abstract category: Evolution & Epidemiology
Keywords: RSV, Nirsevimab, Palivizumab, Antigenic Site, Mutation, Fusion Protein
Conflict of Interest: None declared.
DETECTION OF RESPIRATORY SYNCYTIAL VIRUS (RSV) USING NASOPHARYNGEAL SPECIMENS (NP) ALONE SIGNIFICANTLY UNDERESTIMATES DISEASE INCIDENCE IN ADULTS HOSPITALIZED WITH ACUTE RESPIRATORY INFECTIONS: A POOLED ANALYSIS


1. Pfizer, Inc 2. Norton Infectious Disease Institute, Louisville Kentucky, USA 3. Sinai Health System, Toronto Ontario, Canada 4. University of Rochester School of Medicine

Presenting author: Negar Aliabadi

Background: Collecting >1 diagnostic specimen boosts RSV detection in adults; prior studies have not assessed benefit of adding saliva or ≥2 specimen types. We quantified RSV detection increase with multiple additional specimens compared to NP alone.

Methods: Adults ≥40 years hospitalized with acute respiratory illness were prospectively enrolled during 2021–2023. Collected NP swabs, saliva, and sputa were tested by RT-PCR, and acute/convalescent serology specimens by Luminex-based immunoassay. Fold increase in RSV detection rate associated with adding additional specimens was calculated, comparing RSV prevalence using NP swab plus other specimen types to RSV prevalence using NP alone.

Results: Among 3,651 patients enrolled, 100% had NP swabs, 97.7% saliva, 33.2% sputum, and 33.4% paired serologies. RSV detection was 2.03-fold higher (103% increase; 95% CI 79%–230%) using all specimen types compared to NP alone. Prevalence increase associated with additional specimen types was higher among those with common cardiac diagnoses (e.g., CHF: 3.14-fold/214% increase [95%CI: 70%–479%], with about half of additional infections detected by saliva. Among the entire study population, saliva identified the highest percentage of RSV (61.6%) because of its higher sensitivity than NP swab (63.1% versus 49.2%) and greater ease of collection versus serology/sputum.

Conclusions: RSV detection increased by 103% using four specimen types, with all specimens contributing to additional identification. Saliva may be more sensitive than NP swab for routine use. These data provide an estimate of the potential correction factor to use for estimating RSV incidence in studies relying on NP swabs alone.

Abstract category: Evolution & Epidemiology

Keywords: Respiratory Syncytial Virus, Acute Respiratory Infection, Sensitivity, RSV Detection

Conflict of Interest: Negar Aliabadi, Qing Liu, Sonal Uppal, Robin Hubler, Paula Peyrani, Warren V Kalina, Malak Elsobky, Kari Yacisin, Elisa Gonzalez, Luis Jodar, Bradford D. Gessner, and Elizabeth Begier are employees of Pfizer and may hold Pfizer stock and/or stock options.
RESPIRATORY SYNCYTIAL VIRUS (RSV) TESTING FREQUENCY AMONG ADULTS ADMITTED WITH LOWER RESPIRATORY TRACT INFECTION (LRTI) IN A LARGE US HEALTHCARE NETWORK

Negar Aliabadi(1), Sara Y Tartof(2), Bradley K Ackerson(2), Vennis Hong(2), Sabrina Welsh(1), Sally Shaw(2), Qing Liu(1), Parag Mahale(2), Banshri Kapadia(2), Elisa Gonzalez(1), Robin Hubler(1), Brigitte Spence(2), Sarah Simmons(2), Jeff Slezak(2), Gabriella Goodwin(2), Rudy Patrick(2), Erica Chilson(1), Kari Yacisin(1), Bradford D Gessner(1), Elizabeth Begier(1)

1. Pfizer, Inc.
2. Kaiser Permanente, Southern California

Presenting author: Negar Aliabadi

Background: RSV is a leading cause of LRTI, however testing is infrequent among older adults (aged ≥60 years); characteristics of those tested are not well described.

Objective: To describe RSV testing patterns among adults hospitalized with LRTI.

Methods: Kaiser Permanente Southern California (KPSC) electronic medical records of older adults were analyzed for LRTI hospitalizations, and the proportions therein with respiratory specimens collected, RSV testing conducted, and testing results during 01January2022–19May2023.

Results: Overall, 77,298 LRTI hospitalizations occurred among 1,127,099 KPSC beneficiaries aged ≥60 years. Nasopharyngeal swabs (NPS) were collected for 63,863 (83%) of these hospitalizations, ranging from 73–87% by demographics and medical comorbidities. Overall, 5,147 hospitalizations (6.7% of LRTI hospitalizations and 8.1% of those with NPS collected) had RSV testing. Peak RSV testing during the study period was 12.6% of LRTI hospitalizations (Figure 1). The percentage of RSV testing among LRTI hospitalizations varied little by demographics (Range 7%–9%, Figure 2); there was slightly more variation by comorbidities (Range 6%–15%, Figure 3), with the greatest percentage of RSV testing among those with immunocompromise and organ transplant (12%, and 15% tested, respectively). Of tested specimens, 3.6% were RSV positive, with similar results by comorbidity (Range: 2–5%).

Discussion: Most LRTI hospitalizations had an NPS obtained but RSV testing was infrequent regardless of patient RSV risk or RSV activity, indicating that NPS collection was likely driven by testing for other viral pathogens such as SARS-CoV-2. Low testing frequency among older adults likely results in missed RSV infections in standard-of-care settings.

Abstract category: Evolution & Epidemiology

Keywords: Respiratory Syncytial Virus, Lower Respiratory Tract Infection, Testing Patterns

Conflict of Interest: Negar Aliabadi, Sabrina Welsh, Qing Liu, Elisa Gonzalez, Robin Hubler, Erica Chilson, Kari Yacisin, Bradford D. Gessner, Elizabeth Begier are employees of Pfizer and may hold Pfizer stock and/or stock options. KPSC authors received funding from Pfizer to conduct the study, and these funds were paid directly to the organization. Additional CDIs from KPSC authors: Sara Tartof has received funds from GlaxoSmithKline that are unrelated to this study and were paid directly to the organization. Sarah Simmons has received funds from GlaxoSmithKline that are unrelated to this study and were paid directly to the organization. Brad Ackerson has received funds from GlaxoSmithKline, Moderna, Genentech, and Dynavax that are unrelated to this study and were paid directly to the organization.
REAL-WORLD STANDARD OF CARE RESPIRATORY SYNCYTIAL VIRUS (RSV) TESTING RATES IN OUTPATIENT SETTINGS AMONG U.S. ADULTS WITH LOWER RESPIRATORY TRACT ILLNESS (LRTI)

Suzanne Landi (1), Negar Aliabadi (1), Jennifer Judy (1), Kari Yacisin (2), Bradford D Gessner (1), Elizabeth Begier (1)

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2. U.S. Medical Affairs, Pfizer Inc.

Presenting author: Negar Aliabadi

Background: RSV is a leading cause of LRTI among adults and can cause severe outcomes. RSV testing is infrequent, partly due to a lack of treatment options. We quantified RSV versus influenza testing frequency among adults with LRTIs.

Methods: We conducted a retrospective cohort study identifying U.S. adults aged ≥18 years in Optum Electronic Health Records (EHR) Database and identified LRTIs (by ICD-10-CM codes) in any outpatient healthcare setting between Aug 2017–Mar 2023. Proportions of those tested for influenza and RSV were quantified over time and by patient characteristics. Episodes were defined as the 7-day window following the LRTI diagnosis date, separated by a 30-day washout period.

Results: Among 9,176,304 adults, we identified 3,540,040 outpatient LRTI episodes, of which 63,538 (1.8%) had RSV testing and 520,269 (14.7%) had influenza testing. RSV testing was less frequent than influenza testing among LRTI episodes but increased 3-fold (1.8–5.4%) over time (Figure 1). Among LRTI episodes with RSV testing, 79% were tested on the day of LRTI diagnosis. RSV testing was more frequent in the Northeast (3.9%) and emergency care settings (4.6%) and among immunocompromised adults (2.1%). Outpatient influenza testing was more frequent in emergency care settings (26.1%), the South (19.3%), and among patients with asthma (12.5%).

Conclusions: Outpatient RSV and influenza testing of LRTI episodes remains infrequent among U.S. adults in a large EHR database but increased over time with variation by geography, care setting and patient comorbidity.

Abstract category: Evolution & Epidemiology

Keywords: Respiratory Syncytial Virus, Lower Respiratory Tract Infection, Testing, Healthcare Utilization, Outpatient Care

Conflict of Interest: All authors are employees of and may hold stock/stock options in Pfizer Inc.

RSV INFECTIONS IN ADULTS AGED 50 YEARS AND OLDER WITH ACUTE RESPIRATORY TRACT INFECTIONS IN GHANA

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Presenting author: Comfort Nuamah Antwi

Respiratory Syncytial Virus (RSV) associated Acute Respiratory Tract Infections (ARI) contributes to ≥10,000 deaths yearly among people aged ≥65 years but is woefully understudied as a problem in the Ghanaian adult population. The current study assessed the rate of RSV infections and its monthly circulation pattern in older adults both hospitalized and non-hospitalized in Ghana.

This is an ongoing prospective study of adults ≥50 years who visited the University of Ghana Hospital, University of Ghana Medical Centre, and Korle-Bu Teaching Hospital with ARI. Participants were recruited with consent. Throat and/or nasal swabs were obtained and tested for RSV and influenza using real-time PCR at Noguchi Memorial Institute for Medical Research.

So far, forty-five adults have been enrolled from May to June 2023. No cases of RSV were recorded, but one patient tested positive for influenza. Pneumonia was seen among 35 (78%) cases, and 22 (62.9%) were adults ≥60 years. One case of bronchitis was recorded. Among those hospitalized, 18/32 (56%) patients received oxygen therapy, and average length of stay in the ward was 10 days. 4 (8.9%) deaths occurred and 2 (4%) of patients have some knowledge about RSV.

Although no cases have yet been recorded in this study, RSV-associated ARI remained an important contributor to mortality in older adults. The absence of RSV in May and June may be attributed to the shift in the disease seasonality as seen globally after the COVID-19 pandemic. RSV awareness and targeted therapeutics are needed against the disease in this frail population.
Abstract category: Evolution & Epidemiology

Keywords: Acute Respiratory Tract Infections, Respiratory Syncytial Virus, Older Adults, Ghana.

Conflict of Interest: None declared

RSV GENOTYPES CIRCULATING IN ADULTS AGED 50 YEARS AND OLDER WITH ACUTE RESPIRATORY TRACT INFECTIONS IN GHANA.

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Respiratory Syncytial Virus (RSV) associated acute respiratory tract infections (ARI) contributes to ≥10,000 deaths yearly among people aged ≥65 years but is woefully understudied as a problem in the Ghanaian adult population. This study aimed to characterized RSV genotypes isolated from adults ≥50 years with acute respiratory tract infections (ARI) in Ghana.

Adults ≥50 years who visited hospitals in Accra with ARI were recruited with consent. Nasal samples were obtained. Samples were screened for both RSV and influenza using RT-qPCR. RSV genotypes were selected for sanger sequencing, and bioinformatic analysis was carried out to identify the predominant circulating strains. Circulating strains were further phylogenetically analyzed, and a relationship established between them and other globally circulating RSV strains.

Two hundred and twelve adults were enrolled from April to October of 2023. RSV was confirmed in 11/212 (5.19%) of the adults who were between the ages of 50 and 89 years, with the first case recorded in July. Pneumonia was associated with 5/11 cases and cough was the most significant symptom (p=0.023). RSV B predominated (100%) cases and clustered as RSV B BAIX in two lineages. One lineage aligned closely with strains circulating in 2022 in Seattle, while the other was similar to a Japan isolate in 2016.

BAIX dominated the RSV season in Accra, 2023. The absence of RSV in May and June may be attributed to the shift in the disease seasonality as seen globally after the COVID-19 pandemic. RSV targeted therapeutics are needed against the disease in this frail population.

Abstract category: Evolution & Epidemiology

Keywords: Acute Respiratory Tract Infections, Respiratory Syncytial Virus, Older Adults, Ghana.

Conflict of Interest: None declared

SHORT AND MID-TERM BURDEN OF SEVERE RSV INFECTIONS ON PRIMARY CARE RESOURCES UTILIZATION. THE NIRSE-GAL STUDY (WWW.NIRSEGAL.ES)

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Presenting author: Maria Sonia Ares-Gomez

Background: RSV burden on primary care/emergency department (PC/ED) resources is not well established. With the implementation of nirsevimab in Galicia’s (Spain) immunization program, the NIRSE-GAL study* aims to explore its eventual short-mid term impact and to provide historical, reference background data as comparator. Thus, a population-based cohort study was conducted to investigate the impact of RSV hospitalization on subsequent healthcare resource utilization.

Methods: Infants hospitalized for RSV between January 1st-2016, and March 3rd-2022, were compared to infants without RSV-related hospitalization matched by birth-date and gender. The total number of PC visits (pediatric or nurse), PC/ED, and prescriptions for antibacterial and/or drugs for obstructive airways diseases were analyzed. Adjusted incidence rate ratios (IRR) were calculated to assess the association between RSV hospitalization and PC/ED resource use, employing Poisson regression models.

Results: We included 3,313 hospitalized and 3,313 non-hospitalized children (median follow up 50.3 months). Pediatric visits [IRR = 1.20 (95% CI: 1.04, 1.37)] and nurse visits [IRR = 1.32 (95% CI: 1.08, 1.63)] were increased, persisting up to 24 months. ED attendance was increased both in the 4-month [IRR = 1.05 (95% CI: 0.98, 1.12)] and 24-month follow-up periods [IRR = 1.14 (95% CI: 1.05, 1.23)]. Use of medication for obstructive airway diseases in the 4-months [IRR = 1.27 (95% CI: 1.00, 1.62)] and 24-months post-hospitalization [IRR = 1.28 (95% CI: 1.19, 1.38)] were also increased (Figure 1).

Conclusions: Severe RSV significantly increments PC/ED use for up to two years. These findings provide crucial insights for evaluating the cost-effectiveness of RSV prevention programs in children.
Abstract category: Evolution & Epidemiology
Keywords: severe RSV, healthcare resource utilization, antibacterial and/or drugs for obstructive airways diseases, primary care, emergency department resources

Conflict of Interest: *The NIRSE-GAL study (CEIC 2023–377) is funded by Sanofi Pasteur/AstraZeneca through a research grant to the Healthcare Research Institute of Santiago.

NEW MATERNAL IMMUNIZATION INTRODUCTION IN LOW- AND MIDDLE- INCOME COUNTRIES: LEARNINGS FROM IN-COUNTRY STAKEHOLDER CONVENINGS IN FIVE COUNTRIES

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Presenting author: Ranju Baral

Background: Successful implementation of upcoming maternal immunization (MI) will require health system adaptations, specifically within immunization and maternal health service programs. We gathered perspectives from key stakeholders in five-countries (Bangladesh, Ghana, Kenya, Mozambique, and Nepal) regarding what it would take to introduce new maternal vaccines.

Methods: In each country, we convened approximately 40 stakeholders for a workshop to deliberate on potential delivery strategies and opportunities and constraints for implementing new MI interventions. Participants were divided into thematic areas and discussed the need for health system adaptations to establish or strengthen a MI platform.

Results: Stakeholders underscored that existing MI programs (TD vaccination) provide a proven path for future MI. Maternal health and immunization program integration was strongest at the delivery level and weakest at the national level. Concerted coordination at the national level was identified as critical to the success of introducing new interventions. While the health workforce providing immunization and antenatal care (ANC) services undergo similar training, with transferrable skills, developing operational guidelines with clear roles and responsibilities was deemed critical for ownership and accountability. Human resource constraints pose challenges for some countries. Raising awareness of disease burden and new MI interventions were important. Sustainable financing was a recurring theme across all countries, especially inconsidering transitions from Gavi support.

Conclusions: While circumstances and needs varied between countries, the workshops created an opportunity for experts from immunization and ANC programs to collaborate and identify recommendations for building a platform for new maternal vaccines.

Abstract category: Evolution & Epidemiology
Keywords: Maternal Immunization, implementation, low and middle income countries

Conflict of Interest: None
COST OF IMPLEMENTING FUTURE RSV MATERNAL IMMUNIZATION IN LOW-AND MIDDLE-INCOME COUNTRIES

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Background: Delivering new maternal vaccines will require adaptations to existing immunization platforms and will have cost implications. Evidence on costs of delivering maternal vaccines in low- and middle-income countries (LMIC) is nearly non-existent. We generate cost projections of delivering maternal respiratory syncytial virus (RSV) vaccines in Ghana, Kenya, and Bangladesh.

Methods: We gathered perspectives from country stakeholders to explore potential delivery mechanisms and program adaptations needed to establish/strengthen Maternal Immunization (MI) platforms. Using an activity-based micro-costing approach, we generated MI introduction and delivery costs. Costs considered cold chain storage expansion, transport and logistics, social mobilization, advocacy and communication, and health worker training, among other aspects. We collected key data inputs and assumptions on resource requirements through interviews with ministry of health staff, a survey of select health facilities, and administrative/financial record reviews. We present financial and economic costs to governments over a period of five years.

Results: Data collection to inform delivery cost projections is currently underway; preliminary results are anticipated by December 2023. Stakeholders viewed the existing MI program (tetanus immunization) as successful and recommended leveraging it for upcoming MI interventions. Cost estimates will incorporate recommended health system strengthening activities viewed as critical for successful maternal RSV vaccine delivery.

Conclusions: Our cost estimates will provide much needed data on implementation feasibility and affordability of RSV maternal vaccines and other forthcoming products.

Abstract category: Evolution & Epidemiology

Keywords: Cost, Cost Of Introduction, Maternal Immunization

Conflict of Interest: None declared
Conclusion: The results of our study indicate a substantial economic burden, particularly in older patients and those with underlying risk factors, highlighting the need for effective prevention in these patient groups.

Abstract category: Evolution & Epidemiology

Keywords: Respiratory Syncytial Virus, RSV, Economic Burden, Costs, Inpatient, Outpatient, Prevention

Conflict of Interest: Lea Bayer, Caroline Beese, Bennet Huebbe, and Christof von Eiff are employees of Pfizer Pharma GmbH. Karina C. Manz and Anja Mocek are employees of the IGES Institut GmbH, which is a paid consultant to Pfizer Pharma GmbH for conducting the study and preparatory work.

HOSPITALISATION BURDEN ESTIMATES OF RESPIRATORY SYNCYTIAL VIRUS (RSV) WITH ADJUSTMENT FOR CASE UNDERASCERTAINMENT IN ADULTS AGED 18 TO 64 YEARS IN HIGH-INCOME COUNTRIES

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3 Pfizer Vaccines, Dublin, Ireland
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Presenting author: Elizabeth Begier

Introduction: RSV represents a substantial health burden for both young children and older adults (aged>65 years), but its impact on adults aged 18-64 years is not well documented. We estimated the hospitalisation burden of RSV in adults aged 18-64 years in high-income countries. For each study included, we followed a two-step statistical approach to adjust for RSV case under-ascertainment related to the use of clinical specimen and diagnostic test, considering the combination of sputum, saliva, and nasopharyngeal specimens testing through PCR plus paired serology as the reference. Random-effects meta-analysis was conducted to estimate RSV hospitalisation rate, proportion of acute respiratory infection (ARI) hospitalisations positive for RSV, and in-hospital RSV-related mortality.

Results: Fifteen studies were included. The adjusted annual RSV-associated hospitalisation incidence was 70/100,000 population (95% CI: 43-117) in persons aged 18-64 years, which increased over time (Figure), and which translated into 537,000 hospitalisations in 2019 across high-income countries. Among adults aged 18-64 years, RSV accounted for 9.7% (7.0-13.2%) of ARI hospitalisations, in-hospital case fatality ratio was 5.7% (4.7-7.0%). After correcting for under-ascertainment in documentation of RSV hospitalisations, we estimated the overall number of RSV-associated in-hospital deaths as 24,700 (9,500-82,900).

Conclusion: RSV contributes a substantial hospitalisation and mortality burden in adults aged 18-64 years in high-income countries, especially those aged 50-64 years.

Abstract category: Evolution & Epidemiology

Conflict of Interest: This work received funding support from Pfizer.

RSV GENOMIC DIVERSITY IN COMMUNITY SETTINGS PRE- AND POST-COVID-19 PANDEMIC PERIODS IN SEATTLE, WASHINGTON, USA

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Presenting author: Julia Bennett

Globally, RSV declined to historically low levels following stay-at-home orders in 2020 and re-emerged as restrictions lifted, with large inter-seasonal outbreaks and other shifts in epidemiology. We used data from a community-based respiratory virus surveillance study in Seattle, USA to assess RSV clinical features and genomic diversity over three respiratory seasons (2019-2022). Individuals with respiratory symptoms were enrolled and provided nasal swabs. Samples were tested for RSV by RT-qPCR, with whole genome sequencing performed for a subset. Among children (<18 years) and adults respectively, 1.8% (232/13014) and 0.2% (86/46042) of samples tested positive for RSV-A and 1.1% (139/13016) and 0.3% (119/46043) for RSV-B. Positive samples came from childcare (n=39), clinic (270), university (20), workplace (32), or nursing facility (1) sites and at-home self-administered testing (253). Median age for all participants was 32 years (IQR:22-48) and 3 years (3-33) for those who tested positive. Cough (28%) and rhinorrhea (28%) were the most common symptoms for RSV-positive children and adults, with lower median relative cycle threshold values observed in children. During 2019-2020, RSV-A and RSV-B co-circulated with 6 RSV-A and 4 RSV-B clades observed. Almost no RSV was observed during 2020-2021. During 2021-2022, RSV-B clade B.D.5.2.1.1 was dominant with a few cases of B.D.5.2.1 and RSV-A (Figure). Genomic diversity trends were similar for all ages, but less prevalent clades (A.D.2/A.D.2.2/AD.5/B.D.5.2.1.2) were only observed among children, possibly due to fewer positives among adults. From pre- to post-implementation of pandemic restrictions, RSV genomic diversity in Seattle shifted and appeared to decline for RSV-B.
RESURGENCE OF RESPIRATORY SYNCYTIAL VIRUS INFECTION DURING COVID-19 PANDEMIC IN PUNE, INDIA

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Presenting author: Sumit Dutt Bhardwaj

Background: Respiratory Syncytial Virus (RSV) is a leading cause of acute lower respiratory infection in children worldwide. Understanding its prevalence, variations, and characteristics is vital, particularly in the context of the COVID-19 pandemic. The study aimed to investigate the RSV positivity rate, subtype prevalence, age and gender distribution, symptomatology, and co-infection rates during pre-pandemic and pandemic periods.

Methods: We analyzed data from 15,381 patients tested for RSV between 2016 and 2023.

Results: Our analysis revealed a 7.2% average RSV positivity rate in the pre-pandemic period, with significant fluctuations during the pandemic (1.5% in 2020 to 32.0% in 2021). We observed variations in RSVA and RSVB detection rates. The 0-4 year’s age group was consistently the most affected, with a slight male predominance. Fever and cough were common symptoms. Therapeutic interventions, particularly antiviral usage and ventilation requirements, decreased during the pandemic. We also identified variations in co-infection rates with other respiratory viruses.

Conclusion: Our study offers critical insights into the impact of the COVID-19 pandemic on RSV prevalence, subtype distribution, patient characteristics, and clinical management. These findings underscore the need for ongoing surveillance and adaptive public health responses.

Abstract category: Evolution & Epidemiology

Keywords: Respiratory Syncytial Virus, RSV Subtypes, COVID-19 Pandemic, Prevalence, Co-Infections, Symptomatology, Therapeutic Interventions.

Conflict of Interest: None declared

RESPIRATORY VIRUS SEASONALITY, IMPLICATIONS ON IMMUNISATION STRATEGY, AND PROPOSED STRATEGIES

Jonathan Broad (1, 2)

1. UK Health Security Agency
2. NHS

Presenting author: Jonathan Broad

Background: With a range of Respiratory Syncytial Virus (RSV) maternal and infant immunisations recently approaching licensure, it is important to consider how seasonality might impact deployment policy. This article reviews current literature on seasonality and appraises a range of immunisation approaches in different potential settings.

Methods: This undertakes a narrative review of the literature on seasonality and trial papers on near-licensure immunisations. Near-licensure immunisations are then appraised using a framework adapted from the GAVI vaccine evaluation framework to include seasonality.
RESULTS: RSV seasonality varies largely across the globe, with short seasons in temperate global north and global south countries, compared to prolonged (e.g. 10 month) seasons in several equatorial countries. 3 immunisations are appraised, including Palivizumab, Nirsevimab, and Pfizer’s maternal vaccine offering 1, 5, and 6 months protection respectively. A year-round maternal vaccine strategy would likely prevent disease in the highest burden and be most easily implementable and affordable, though lower uptake and late impact. A seasonal maternal vaccine strategy may have more theoretical cost effectiveness, but may be more difficult to implement on/off. A year-round infant immunisation after birth and at 6 months would potentially have most benefit but is most costly.

Conclusion: Given RSV seasonality, and the burden in early infancy, it is likely that a range of approaches may be adopted globally. A maternal universal programme potentially has the greatest range of likely benefits but may have reduced uptake and reduced benefit in later infancy. Further research is needed on different vaccine strategies, and potential combined programmes.

Abstract category: Evolution & Epidemiology
Keywords: RSV, Immunisation, Seasonality

Conflict of Interest: None declared

PREVALENCE OF RESPIRATORY SYNCYTIAL VIRUS (RSV) AMONG CHILDREN IN GEORGIA, 2019-2022

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Presenting author: Giorgi Chakhunashvili

Background: RSV poses a global burden, particularly in low- and middle-income countries, and causes severe respiratory illness in young children, resulting in significant morbidity and mortality. RSV-associated acute lower respiratory infections cause 3.4 million hospitalizations and over 100,000 deaths annually among children under five. Strengthening surveillance systems is essential for timely detection and monitoring of RSV.

Methods: To determine prevalence of RSV in Georgia among children below 5, data of 2019-2022 (including May) was obtained from national SARI sentinel surveillance system. Sample was filtered by availability of laboratory test results. Combination of single- and multiplex PCR diagnostic kits were used for confirmation of RSV.

Results: 2,287 SARI cases were identified. Among them 451 (15.37%) were positive on RSV. Results were stratified by years and months. Highest positivity was registered in April, 2019 - 64.29%; March-April, 2020 - 58.67% and 50.00% respectively; and January, 2022 - 54.43%. All samples were negative on RSV between July-November, 2019; in June, August-November, 2020; and in January, March, and April, 2022. RSV was positive in more than 20% of samples in 2019 February and May; in 2020, February-April; in 2021, September-December; and in 2022, January-March.

Conclusion: Seasonal variations in RSV prevalence was revealed with the highest percentage of positivity mostly in late winter and spring of 2019-2020. Active phase of COVID-19 in 2021 has seemed to have “delayed” the circulation of RSV to summer, autumn, with a peak throughout winter. These findings emphasize the importance of continuous surveillance efforts to monitor RSV.

Abstract category: Evolution & Epidemiology
Keywords: Georgia; RSV; prevalence

Conflict of Interest: None declared

THE ECONOMIC BURDEN OF RSV-ASSOCIATED ILLNESS IN CHILDREN AGED <5 YEARS IN TAIWAN: A POPULATION-BASED STUDY

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Presenting author: Hsin Chi

Background: Respiratory syncytial virus (RSV) is a common cause of hospitalizations in young children. This study aims to estimate the cost of RSV-associated illness in Taiwan using the National Health Insurance (NHI) database.

Methods: Among the 2008-2021 Taiwan birth cohort, children <5 years who had RSV were identified by ICD-9 or 10 coding in outpatient or in-hospital records from the NHI database. Data for resource utilization and direct medical costs were collected.

Results: The mean annual cost of RSV-associated hospitalization (RSVH) in children aged <5 years increased from US dollars ($) 2,954,387 with an average of 2,970 hospitalizations for 2008-2014 to $4,941,570 with an average of 4,740 hospitalizations for 2015-2021. The average lengths of stay were 5.8 days in 2008-2014 and 5.3 days in 2015-2021. Of these RSVH, 7.4% and 5.0% of children required intensive care in 2008 and 2014 respectively. Accordingly, the average lengths of stay were 10.8 days in 2008-2014 and 10.6 days in 2015-2021, which were significantly higher than RSVH without intensive care. Among children aged <5 years, the average annual costs of RSV related outpatient visits were $1,616,511 with an average of 91,814 visits per year in 2008-2014 and $1,554,404 with an average of 77,714 visits per year in 2015-2021.

Conclusion: The study reveals for the first time the substantial economic burden of RSV-associated illness among young children in Taiwan. Interventions targeting RSV are important to reduce the economic burden of RSV-associated illness.

Acknowledgements: This study is co-funded by Sanofi and AstraZeneca.

Abstract category: Evolution & Epidemiology
Keywords: Respiratory Syncytial Virus (RSV), Cost

Conflict of Interest: None declared
EXPLORING THE USE OF A COMMON DATA MODEL TO EVALUATE INTENSIVE CARE UNIT ADMISSION RISK IN PEDIATRIC RESPIRATORY SYNCYTIAL VIRUS INFECTION: A PILOT STUDY

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Presenting author: Young June Choe

Respiratory Syncytial Virus (RSV) poses a pervasive threat, particularly causing severe lower respiratory tract infections in children. This study explores the occurrence and risk factors associated with severe RSV infections in Korean children. Analyzing electronic medical records transformed into the Observational Medical Outcome Partnership (OMOP) CDM, we conducted a retrospective study from August 2008 to December 2022 at three Korean hospitals. Of 33,674 pediatric patients hospitalized with respiratory symptoms, 4.5% tested positive for RSV. RSV-positive patients admitted to the intensive care unit (ICU) were predominantly under 5 months old, with shorter gestational lengths and lower birth weights.

Regression analyses, considering multicollinearity between gestational length and birth weight, revealed that infants aged 0-5 months had significantly higher odds of ICU admission compared to the 24-59 months age group. Sex and congenital cardiac disease were not significant predictors. Notably, patients with shorter gestational lengths (<27 weeks) and extremely low birth weights had elevated odds of ICU admission.

Utilizing OMOP CDM, our study offers crucial insights into severe RSV infection risk factors in children. Future research should extend beyond individual institutions, encompassing multiple sources for a comprehensive risk analysis, enhancing our understanding of the RSV epidemic.

Table 1. General characteristics of RSV-positive and negative patients

<table>
<thead>
<tr>
<th>Age at diagnosis (months)</th>
<th>All Patients (n=33,674)</th>
<th>RSV-positive patients, n (%)</th>
<th>RSV-positive patients, n (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-27</td>
<td>21,623 (64.1)</td>
<td>2,046 (94.0)</td>
<td>1,859 (90.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>28-59</td>
<td>12,051 (35.9)</td>
<td>277 (13.4)</td>
<td>206 (10.7)</td>
<td>0.0210</td>
</tr>
</tbody>
</table>

Table 2. The distribution of potential risk factors among ICU and non-ICU admission patients

<table>
<thead>
<tr>
<th>Age at diagnosis (months)</th>
<th>All RSV-positive patients, n (%)</th>
<th>ICU admission patients, n (%)</th>
<th>Non-ICU admission patients, n (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-27</td>
<td>2,046 (94.0)</td>
<td>1,859 (90.9)</td>
<td>187 (9.1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>28-59</td>
<td>277 (13.4)</td>
<td>206 (10.7)</td>
<td>71 (3.3)</td>
<td>0.0484</td>
</tr>
</tbody>
</table>

*The records of 60 patients were missing.*
GENOMIC DIVERSITY AND HOUSEHOLD TRANSMISSION PATTERNS OF RESPIRATORY SYNCYTIAL VIRUS (RSV) IN WASHINGTON AND OREGON, USA (2022-2023)

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Presenting author: Sarah Cox

Introduction: Household transmission of respiratory viruses is a driver of community spread. Few population-based studies have examined household RSV transmission in the United States, particularly since the advent of SARS-CoV-2.

Methods: We analyzed data from CASCADIA, a prospective community-based US cohort study from August 2022 through May 2023. Participants completed symptom surveys and collected nasal swabs at least weekly, with additional surveys and swabs when symptoms occurred. We tested nasal swabs for RSV-A by RT-PCR and performed whole genome sequencing.

Results: Among 3,060 participants within 1,010 multi-person households during the 2022-2023 season, RSV-A was detected among 130 individuals within 96 households (Figure 1). Of 107 index and co-primary index cases, 96 (90%) were symptomatic within ±7 days of their first positive/inconclusive RSV-A result. Secondary transmission ≤14 days was detected in 18 (17%) of 96 RSV-A positive households; median age of index and secondary cases were 7 (IQR: 3-15) and 9 (5-40), respectively. Sequence data were generated for 85 RSV-A samples collected between September 2022 and February 2023. Main RSV-A lineages represented were A.D.5 (n=40), A.D.1 (n=28), A.D.3 (n=11), and A.D.2 (n=6) (Figure 2 – next page). Within households with ≥2 RSV-A cases, sequenced viruses were more similar where transmission occurred ≤14 (mean pairwise difference 2.85 [range 0-5], n=7 households) versus >14 days after the index case (136.5 [37-236], n=2).

Conclusion: Secondary cases that occur >14 days after the index case may be more likely due to independent introductions than within-household transmission. Findings that most index cases were children can inform future RSV prevention efforts.
HIGH CIRCULATION OF RESPIRATORY SYNCTIAL VIRUS IN PEDIATRIC PATIENTS HOSPITALIZED WITH SEVERE ACUTE RESPIRATORY INFECTION IN SENEGAL, 2022–2023.

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Presenting author: Ndongo Dia

Background: Acute respiratory infections caused by the respiratory syncytial virus (RSV) can be severe, resulting in pediatric hospitalizations and childhood deaths, mostly in developing countries. So here, we investigated the epidemiology and the genetic characteristics of RSV infections among patients hospitalized with severe acute respiratory infections using data from the 2022-2023 sentinel surveillance.

Methods: Nasopharyngeal swab samples were collected from hospitalized patients as part of the SARI surveillance in Senegal from 2022 to 2023. A multiplex RT-PCR was used for the detection of respiratory pathogens, including RSV as well as the most common respiratory bacteria. Subsequently, a subset of RSV positive samples was randomly selected to undergo whole genome sequencing (WGS).

Results: Overall, 1570 SARI samples were received and analyzed at the Senegalese NIC from January, 1 2022 through November 2023. Among enrolled patients, 861 (54.8%) were males, 710 (45.2%) were children aged under 1 year and children above 5 years represented 471 (30%). RSV was detected in 14.6% (230/1570), among which RSV-A was confirmed in 40.4% and RSV-B in 59.1%. RSV positivity was significantly higher in infants aged ≤11 months (58.3%) than in the other age groups and a co-circulation of both type of RSV during seasonal epidemic periods with alternating patterns of predominance over time was observed. Phylogenetic analyses revealed that all RSV-A strains belonged to GA2.3.5 genotype and all RSV-B strains to GB5.0.5a genotype.

Conclusion: Globally, our findings from the 2022-2023 sentinel surveillance seasons reveal a high prevalence of RSV infection among hospitalized pediatric patients in Senegal.

Abstract category: Evolution & Epidemiology
Keywords: RSV, SARI, Children
Conflict of Interest: None declared

THE BURDEN UNVEILED: A COMPREHENSIVE ANALYSIS OF THE COST OF ILLNESS OF RECURRENT WHEEZING IN CHILDREN FOLLOWING SEVERE RSV DISEASE IN ARGENTINA

Julia Dvorkin (1,2,3); Carlos Rojas-Roque (4); Emiliano Sosa (1,2); Elizabeth Vodicka (5); Ranju Baral (5); Andrea Sancilio (1,6); Karina Dueñas (1,6); Andrea Rodriguez (1,7); Patricia B. Carruitero (8); Ana B. Ramos Aloí (1); Veronica Bianchi (1); Fernando P. Polack (1); Clint Pecenka (5); Romina Libster (1); and Mauricio T. Caballero (1,2,3).

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Presenting author: Julia Dvorkin

Background: There is a lack of available data on the economic burden of wheezing episodes resulting from prior severe respiratory syncytial virus (RSV) infections in resource-constrained environments. This study aimed to assess the cost incurred for wheezing episodes in Argentina, considering the public health system and societal perspectives.

Methods: Prospective, multi-center cohort study that gathered data from 256 infants aged under 12 months who experienced severe RSV disease in two public hospitals within Buenos Aires from 2014 to 2016. Subsequently, patients were followed up for five years through phone calls and scheduled health visits. Data
pertaining to healthcare resource utilization, indirect expenses, and parental out-of-pocket costs were obtained from patient accounts and assessed using financial databases and records maintained by the hospitals. The overall cost per wheezing episode was calculated from the perspectives of the healthcare system and society. Costs were quantified in US dollars.

Results: 150 patients presented wheezing episodes after an acute severe RSV infection. The mean costs per RSV wheezing episode was US$626.58 (95% CI 499.97-753.18) for those who required hospitalization. For outpatients, the mean cost (considering all visits until recovery) was US$85.92 (95% CI 80.51-91.34). Parental out-of-pocket costs per patient was estimated in US$16.36 for all episodes (CI 95% 13.45-19.27).

Conclusions: This study shows the direct and indirect economic impact of wheezing after an acute severe RSV infection on the public health system in Argentina. The estimates obtained from this study could be used to inform cost-effectiveness analyses of new preventive RSV interventions being developed.

Abstract category: Evolution & Epidemiology

Conflict of Interest: Cost of Illness, Medical Cost, Respiratory Syncytial Virus, Wheezing Episodes, Economic Burden

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.

COST OF ILLNESS DUE TO RESPIRATORY SYNCTIAL VIRUS ACUTE LOWER RESPIRATORY TRACT INFECTION AMONG INFANTS HOSPITALIZED IN ARGENTINA

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Presenting author: Julia Dvorkin

Background: Respiratory syncytial virus (RSV) is the leading cause of acute lower respiratory tract illness (ALRTI), a major cause of hospitalizations and a significant cause of mortality among post neonatal children worldwide. There is scarce information regarding the economic burden of RSV disease in low-resource settings.

Methods: We established a nested study in a major cohort program to collect economic information regarding 256 infants under 12 months of age with ALRTI due to RSV in 2 public hospitals of Buenos Aires, Argentina, between May and September 2014-2016. We estimated the total cost per hospitalization due to RSV by the public health system in a low-income population. The costs were estimated in 2022 US Dollars.

Results: The mean costs per RSV hospitalization in infants for the health system were $587.79 (95% confidence interval [CI] $535.25 – $5640.33). The mean costs associated with PICU admission almost tripled from those at regular ward (USD 1556.81 [95%CI 512.21 – 2601.40] vs $56.53 [95%CI 512.21 – 2601.40]). Staff expenses were the main driver of the total cost of hospitalizations. In a higher burden scenario of 22,463 hospitalizations (incidence rate of 32.9/1000 infants), we found a total cost of 13,203,585 USD (95%CI 12,023,374 - 14,383,796) in Argentina.

Conclusions: This study shows for the first time the direct economic impact of severe RSV infection on the public health system and the low-income households in Buenos Aires, Argentina. The estimates obtained from this study could be used to inform cost-effectiveness analyses of new preventive RSV interventions being developed.

Abstract category: Evolution & Epidemiology

Keywords: Acute respiratory infections (ARIs); cost per episode; cost of illness; Low- and middle-income countries; Respiratory Syncytial Virus (RSV);

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.

RESPIRATORY SYNCTIAL VIRUS SEROPREVALENCE AND EPIDEMIOLOGICAL CHARACTERISTICS AMONG CHILDREN IN THE SUEZ CANAL AREA, EGYPT, 2019–2022

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Presenting author: Mohamed Fawzy

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 2022. 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 265 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, 72 (27.71%) of the 265 samples tested were positive for RSV. In 53/72 (73.6%) samples, RSVA was found, while in 19/72 (26.4%) samples, RSVB was identified. IgM and IgG seroprevalence for HRSA were 9.7% and 74%, respectively. Cough was the main clinical sign seen in RSV positive patients (60/72, 83.3%), followed by rhinorrhea (53/72, 73.6%), and nasal congestion (46/72, 63.8%). There were a 2:1 male to female ratio among the examined children. Twenty-three (31.9%) out of the 72 positive patients were less than 5 years old. RSV levels were at their peak in winter, particularly from December to February. Our study found that RSVA infections were common than RSVB infections in Ismailia Province, 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 in Egypt particularly Suez Canal Area.
Abstract category: Evolution & Epidemiology  
Keywords: Occurrence, Respiratory Syncytial Virus, RSV, Seroprevalence, Serological investigation  
Conflict of Interest: The authors declare no conflict of interest.

SEASONALITY OF BRONCHIOLITIS IN INFANTS — BRAZIL, 2016–2022

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Presenting author: Frederico Friedrich

Background: More than a year into the COVID-19 pandemic, intensified infection control measures have controlled most viral respiratory infections in Brazil. From March to June 2022, however, an increasing number of hospitalizations for acute bronchiolitis were reported in Brazil. This resurgence may have resulted from restarting social activities for children.

Methods: Data from hospitalizations of acute bronchiolitis in infants <1 year of age were obtained from the Department of Informatics of the Brazilian Public Health database for the period between 2016 and 2022. We performed a time series analysis using Seasonal-Autoregressive Integrated Moving Average (SARIMA) model in the R computing environment.

Results: In terms of seasonal trends, a pattern was observed in hospitalizations for AB during the pre-COVID-19 period (p < 0.01). However, this pattern was lost in 2020–2021 (p = 0.20). In 2022, we observed a recovery of the seasonal pattern when compared to the pre-COVID-19 period (p < 0.01), with the peak of cases occurring in May and presenting a value approximately 4% higher than the peak recorded from 2016–2019 (4218/100,000 vs. 4045/100,000). During the counterfactual period of school closure, there was an average reduction of 1400/100,000 hospitalizations. When comparing the counterfactual for 2022 with the observed data, we found an increase of 94/100,000 hospitalizations than expected.

Conclusion: the study identified a significant seasonal pattern in hospitalizations for AB before the COVID-19 pandemic, which was disrupted in 2020-2021 but recovered in 2022.

Abstract category: Evolution & Epidemiology  
Keywords: Bronchiolitis, Pandemics, Pediatric Epidemiology  
Conflict of Interest: No.
RSV causes significant morbidity and mortality among infants, young children, and the elderly. Few population-based studies have evaluated the RSV disease burden among older children and adults. This study examines incident RSV A infections and the baseline distribution of pre-F IgG antibody levels in a community setting.

We analyzed data from the ongoing CASCADIA Study—a prospective cohort study evaluating COVID-19 vaccine effectiveness in the United States—between August 2022 and May 2023. Participants completed weekly online symptom surveys and self-collected nasal swabs, irrespective of symptoms, which were tested for multiple respiratory viruses including RSV using RT-PCR. Enrollment serum samples were tested for anti-pre-F IgG antibody concentration (Mesoscale Diagnostics [MSD], Rockville, MD).

This study included 3,133 participants in 1,147 households (Table 1). RSV A was detected among 135 individuals within 101 (8.8%) households in the following age groups: 6 months to 1 year (n=15; 15.5%), 2-4 years (n=29; 13.4%), 5-12 years (n=48; 5.2%), 13-17 years (n=4; 1.2%), 18-39 years (n=16; 3.0%); 40-50 years (n=23; 2.2%). As age increased, mean baseline pre-F antibody concentration (AU/mL) increased while the range decreased (Figure 1). There was a statistically significant difference in geometric mean titer by age group (p-value<0.001).

We identified a difference in baseline pre-F antibody titers by age group in a large, community-based cohort. We detected RSV infections among children and adults including those not seeking medical care via home-based self-swabbing. Analyses describing RSV incidence, clinical outcomes, and the impact of pre-F IgG antibody concentration on subsequent RSV infection are ongoing.

Abstract category: Evolution & Epidemiology

Keywords: Respiratory Syncytial Virus, Pre-F Antibodies, Epidemiology, Community Surveillance, Adult, Adolescent, Pediatric

Conflict of Interest: CF: None declared. HYC reported consulting with Ellume, Pfizer, the Bill & Melinda Gates Foundation, Glaxo Smith Kline, and Merck. She has received research funding from Emergent Ventures, Gates Ventures, Sanofi Pasteur, the Bill & Melinda Gates Foundation.
EXPLORATORY ASSESSMENT OF MID-TERM RESPIRATORY NIRSE-GAL STUDY (WWW.NIRSEGALES)

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7. Sanofi Vaccines Medical, Lyon, France.
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9. Unidade de Xenética, Instituto de Ciencias Forenses, Facultade de Medicina, Universidade de Santiago de Compostela (USC), and GenPoB Research Group, Instituto de Investigación Sanitaria (IDIS), Hospital Clínico Universitario de Santiago, Servizo Galego de Saúde, Galicia, Spain.

Presenting author: Maria Sonia Gomez

Background: The mid-term respiratory morbidity of RSV is significant. With the implementation of nirsevimab into Galicia’s (Spain) immunization program, the NIRSE-GAL study* aims to establish reference background data using a population-based cohort study to examine its potential impact on short-to-mid-term RSV morbidity.

Methods: Infants hospitalized for RSV between January 1st, 2016, and March 3rd, 2022, were compared to infants without RSV-related hospitalization, matched by day of birth and sex. All analysed data come from the Primary Care (PC) registries from the Galician Health Care Services (SERGAS). The PC episodes were categorized as individual outcomes linked to specific diagnostic codes in primary care (CIAP-2), and as composite outcomes through the combination of relevant CIAP-2 codes (Figure). Adjusted incidence rate ratios (IRR), with 95%CI, by follow up period (from prior 30 days to 2 years post-hospitalization) were calculated employing Poisson regression models to assess the association between RSV hospitalization and CIAP-2 episodes.

Results: We included 3,313 RSV-hospitalized and 3,313 non-hospitalized children (2016:630, 2017:538, 2018:510, 2019:551, 2020:52, 2021:427, 2022:605). Figure 1 shows consistently high IRRs (95%CI) up to 24 months post-hospitalization: Bronchitis [IRR= 2.68 (95% CI: 2.49, 2.9)], bronchiolitis [IRR= 3.3 (95% CI: 2.66, 4.11)] and the composite PC variables Wheezing or Asthma [IRR= 2.31 (95% CI: 2.15, 2.47), Lower Respiratory Infections [IRR= 2.67 (95% CI: 2.47, 2.88), and Acute Respiratory Infections [IRR= 1.52 (95% CI: 1.43, 1.6)].

Conclusions: The mid-term respiratory morbidity of RSV is significant and may be a valuable tool for assessing the cost-effectiveness of RSV prevention programs in this regard.

Abstract category: Evolution & Epidemiology

Keywords: Mid-term Respiratory Morbidity of RSV, Bronchiolitis, Wheezing or Asthma, Primary Care Resources

Conflict of Interest: *The NIRSE-GAL study (CEIC 2023–377) is funded by Sanofi Pasteur/AstraZeneca through a research grant to the Healthcare Research Institute of Santiago.
ESTIMATION OF THE RESPIRATORY SYNCYTIAL VIRUS BURDEN IN ADULTS OF MIDDLE-INCOME COUNTRIES; ARE WE OVERLOOKING ITS BURDEN IN ARGENTINA, BRAZIL, CHILE, MALAYSIA AND MEXICO?

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3. GSK London, UK
4. GSK, Dubai, United Arab Emirates
5. GSK, Ware, Belgium

Presenting author: Jorge A. Gomez

BACKGROUND: Respiratory Syncytial Virus (RSV) has long been considered a disease of young children, but evidence suggests that adult population faces an even more substantial burden worldwide. Its epidemiology is underestimated among older adults due to nonspecific symptomatology, lack of surveillance and routine testing. However, understanding its burden is crucial for developing effective prevention and control strategies. Present study provides an estimation of the burden of RSV in adults of selected middle-income countries: Argentina, Brazil, Chile, Malaysia, and Mexico.

METHODS: We used hospital discharges (HD) and deaths statistics due to any respiratory disease (RD; ICD10 codes J00-J99) by age from each country and the RSV attributable risk reported for RD by outcome (HD or death) and age from the UK, to estimate the rate of RSV HD, RSV mortality and the annual (2019) number of RSV HD & RSV deaths in each country by age group.

RESULTS: Among adults aged ≥20 years, we estimated RSV-HD rates (/100,000) between 29.6-48.0 and RSV mortality rates (/100,000) between 3.1-11.6 in each country. In addition, we estimated the annual RSV-HD and RSV deaths (2019). Increasing RSV rates and burden was identified with increasing age.

CONCLUSIONS: Despite the limited data available, RSV burden in adults should not be overlooked. This study suggests a substantial amount of RSV cases lead to hospitalization and death in middle-income countries, with the highest burden in the elderly. RSV preventive measures could have a major impact on this burden, especially in those ≥50 years old.

<table>
<thead>
<tr>
<th>Age groups</th>
<th>Mexico</th>
<th>Malaysia</th>
<th>Brazil</th>
<th>Argentina</th>
<th>Chile</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 to 64 years</td>
<td>770</td>
<td>257</td>
<td>603</td>
<td>70</td>
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<tr>
<td>65 to 74 years</td>
<td>2,147</td>
<td>555</td>
<td>2,388</td>
<td>168</td>
<td>9,961</td>
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<td>673</td>
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<td>173</td>
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<td>2,29%</td>
<td>251</td>
<td>21,02%</td>
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<tr>
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<td>3,846</td>
<td>4,714</td>
<td>704</td>
<td>56,921</td>
</tr>
</tbody>
</table>

Note: The RSV attributable risk reported by Fleming DJ, et al., Modelling estimate of the burden of Respiratory Syncytial Virus infection in adults and the elderly in the United Kingdom, BMJ, impact 26, 2013

Abstract category: Evolution & Epidemiology

Keywords: RSV Epidemiology, Adult Population, Disease Burden, Hospital Discharges, Deaths

Conflict of Interest: Jorge A. Gómez, Otavio Cintra, Arnas Berzanskis, Abdelkader El Hasnouai, Desirée A.M. van Oorschot, Adriana Guzman-Holst are employed by and hold shares in GSK. The authors declare no other financial and non-financial relationships and activities and no c

EPIDEMIOLOGY AND BURDEN OF HOSPITAL ADMISSIONS DUE TO RESPIRATORY SYNCYTIAL VIRUS IN CENTRAL QUEENSLAND, A SUB-TROPICAL REGION.

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Presenting author: Reema Goswami

Background: There is limited data on RSV circulation and related hospital admissions in sub-tropical regions of Australia. We assessed the epidemiology and hospital burden of RSV in Central Queensland (CQ), a sub-tropical region in Australia.

Methods: As part of RSV surveillance, RSV-specific ICD-10-AM codes (J12.1, J12.5, J21.0 and B97.4) and Palivizumab administrations data between January-2010 and September-2023, and RSV notification data from July-2021 to September-2023 were collected and analysed.

Results: 1,610 RSV-related hospital admissions were documented: mean age 21.3±28.6 years, 46.5%(n=749) female and 20.9%(n=336) Indigenous population. RSV was the primary diagnosis in 59.9%(n=964) of admissions. Among these, 12.8%(n=204) were in infants aged <12 months and 17.6%(n=283) were aged 60 years and over. The mean length of stay was 4.5±2.0 days. Ventilation was required in 13.5%(n=218) of cases, with 2.2%(n=35) needing ICU support and 0.7%(n=11) resulting in deaths. During the study period, 56 high-risk infants were administered Palivizumab. Notably, 27.0%(n=434) of hospital admissions occurred outside the recommended Palivizumab administration period (March-August). Between July-2021 and September-2023, 2,274 lab-confirmed RSV notifications were
reported, with 22.1%(n=502) necessitating hospital admissions. Of all RSV notifications in CQ, 82.1%(n=1,867) were reported between March-August.

Conclusion: The burden of RSV-related hospital admission is markedly high in CQ, with notifications and hospital admissions occurring throughout the year with a winter peak. A substantial proportion of hospital admissions transpire outside the Palivizumab recommended period, suggesting a need for a reassessment of existing preventive policies for RSV.

Funding: The authors acknowledge that this work was supported by Sanofi and AstraZeneca.

Abstract category: Evolution & Epidemiology

Keywords: RSV, Palivizumab, Hospitalisation

Conflict of Interest: None declared

**IMPACT OF EXCLUDING NON-ENGLISH LANGUAGE DATABASES IN SYSTEMATIC LITERATURE REVIEWS ESTIMATING RESPIRATORY SYNCYTIAL VIRUS AND INFLUENZA DISEASE BURDEN IN ADULTS: AN ASIAN PERSPECTIVE**

Aruni Seneviratna (1), Victor Preckler Moreno (2), Maria Moitinho de Almeida (2), Yufan Ho (1)

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2. GSK, Wavre, Belgium

**Presenting author:** Yufan Ho

**BACKGROUND:** Studies reporting respiratory syncytial virus (RSV) burden in Asian adults are limited. Excluding non-English language publications from systematic literature reviews (SLRs) could impact the conclusions of evidence syntheses.

**METHODS:** We reviewed literature between January 1, 2000, and December 13, 2022, examining RSV and Influenza burden in elderly (60+) and 18+ high-risk adults in Japan, South Korea, and Taiwan. PubMed (English), ICHUSHI (Japanese), RISS (Korean), and Airiti (Traditional Chinese) databases were searched. Abstracts were first screened for eligibility, and eligible studies underwent full-text review by two independent reviewers. Data from the final selected studies were extracted.

**RESULTS:** Out of 2,467 citations for RSV and Influenza, 66.3% were from non-English databases. Abstract screening yielded 535 citations (60.7% from non-English databases: RISS=23, Airiti=10, ICHUSHI=292) of which 155 studies (49.0% from non-English databases: RISS=3, Airiti=1, ICHUSHI=72) were finally included for both RSV and Influenza. Non-English citations for Taiwan (5.6%) and Korea (12.0%) were lower compared to Japan (64.3%). For RSV, non-English citations were not found for Korea and Taiwan while Japan had 8 publications, covering incidence, prevalence, and mortality. From English databases, Korea had 3 articles reporting prevalence (including one reporting mortality) and Taiwan had 2 articles reporting prevalence. Japan’s 8 English articles on RSV included 6 reporting prevalence, 4 reporting incidence, and 2 reporting mortality.

**CONCLUSIONS:** Impact of excluding non-English publications from SLRs estimating RSV and Influenza burden in adults vary by country, with potential greater impact in the overall estimates for Japan.

**Abstract category:** Evolution & Epidemiology

**Keywords:** Respiratory Syncytial Viruses; Disease Burden; Healthcare Resource; Asia Pacific; Respiratory Infection; Literature Review

**Conflict of Interest:** All authors are employed by and hold shares in GSK and declare no other financial and non-financial relationships and activities.
THE TREND AND SEVERITY OF RESPIRATORY SYNCYTIAL VIRUS INFECTIONS IN THE GAMBIA (A SCOPING LITERATURE REVIEW)

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2. Study Coordinator in Clinical Research
3. Research Clinician

Presenting author: Abdoulie E. Jallow

RSV is a leading cause of ALRI in children. Influenced by climate and weather conditions, RSV infections in The Gambia follow a similar trend as equatorial and tropical climate countries.

This review assesses the epidemiology, trend and severity of RSV infections over a three-decade period. RSV infections peaked between August and October, affecting infants mainly.

RSV infections were responsible for 19% of all ALRI admissions from 1994 to 1997. A review in 1999 showed risk factors including social, environmental, dietary factors (socio-economic conditions). Interestingly, from December 1999 to October 2000, an uncommon epidemic spread, with one peak occurring in March (during the dry season). From 2001 onwards, epidemics followed a regular pattern during summer months. RSV was more prevalent than other viral infections and was linked to eight times as many ALRI infections as Parainfluenza Virus or Influenza Virus, and during the initial stages of the COVID-19 pandemic, a dramatic reduction in RSV cases in the country.

With infection severity, RSV was discovered as the dominant pathogen to cause severe pneumonia in all Pneumonia Etiology Research for Child Health (PERCH) study sites including The Gambia. RSV accounted for 31.1% of the etiologic distribution of pathogens causing severe pneumonia in children (0-60 months).

In conclusion, RSV remains an important pathogen causing Acute Lower Respiratory infections in Gambian children (0-60 months), and changes in socio-economic status have led to marked improvements in disease prevalence and case management.

Abstract category: Evolution & Epidemiology

Keywords: Acute Lower Respiratory Infections, Respiratory Syncytial Virus (RSV), Severe Pneumonia.

Conflict of Interest: None declared.

EPIDEMIOLOGICAL CHARACTERISTICS OF RESPIRATORY SYNCYTIAL VIRUS INFECTION IN HOSPITALIZED CHILDREN

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Presenting author: Deng Jikui

Objective: To analyze the epidemiological characteristics of acute respiratory infections (ARTI) in children caused by respiratory syncytial virus (RSV) in Shenzhen, and provide reference for RSV prevention.

Methods: From January 2020 to December 2022, children with ARTI who were hospitalized at Shenzhen Children’s Hospital were collected nasopharyngeal swabs for fluorescence PCR detection of 13 respiratory pathogens during hospitalization. This method detected influenza A virus, Bocavirus, coronavirus, H1N1, adenovirus, rhinovirus, PIV, Chlamydia trachomatis, metapneumovirus, influenza B virus, H3N2, and Mycoplasma pneumoniae. Epidemiological analysis was conducted based on clinical data.

Results: The total positive rate of RSV among ARTI patients in Shenzhen from 2020 to 2022 was 12.7% (4689/36945), with annual rates of 19.2%, 17.0% and 4.6% respectively. Male accounts for 62%. 45.6% of cases occur within one year of age. RSV has the highest detection rate from July to October, with an average detection rate of 25.4%. The mixed infection rate of RSV and other respiratory pathogens is 11.5%, mainly nasal viruses (383 cases). 17 cases of reinfection. 534/4675 (11.4%) of the children were premature infants, while other underlying diseases included congenital heart disease, bronchopulmonary dysplasia and immunodeficiency.

Conclusions: RSV is a common pathogen of ARTI in children in Shenzhen, and its prevalence varies in different years. The epidemic period is from July to October, and it is more common in males. The younger the patients, the more susceptible they are. RSV is prone to coinfection with rhinovirus. Reinfection is not uncommon. Immunization strategies should be paid attention to the peak outbreaks in different regions.

Abstract category: Evolution & Epidemiology

Keywords: Respiratory Syncytial Virus; Acute Respiratory Tract Infection; Epidemiological Characteristics

Conflict of Interest: None declared.
RISK OF RSV-ASSOCIATED HOSPITALIZATIONS AMONG U.S. CHILDREN WITH AND WITHOUT SELECT UNDERLYING CONDITIONS, 2015-2021

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Presenting author: Jefferson Jones

Background: CDC recommends nirsevimab to prevent RSV disease for infants born during or entering their first RSV season. For children entering their second RSV season, nirsevimab is recommended for certain children at increased risk for severe disease. Limited data are available to quantify the risk of severe RSV disease for most chronic conditions in children in their second season.

Methods: International Classification of Diseases 9 and 10 codes were used to identify children with and without select underlying chronic conditions and RSV-associated hospitalizations in the Merative™ MarketScan® Commercial and Multistate-Medicaid Databases. Adjusted prevalence ratios (aPR) for RSV-associated hospitalization were estimated for U.S. children aged 12-23 months with a single underlying condition compared with 2 groups of children without select underlying conditions (aged 12-23 months and aged 0-11 months), adjusting for demographic variables.

Results: Compared with children aged 12-23 months without underlying conditions, children with each underlying condition had increased prevalence of RSV-associated hospitalization (aPR for commercial insurance database ranged from 3.5 [95% CI, 2.4–5.0] for non-severe congenital heart disease to 64.2 [95% CI, 35.4–116.5] for chronic lung disease). Results were similar for children with Medicaid (Figure 1). Among children aged 12–23 months, most underlying conditions were associated with increased prevalence of RSV-associated hospitalization compared with infants without select underlying conditions (Figure 2).

Conclusion: Several chronic conditions may be associated with increased risk of RSV hospitalization in children aged 12-23 months. Studies accounting for testing bias are needed to estimate RSV disease burden by chronic condition.

Abstract category: Evolution & Epidemiology
Keywords: RSV, Epidemiology, Risk Factors, Hospitalization
Conflict of Interest: None declared.

SUPPORTING PEDIATRIC RSV CLINICAL TRIALS THROUGH CLOSE EPIDEMIOLOGICAL SURVEILLANCE DURING THE SARS-COV-2 PANDEMIC

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Presenting author: Rennie Joshi

Background:Clesrovimab is an extended half-life monoclonal antibody against respiratory syncytial virus (RSV), intended to protect infants for an entire RSV season. The clesrovimab clinical trials teams have faced significant difficulties to conduct trials due to SARS-CoV-2’s disruption of RSV seasonality. The anticipated enrollment of approximately 4000 infants in 300 sites across 30 countries has been challenging.

Objective:To describe the pandemic’s impact on RSV epidemiology and the mitigations implemented to support clinical development of clesrovimab.

Methods:During the pandemic, several activities were implemented to monitor RSV in near real-time. Specifically, RSV and SARS-CoV-2 surveillance data sources were investigated, and a country-specific data dashboard was established. Disruptions to the timing and severity of RSV seasonal circulation were monitored to recommend optimal enrollment windows.

Results:In 2020, RSV activity was very low or absent in most countries. In 2021, RSV resurfaced early in some countries like Denmark where circulation was observed from late summer. In others, such as South Korea, circulation was delayed. This resulted in significant disruption of trial enrollment windows in most countries. Anticipating a similar disruption in 2022, strict monitoring of RSV and SARS-CoV-2 surveillance data, coupled with site-level investigators’ feedback, allowed the determination of enrollment windows to match real or predicted RSV circulation patterns for each country/site. This strategy enabled us to capture the peak RSV circulation, allowing timely administration of clesrovimab to participants per study protocols.

Conclusion: RSV epidemiology was significantly disrupted during the pandemic. Vigilant monitoring of RSV and SARS-CoV-2 activity was crucial in supporting optimal enrollment in clinical trials.

Abstract category: Evolution & Epidemiology
Keywords: Clesrovimab, SARS-COV-2, RSV, RSV seasonality, monoclonal antibody, RSV epidemiology
Conflict of Interest: All authors are employed by Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

RSV: CLINICAL AN EPIDEMIOLOGICAL PATTERN IN CHILDREN ADMITTED IN A PEDIATRIC HOSPITAL IN BUENOS AIRES AFTER COVID-19 PANDEMIC

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3. Commission of Investigations, Buenos Aires Province (CIC), Argentina

Presenting author: Maria del Valle Juarez

Introduction: Respiratory syncytial virus (RSV) is a significant pathogen affecting infants and young children. This study aims to characterize the clinical and epidemiological patterns of acute lower respiratory tract infection (ALRI) cases caused by RSV in a pediatric hospital in Buenos Aires city during 2023.

Materials and Methods: observational, cross-sectional, descriptive design including patients hospitalized for ALRI between weeks 1 and 27 of 2023. Virological diagnosis was conducted using RT-PCR.

Results: A total of 256 ALRI patients were hospitalized, of which 88% tested positive for a viral infection. RSV was the most prevalent (145;66%), with early-onset circulation in peak 17 and peaking in week 21. Rhinovirus (n=57;26%) ranked second. Influenza A (n=20;9%) cases started increasing when RSV cases reached their maximum (EW19).
RSV cases median age of 6.5 months, 56.5% male. Comorbidities were present in 42% of cases (chronic lung disease being the most common). Additionally, 10% were preterm infants, and 9% had congenital heart disease. Nearly 60% had an incomplete vaccination schedule. The most frequent symptoms were cough (65%), fever (63%), and respiratory difficulty (86%). Bronchiolitis was the predominant clinical presentation (85%). Coinfections were observed in 17% of cases, primarily with rhinovirus. The median hospitalization duration was 7 days, with 25% requiring intensive care. No fatal cases were reported.

Conclusion: In the first half of 2023, RSV circulation began earlier than in previous years. It predominantly affected previously healthy infants, and a significant portion required intensive care. Molecular techniques allowed the detection of coinfections in 17% of cases.

Abstract category: Evolution & Epidemiology

Keywords: RSV, Epidemiological Patterns, Acute Lower Respiratory Tract Infection, Cross-Sectional Study

Conflict of Interest: None declared.

### PATTERNS AND INCIDENCE OF OTITIS MEDIA (OM) AFTER FIRST MEDICALLY ATTENDED RESPIRATORY SYNCYTIAL VIRUS (MA-RSV) DIAGNOSIS IN US INFANTS BETWEEN 2017-2022

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2. Pfizer, USA - PA - Remote
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5. Pfizer, USA - CA - Remote
6. Pfizer, CAN - ON - Remote

Presenting author: Jennifer Judy

Otitis media (OM, middle ear infection) has a seasonal pattern that parallels the respiratory virus season and often coincides with or follows a respiratory tract infection (e.g., pneumonia, RSV, influenza). Given the decrease in OM in the US after the introduction of pediatric pneumococcal conjugate vaccines, a future decline in RSV-associated OM is plausible after the recent introduction of RSV preventatives. We described baseline patterns and incidence of OM following first medically attended RSV (MA-RSV) diagnosis among infants in the US.

This was a retrospective cohort study of infants with a first MA-RSV diagnosis at ≤1 year of age between 2017-2022 using Pharmetrics data, which provides longitudinal healthcare and pharmacy claims for a generally representative population of commercially-insured individuals in the US. We estimated the incidence proportion of OM (ICD-10-CM H66*) within 90 days after MA-RSV, overall and by age and care setting of MA-RSV.

Among 120,375 infants with a first MA-RSV (red data bars), most were treated in the outpatient setting (75%) and 38,518 (32%) developed OM (dark blue). The number of MA-RSV and OM cases peaked at age 5 months. The proportion of infants who developed OM (light blue) increased with increasing age of first MA-RSV until approximately 6 months of age, then stabilized. Infants <3 months—who were more likely to require emergent/inpatient RSV care—had a lower incidence of subsequent OM.

These results provide a baseline for the relationship between MA-RSV in infants and OM ahead of widespread availability and uptake of RSV prophylaxis.

### Figure 1: Patterns of 1st Medically-Attended RSV Infections and Subsequent Otitis Media Diagnoses; Overall, by Age of RSV Infection, and Setting of Care for RSV

<table>
<thead>
<tr>
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<th>Emergency Room (OM)</th>
<th>Inpatient (OM)</th>
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<tr>
<td></td>
<td>RSV Patients</td>
<td>Subsequent OM</td>
<td>RSV Patients</td>
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<tr>
<td>N</td>
<td>N (%)</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
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<td>38,518</td>
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Abstract category: Evolution & Epidemiology

Keywords: RSV, Infants, Otitis Media, Real-World Evidence

Conflict of Interest: All authors are employees of Pfizer and may hold stock/stick options in Pfizer Inc.
PREVALENCE OF VIRAL INFECTIONS: HIV, COVID-19 AND HEPATITIS B VIRUS IN TUBERCULOSIS PATIENTS AT THE JAMOT HOSPITAL OF YAOUNDE, CAMEROON

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Presenting author: Diane Kamdem Thiomo

BACKGROUND: Tuberculosis is a major public health problem in the world, particularly in developing countries. Its association with viral infections forms a deadly combination. The number of deaths related to tuberculosis is estimated at 1.6 million people (WHO, 2022). Morbidity and mortality are still high, this could be due to co-infection by viruses and by emergence of resistant strains. The aim of this study was to determine the prevalence of HIV, COVID-19 and Hepatitis B Virus in tuberculosis patients in Yaoundé Jamot hospital.

METHODS: We carried out a cross-sectional study. Sputum, blood and nasopharyngeal samples were collected from 271 tuberculosis (TB) patients aged 21 or above, from September 2022 to April 2023. A microscopic examination was performed, the determination of the anti HIV 1/2 antibody, the antigens of Hepatitis B Virus (HBV) and the antigens of COVID-19 were made by rapid diagnostic tests based on the immuno-chrommatographic method.

RESULTS: The male sex was predominantly represented 70.5% (191) compared to the female sex 29.5% (80) among the 271 patients recruited. 73.8% (200) were mono-infected TB patients. The prevalence of TB/HIV co-infection was 13.6% (37), for the TB/HBV co-infection was 10.7% (29) and 0.4% (01) for TB/COVID-19 co-infection. We also obtained the triple infections prevalence of TB/HIV/HBV 1.1% (03) and 0.4% (01) TB/HIV/COVID-19.

CONCLUSION: These results show that the prevalence of viral infections remains high in tuberculosis patients. Their diagnosis is necessary for a better management of tuberculosis patients by the initiation of a bi or tri-therapy.

Abstract category: Evolution & Epidemiology
Keywords: Co-Infections, HIV, Hepatitis B Virus, COVID-19, Tuberculosis

Conflict of Interest: None declared.

SEVERITY OF HUMAN METAPNEUMOVIRUS (HMPV) DISEASE IN OLDER AND HIGH-RISK ADULTS: A SYSTEMATIC LITERATURE REVIEW

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Presenting author: Niranjan Kanesa-thasan

Background: HMPV causes respiratory infections in older and high-risk adults. We summarized evidence on HMPV disease burden in both populations.

Methods: We searched Embase and MEDLINE for articles published between 01/01/2000 and 12/06/2023 reporting the burden of HMPV disease in adults ≥ 50 years or ≥ 18 years with comorbidities (high-risk) in developed countries. A random-effects meta-analysis was used to summarize the outcomes.

Results: Out of 2,847 articles, 119 were included (Figure). In symptomatic older adults, HMPV prevalence was 3.4% (95% CI: 2.7–4.2) in annual studies and 4.0% (95% CI: 2.9–5.3) in seasonal studies. 3.8% (95% CI: 0.5–22.8%) of HMPV cases were hospitalized and 11.9% (95% CI: 7.3–18.8%) admitted to the ICU. The case fatality rate (CFR) was 5.2% (95% CI: 2.6–10.0). In symptomatic high-risk adults, HMPV prevalence was 4.3% (95% CI: 3.2–5.7) in annual studies and 5.1% (95% CI: 3.2–7.9) in seasonal studies. Hospitalization, ICU admission, and CFR were 51.4% (95% CI: 33.2–69.3%), 6.2% (95% CI 4.4–8.7%), and 9.3% (95% CI: 4.6–18.0), respectively. Limited incidence, complications, seasonality, transmission, or risk factor data precluded further meta-analyses.

Discussion: While viruses such as RSV are considered major pathogens in older adults, our findings reveal HMPV is also a relevant agent in developed countries.

Abstract category: Evolution & Epidemiology
Keywords: human metapneumovirus; hMPV; systematic literature review; SLR; epidemiology; severe disease

Conflict of Interest: None declared.

A SCOPING REVIEW OF BURDEN OF RSV INFECTION IN YOUNG CHILDREN IN INDIA

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2. Bill and Melinda Gates Foundation

Presenting author: Amanjot Kaur

Background: Respiratory Syncytial Virus (RSV), is one of the major causative agents of Lower Respiratory Tract Infections (LRTI) in young children across the globe including India. Multiple studies report varying prevalence of RSV ranging from 2.1% to 62.4%. Therefore, the aim of this study is to review the prevalence of RSV across different regions in India to generate evidence for planning future interventions to reduce the burden of RSV.

Method: A search strategy, including appropriate key words, was used to conduct a literature search using multiple databases (Google Scholar, PubMed, EbeSco).

Grey literature including official reports and fact sheets were also referred to. Only English language publications which reported RSV in young children (less than 5 years) were included.

RESULTS: Out of 2,847 articles, 119 were included (Figure). In symptomatic young children, the prevalence of RSV was 3.4% (95% CI: 2.7–4.2). RSV was associated with hospitalization (33.2%, 95% CI: 22.8–45.9%), intensive care unit admission (9.4%, 95% CI: 3.4–16.0%), mechanical ventilation (2.7%, 95% CI: 0.4–9.1%), and death (0.9%, 95% CI: 0.4–1.5%). Among these, the CFR was 5.2% (95% CI: 2.6–10.0).

CONCLUSION: These results show that the prevalence of RSV infection remains high in young children. Their diagnosis is necessary for a better management of RSV patients by the initiation of appropriate treatment.

Abstract category: Evolution & Epidemiology
Keywords: Respiratory Syncytial Virus, RSV; systematic literature review; SLR; epidemiology; severe disease

Conflict of Interest: None declared.
5 years of age) and published in the last 10 years were included in the review.

Results: The preliminary findings show that the rate of new episodes of RSV-associated Acute Lower Respiratory Infection and the morbidity and mortality is higher among children less than 5 years of age. In India, RSV mainly peaks in winter in North India and some correlation with low temperature has been observed. A few studies also document the seasonal peak in RSV outbreaks.

Conclusion: As the review is still underway, it is anticipated that the comprehensive analysis will help in designing efforts towards prevention of RSV LRTIs. Majority studies suggest that RSV vaccination plays a key role in reducing the disease burden.

Abstract category: Evolution & Epidemiology

Keywords: RSV burden, Children under Five, India

Conflict of Interest: None declared.

BURDEN OF RESPIRATORY SYNCYTIAL VIRUS-ASSOCIATED ACUTE RESPIRATORY INFECTIONS DURING PREGNANCY

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3. Centers for Disease Control and Prevention, Atlanta, Georgia, USA.
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6. School of Public Health, Nanjing Medical University, Nanjing, Jiangsu, China.

Presenting author: Sebastien Kenmoe

Introduction: With the licensure of maternal RSV vaccines in Europe and USA, data are needed to better characterize the burden of respiratory syncytial virus (RSV)-associated acute respiratory infections (ARI) in pregnancy. This study aims to determine among pregnant individuals (PI) the proportion of ARI testing positive for RSV and RSV incidence rate, RSV-associated hospitalizations, deaths, and perinatal outcomes.

Methods: We conducted a systematic review following PRISMA 2020 guidelines using five databases (Medline, Embase, Global Health, Web of Science and Global Index Medicus) and included additional unpublished data. Pregnant individuals with respiratory infections who had respiratory samples tested for RSV were included. We used a random-effects meta-analysis to generate overall proportions and rate estimates across studies.

Results: Eleven studies with PI recruited between 2010 and 2022 were identified, most of which recruited PI in community, inpatient and outpatient settings. Among 8126 PI, the proportion with respiratory infections that tested positive for RSV ranged from 0.9% to 10.7%, with a meta-estimate of 3.4% (95% CI: 1.9; 5.4). The pooled incidence rate of RSV infection episodes among PI was 26.0 (15.8; 36.2) per 1000 person-years. RSV hospitalization rates reported in two studies were 2.4 and 3.0 per 1000 person-years. Of five studies that ascertained RSV-associated deaths among 4708 PI, no deaths were reported. Three studies comparing RSV-positive and RSV-negative PI found no difference in odds of miscarriage, stillbirth, low birth weight, and small for gestational age. RSV-positive PI had higher odds of preterm delivery (odds ratio 3.6 [1.3; 10.3]).

Conclusion: Data on RSV-associated hospitalization incidence rates in PI are limited but available estimates are lower than those reported in older adults and young children. As countries debate whether to include RSV vaccines in maternal vaccination programs, which are primarily intended to protect infants, this information could be useful in shaping vaccine policy decisions.

Abstract category: Evolution & Epidemiology

Keywords: Respiratory Syncytial Virus; Pregnant Women; Disease Burden

Conflict of Interest: The study is supported by the Preparing for RSV Immunisation and Surveillance in Europe (PROMISE) project, which 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 programmes and EFPIA.

RSV-ATTRIBUTABLE ANTIBIOTIC PRESCRIPTIONS IN CHILDREN IN THE UNITED STATES, 2008-2018

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2. University of Alabama at Birmingham

Presenting author: Laura King

Background: Respiratory Syncytial Virus (RSV) is a common cause of Acute Respiratory Infections (ARIs) in children. Although viral, RSV contributes to antibiotic prescribing due to etiologic uncertainty in ARIs and concomitant bacterial infections. Thus, vaccination against RSV may reduce antibiotic use. We aimed to estimate the proportion of outpatient antibiotic prescriptions attributable to RSV within a commercially-insured cohort of children in the United States from 2008–2018.

Methods: We measured pediatric antibiotic prescriptions from the Optum Clinformatics™ DataMart. We modeled weekly incidence rates of overall and ARI-associated antibiotic prescriptions among children aged 0–17 years using negative binomial regression. We included harmonic and secular trend terms to capture seasonal patterns and temporal trends, controlling for weekly influenza activity. We estimated RSV-attributable antibiotic prescribing as the difference between observed prescribing rates and model-predicted rates in the absence of RSV.

Results: Within the study population, 4.7% (95% confidence interval 4.0–5.3%) of all antibiotic prescriptions were attributable to RSV among children aged 0–17 years, translating to 88 (76, 100) RSV-associated antibiotic prescriptions per 1000 person-years during the study period. Among children aged <2 years, RSV accounted for 6.0% (5.3–6.8%) of antibiotic prescriptions. In all children 0-17 years, 8.7% (7.3–10.1%) and 8.2% (7.2–9.1%) of antibiotic prescriptions for lower respiratory tract infections and acute otitis media, respectively, were attributable to RSV.

Conclusions: RSV accounts for substantial burdens of antibiotic use in children, especially children <2 years of age. Vaccination against RSV may contribute to reductions in antibiotic use among children.
Abstract category: Evolution & Epidemiology

Keywords: Children, antibiotics, outpatient

Conflict of Interest: Ms. King reports consulting fees from Merck Sharpe & Dohme and Vaxcyte for unrelated work. Dr. Bruxvoort reports research support from Moderna, Dynavax, Gilead, GlaxoSmithKline, and Pfizer for unrelated work. Dr. Tartof reports research grants from Pfizer for unrelated work. Dr. Lewnard reports research grants from Pfizer and Merck Sharpe & Dohme and consulting fees from Pfizer, Merck, Sharpe & Dohme, and Vaxcyte for unrelated work.

MOLECULAR EPIDEMIOLOGY OF RSV CIRCULATING IN PORTUGAL DURING THE 2021/2022 AND 2022/2023 SEASONS

Miguel Lança (1) Ana Paula Rodrigues (2) Maria de Jesus Chasqueira (3) Raquel Guioimar (1) Aryse Melo (1) VigiRSV Network (4)

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2. Department of Epidemiology, National Institute of Health Doctor Ricardo Jorge, Portugal
3. Comprehensive Health Research Center, NOVA Medical School, Faculdade de Ciências Médicas, Universidade NOVA de Lisboa, Portugal
4. VigiRSV network (National Network for RSV Surveillance)

Presenting author: Miguel Lança

Considering the introduction of new therapeutics and vaccines for RSV in the near future, the investigation of the correlation between molecular and clinical epidemiology is crucial. This study aims to assess genetic diversity of RSV according to severity of disease in hospitalized children under 2 years-old, during 2021/2022 and 2022/2023 seasons. Partial sequencing of the G gene was performed in RSV-positive samples from hospitalized children that met the extended ARI case definition. Sequences presenting the same amino acid mutations were grouped in “constellations”. Genomic diversity was explored according to severity, which was established based on the need for ventilation or admission at intensive care unit. Of 245 characterized RSV (101 RSV-A and 144 RSV-B), 32 severe cases (17 RSV-A and 15 RSV-B) were detected. 42 constellations were identified for RSV-A and 45 for RSV-B. Among severe cases, 7 of RSV A and 2 of RSV-B had unique constellations. The most predominant constellation for both subtypes presented less severe cases (6% for RSV-A and 0% for RSV-B) than the second most predominant (14 and 24 samples for RSV-A and RSV-B, respectively), which owned 4 severe cases of RSV-A and 7 of RSV-B. Almost 30% of sequences from the second most predominant constellation for both subtypes were from severe cases. The next step of our project is to perform whole genome sequencing to evaluate RSV phylogenetics and to identify possible genetic markers for severe disease. Knowing the link between genetic diversity and severe disease could support implementation of preventive and therapeutic measures.

Abstract category: Evolution & Epidemiology

Keywords: RSV; Genomic diversity; Severity; Infants; Portugal

Conflict of Interest: None declared.

DISEASE BURDEN AND HEALTHCARE UTILIZATION ASSOCIATED WITH LOWER RESPIRATORY TRACT INFECTIONS ATTRIBUTABLE TO RESPIRATORY SYNCYTIAL VIRUS AMONG ADULTS

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2. Kaiser Permanente Southern California, United States
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Presenting author: Joseph Lewnard

Background: The contribution of RSV to lower respiratory tract infection (LRTI) burden among adults remains uncertain, in part due to the relationship of RSV test sensitivity with timing, number, and type of specimens collected.

Methods: We analyzed electronic health records from 3,681,430 adults enrolled in Kaiser Permanente Southern California from 2016-2019. Inpatient or outpatient ICD-10 codes for pneumonia or other acute LRTI were enumerated. We fit models for individuals’ probability of RSV testing receipt and likelihood of a positive result accounting for demographic, epidemiologic, and clinical characteristics. We used resulting estimates to evaluate individuals’ likelihood of RSV infection via a two-stage estimation procedure accounting for test sensitivity.

Results: In all settings, RSV accounted for 8.7% (95% confidence interval: 7.0-10.9%) of LRTI among adults aged ≥60 years and 5.8% (4.4-7.6%) among adults aged 18-59 years with high-risk conditions. RSV-associated LRTI incidence was 683 (546-851) episodes per 100,000 annually among all adults aged ≥60 years (521 [406-665] per 100,000 at ages 60-79 years and 1,476 [1,146-1,903] per 100,000 at ages ≥80 years). Among adults aged 18-59 years with high-risk conditions, incidence was 316 [238-416] per 100,000 annually. Most RSV-associated LRTI was diagnosed in outpatient versus inpatient settings (525 [413-665]) and 158 [127-196], respectively). LRTI-related mortality associated with RSV totaled 70 [56-87] deaths per 100,000 adults aged ≥60 years.

Conclusions: Among adults, RSV is associated with substantial LRTI burden in inpatient and outpatient settings. Surveillance of all-cause and outpatient-managed LRTI could assist in measuring vaccine impact due to limited RSV testing in adults.
DETECTION OF RESPIRATORY VIRUSES FROM CHILDREN, TEACHERS AND TOUCH SURFACES IN CHILDCARE CENTRES: PRELIMINARY FINDINGS FROM THE DISEASES TRANSMISSION IN CHILDCARE (DISTANCE) COHORT STUDY

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Introduction: Childcare centre is a high-risk setting for transmission of respiratory viruses. We aimed to understand the risk of transmission in childcare centres by establishing a cohort study that collects data on respiratory infections of children and teachers, contact behaviours of children, and detection of respiratory viruses from touch surfaces in childcare centres.

Methods: We reported the preliminary findings from data collected between 26th September 2022 and 7th June 2023 in one childcare centre in Wuxi, China. Throat swabs were collected weekly from 104 children and 15 teachers from four classes; on the same day, samples from 28 touch surfaces (e.g., desks, door knobs) were collected at the childcare centre. All specimens were tested by multiplex PCR for eight common respiratory viruses.

Results: Over the study period, respiratory viruses were detected most commonly among children (9.2%, 233/2544), followed by teachers (5.9%, 23/389) and least commonly from touch surfaces (3.4%, 25/728); teachers generally had lower incidence rate of viral infections than children for most viruses, except for influenza A in which the incidence rate was comparable (Figure). For a given week, the detection of influenza A was strongly correlated between students, teachers, and touch surfaces (student-teacher r=0.82; student-surface: r=0.73; teacher-surface r=0.58). Similar correlation results were observed for RSV and rhinovirus.

Conclusion: Children in childcare centres generally have higher risks for respiratory viral infections than teachers. Highly correlated detection of respiratory viruses from teachers, students, and touch surfaces suggests their joint contribution to the transmission of respiratory viruses in childcare centres.

Abstract category: Evolution & Epidemiology
Keywords: Respiratory Viruses; Children; Childcare Centre; Transmission; Surface
Conflict of Interest: None declared

ESTIMATION OF RSV-ATTRIBUTABLE INCIDENCE OF HOSPITALIZATIONS AMONG ADULTS IN ITALY BETWEEN 2015 AND 2019

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Presenting author: Caihua Liang

Background: RSV can cause severe outcomes, including cardiovascular events, among older adults and adults with underlying comorbidities. However, RSV burden in adults is not well defined due to non-specific symptoms, lack of routine testing, and reduced diagnostic sensitivity among adults. We estimated RSV-attributable incidence of hospitalizations in adults in Italy during 2015–2019.

Methods: A quasi-Poisson regression model was fitted to estimate RSV-attributable counts of respiratory, and cardiovascular hospitalizations, as well as four respiratory and five cardiovascular disease subgroups, using monthly hospitalization data from the Ministry of Health. The model accounted for periodic and aperiodic time trends and viral activity, with stratification by age groups and risk status. Monthly counts of RSV and influenza hospitalizations in children aged <2 years and adults aged ≥65 years, respectively were used as viral activity proxies.
Results: The estimated RSV-attributable hospitalization incidence increased with age and among adults aged ≥65 years was 262–381 respiratory hospitalizations per 100,000 person-years (accounting for 6–9% of all respiratory hospitalizations). Among adults aged ≥75 years, the subgroups with the highest estimated RSV-attributable incidences for respiratory hospitalizations were chronic lower respiratory diseases and influenza/pneumonia. The subgroups with the highest incidences for RSV-attributable cardiovascular hospitalizations were chronic heart failure exacerbation and arrhythmia.

Conclusions: RSV-attributable respiratory hospitalization incidence was comparable to other European countries time-series studies. Adding cardiovascular diseases increased estimated hospitalization burden substantially, especially among older adults.

Abstract category: Evolution & Epidemiology

Conflict of Interest: Chukwuemeka Onwuchekwa, Estelle Méroc, Aleksandra Polkowska-Kramek, Robin Bruyndonckx, Thao Mai Phuong Tran, and Solomon Molain are employees of P95 Epidemiology & Pharmacovigilance, which received funding from Pfizer to conduct the research described in this abstract and for abstract development. Raffaella Iantomasi, Giuseppe Pietro Innocenti, Elizabeth Begier, Caihua Liang, and Bradford D. Gessner are Pfizer employees and may own Pfizer stock. Daniela D’Angela is a data provider and received funding from P95 for providing research data.

ESTIMATION OF SYMPTOMATIC RESPIRATORY SYNCYTIAL VIRUS (RSV) INFECTION INCIDENCE IN ADULTS IN MULTIPLE COUNTRIES: A TIME-SERIES MODEL-BASED ANALYSIS PROTOCOL

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2. Pfizer Inc, USA; Pfizer Inc, France; Pfizer Inc, Ireland.

Presenting author: Caihua Liang

Background: Estimating RSV burden in adults is challenging due to non-specific symptoms, infrequent standard-of-care testing, resolution of viral shedding before seeking medical care, lower diagnostic test sensitivity compared to children, and variable sensitivity based on different upper airways specimen sources. Model-based approaches can be applied to more accurately estimate RSV burden. This study protocol defines a set of core elements for a time-series model-based approach to estimate RSV incidence rate in adults that can be adapted to specific databases.

Methods: Data are analyzed using a quasi-Poisson regression model, considering the effect of seasonal trends and pathogen co-circulation. Outcomes to be modelled are based on ICD code groupings and include the number of cardiorespiratory (I00–I99), respiratory (I00–I99), and cardiovascular (I00–I99) events from hospitalizations, ED visits, outpatient visits and deaths, stratified by age and risk status. Additional subgroup-specific estimates can be obtained by modeling the number of events in specific ICD-based subgroups. Pathogen co-circulation is represented by viral proxies defined as RSV hospitalizations (B97.4, J21.0, J12.1, J09–J11) in adults ≥60/65 years, lagged up to 4 weeks based on the model selection. Model selection is based on p-values and test statistics. The yearly incidence rate and percentage of events attributable to RSV is estimated from the final model. Confidence intervals are calculated using residual bootstrapping.

Conclusions: This time-series analysis protocol is used in countries globally to provide local RSV disease burden estimates to support public health decision making such as immunization policy.

Abstract category: Evolution & Epidemiology

Conflict of Interest: Aleksandra Polkowska-Kramek, Robin Bruyndonckx, and Thao Mai Phuong Tran are employees of P95 Epidemiology & Pharmacovigilance, which received funding from Pfizer to conduct the research described in this abstract and for abstract development. Elizabeth Begier, Caihua Liang, Charles Nuttens, and Bradford D. Gessner are Pfizer employees and may own Pfizer stock.

INCIDENCE OF RSV-ATTRIBUTABLE HOSPITALIZATIONS AMONG ADULTS IN ONTARIO, CANADA BETWEEN 2013 AND 2019

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Presenting author: Caihua Liang

Background: In adults, RSV burden is underestimated due to non-specific symptoms, limited standard-of-care testing, low diagnostic test sensitivity, and variable sensitivity based on upper airway specimen source. We estimated RSV-attributable hospitalization incidence among adults ≥18 years in Ontario (Canada) using a retrospective time-series model-based approach.

Methods: We collected weekly hospitalization data from the Institute for Clinical Evaluative Sciences (ICES) data repository (2013–2019). We estimated RSV-attributable counts of respiratory (ICD10 codes: J00–I99), cardiovascular (I00–I99), and cardiorespiratory (I00–I99, J00–J99) hospitalizations stratified by age-group and risk-group. Corresponding incidence rates were stratified by age-group only, as risk-group-denominator data were unavailable. We used a Quasi-Poisson regression model, accounting for baseline seasonal variation and viral activity (RSV and influenza).

<table>
<thead>
<tr>
<th>Incidence rate range (overall)</th>
</tr>
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<tbody>
<tr>
<td>18–44 years</td>
</tr>
<tr>
<td>All respiratory (I00–I99)</td>
</tr>
<tr>
<td>Influenza/pneumonia</td>
</tr>
<tr>
<td>Bronchitis or bronchiolitis</td>
</tr>
<tr>
<td>Chronic lower respiratory diseases</td>
</tr>
<tr>
<td>Upper respiratory diseases</td>
</tr>
</tbody>
</table>

*Model is based on upper airway specimen source.
**Sensitivity based on different upper airways specimen sources.
Results: RSV-attributable cardiorespiratory hospitalization incidence increased with age, from 14–18 hospitalisations/100,000 person-years (18-49 years) to 317–411/100,000 (≥75 years) (Table). In patients ≥60 years, RSV-attributable incidence rates were highest for cardiorespiratory hospitalizations (186–246/100,000, 3-4% of all-cardiorespiratory hospitalizations), followed by their components: respiratory hospitalizations (144–192/100,000, 5-7% of all-respiratory hospitalizations) and cardiovascular hospitalizations (95–126/100,000, 2–3% of all-cardiovascular hospitalizations).

Conclusion: Estimated RSV-attributable respiratory hospitalization incidence among people ≥60 years is comparable to other incidence estimates from high-income countries, including model-based and pooled prospective estimates adjusted for diagnostic-testing based under-ascertainment. Recently introduced RSV vaccines could have a substantial public health impact.

Abstract category: Evolution & Epidemiology
Keywords: Canada; Disease burden; Hospitalization; Incidence; Modelling; Quasi-Poisson regression; Respiratory Syncytial Virus

Conflict of Interest: Marriana Mitratza, Aleksandra Polkowska-Kramek, Robin Bryundconcx, Thao Mai Phuong Tran, Worku Byadgie Ewetnu, Pimnara Peerawaranan, are employees of P95 Epidemiology & Pharmacovigilance, which received funding from Pfizer to conduct the research described in this abstract and for abstract development. Elizabeth Begier, Caihua Liang, Malak Elsobky, Charles Nuttens, Ana Gabriela Grajales, Sazini Nzula, Bradford D. Gessner are Pfizer employees and may own Pfizer stock.

CHARACTERISTICS OF HUMAN RESPIRATORY SYNCYTIAL VIRUS (HRSV) EPIDEMIC IN CHINA IN THE 2022/2023 SEASON: 1ST YEAR REPORT FROM A SEASONALITY SURVEILLANCE STUDY IN CHINA

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Presenting author: Silu Liu

Background: To ascertain the epidemic trend and characteristics of HRSV in children, a prospective seasonality surveillance is conducted in sentinel hospitals from 7 cities in China.

Methods: Approximately 10 randomly selected children <2 years old with extended severe acute respiratory infection (SARI) were included from each city weekly. Epidemic trend and clinical characteristics of HRSV cases were described based on PCR-confirmed HRSV SARI cases enrolled between June 2022 and July 2023.

Results: A total of 3,029 extended SARI children <2 years old were enrolled. The overall hospitalization incidence for RSV ranged from 203/100,000 person-years in the northern region to 408/100,000 in the southern region. The highest hospitalization incidence was observed in children ≤1 year of age, followed by children aged 1–5 years.

Conclusion: The seasonal peak of HRSV epidemic in China was delayed until April in 2022/2023, probably due to the non-pharmaceutical interventions during the COVID-19 pandemic. Continuous national HRSV surveillance is urgent need.

Acknowledgements: This study is jointly funded by Sanofi and AstraZeneca.

Abstract category: Evolution & Epidemiology
Keywords: Human Respiratory Syncytial Virus, Seasonality, Surveillance, China

Conflict of Interest: None declared

RSV BURDEN OF DISEASE: HOSPITALIZED AND OUTPATIENTS CASES OF ACUTE RESPIRATORY INFECTIONS (ARI)

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Introduction: Acute Respiratory Infections (ARI) are one of the major causes of morbidity and mortality in developing countries, with respiratory syncytial virus (RSV) being the main agent in infants and young children pediatric population. Globally, changes in post-pandemic epidemiological patterns were observed.

Objective: To compare the clinical and epidemiological pattern of ARI cases under 18 years of age with and without hospitalization criteria in a pediatric hospital in Buenos Aires between EW 1-52 of 2023.

Methods: Observational, cross-sectional, descriptive study of patients with respiratory symptoms with and without requirement of hospitalization in 2023. Virolological diagnosis was made by RT-PCR of nasopharyngeal aspirates.

Results: During 2023, a total of 482 hospitalized ARI cases were reported, 83.6% tested positive for viruses; RSV was the most prevalent (n=165; 41%) with an OR of 2.05 (95%CI: 1.38-3.04), followed by influenza A (n=94; 23%), rhinovirus (n=34; 18%), Parainfluenza (n=19; 10%), metapneumovirus (n=7; 9%), CoV (5.8%), adenovirus (4.7%) and SARS-CoV-2 (2.6%). RSV cases had coinfection in 19%, more frequently with influenza A and rhinovirus. RSV outpatient cases had a median age of 1.7 months (IQR 0.7-3.1 months), while inpatients had a median age of 2.7 years (IQR 1.2-3.6 years). The most frequent symptoms of RSV hospitalization were cough (n=62; 98.4%), rhinorrhea (n=61; 96.8%) and fever (n=52; 82.5%). 76% (n=126) of RSV outpatient cases had previous contact with asymptomatic cases; 15% (n=24) had history of hospitalization for respiratory symptoms and 39% had comorbidities being the most frequent chronic lung disease (n=14; 22%); 76% (n=126) had complete vaccination schedules and 31.7% attended educational institutions or kindergarten.

Conclusion: In 2023, RSV was the most frequent agent causing ARI in pediatric population in both outpatient and hospitalized cases, showing an earlier onset of RSV circulation (EW 17). Hospitalized cases were younger with higher frequency of comorbidities compared to outpatients. A fifth of them required intensive care during hospitalization. The use of molecular techniques for viral detection made it possible to show almost 20% of coinfections, mainly with rhinovirus.

Abstract category: Evolution & Epidemiology

Keywords: RSV, Burden Of Disease, Epidemiology, Viral Circulation

Conflict of Interest: None to declare

EXPLORATORY ASSESSMENT OF MID-TERM RESPIRATORY MORBIDITY OF RSV INFECTION IN THE CHILD POPULATION USING RESPIRATORY RELATED PRIMARY CARE VISITS. A POPULATION-BASED LONGITUDINAL STUDY IN GALICIA–SPAIN.

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Presenting author: Narmean Mallah

Aiming at assessing respiratory mid-term morbidity of RSV infection in children, we undertook a longitudinal population-based study that involved all infants born in Galicia-Spain between 2016 and 2021. We evaluated the association of RSV hospitalization with posterior primary healthcare visits (PCV) due to potentially related respiratory diagnosis. We defined RSV hospitalization as exposure and PCV as an outcome. Participants were matched by gender and birth date and followed until June 1st, 2023/death/outcome occurrence, whatever happened first. Odds ratios (ORs) of PCV and their 95% confidence intervals (CI) were estimated by Poisson regression models.

A total of 6630 PCVs were analysed. Compared with infants who had not been hospitalized for RSV, previous RSV hospitalization was associated with >6 folds higher odds of visiting primary healthcare for respiratory fatigue/dyspnea (OR=6.18; 95%CI: 3.41-12.36). It was also associated with increased odds of PCV for ear pain (OR=1.35; 95%CI: 1.13-1.62), ear discharge (OR=2.08; 95%CI: 1.09-4.16), external otitis (OR=1.42; 95%CI: 1.09-1.84), otitis media/acute meningitis (OR=1.45; 95%CI: 1.34-1.57), serous otitis media (OR=1.38; 95%CI: 1.08-1.64), gasping/wheezing (OR=1.98; 1.43-2.78), cough (OR=1.53; 95%CI: 1.4-1.67), sneezing (OR=1.34; 95%CI: 1.1-1.64), signs/symptoms throat/pharynx/tonsil (OR=1.24; 95%CI: 1.06-1.46), streptococcal pharyngitis tonsillitis (OR=1.75; 95%CI: 1.5-2.05), upper acute respiratory infection (OR=1.38; 95%CI: 1.31-1.45), acute tonsillitis (OR=1.56; 95%CI: 1.38-1.77), acute laryngitis/tracheitis (OR=1.52; 95%CI: 1.38-1.68), influenza (OR=1.59; 95%CI: 1.28-1.99), asthma (OR=2.93; 95%CI: 2.48-3.48), and other breathing problems (OR=2.0; 95%CI: 1.45-2.79). Our findings suggest that these endpoints can be valid to explore the impact of RSV preventive measures on short-mid-term respiratory morbidity and assessment of the cost-effectiveness of prevention programs.

Abstract category: Evolution & Epidemiology

Keywords: RSV, Galicia-Spain; Longitudinal Study, Respiratory Morbidity, Children

Conflict of Interest: None declared
RESPIRATORY SYNCTYIAL VIRUS HOSPITALISATION BURDEN IN OLDER ADULTS IN EUROPEAN COUNTRIES: PRELIMINARY RESULTS FROM A SYSTEMATIC ANALYSIS

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Presenting author: Alen Marijam

Background: The disease burden of RSV in older adults is substantial but not well quantified previously. We aimed to estimate country-specific hospitalisation burden of RSV-associated ARI in older adults (>60 years) in Europe.

Methods: We collected published data (through a systematic review) and unpublished data (from GSK-sponsored studies and international collaborators) on RSV hospitalisation burden. We used multiple imputation for missing age bands. We applied stepwise statistical adjustment to account for case underascertainment related to the variations in case definitions, clinical specimens and RSV diagnostic tests in individual studies. We reported country-level RSV hospitalisation rates for countries with ≥1 eligible study reporting point estimate and 95% CI of the rates (a random-effects meta-analysis was conducted when ≥2 studies were available). As an alternative method, we additionally included studies not reporting 95% CI and calculated the median of the rate point estimates.

Results: Seven studies were included from five countries: Denmark (1), Finland (1), Netherlands (1), Spain (1) and UK (3). Denmark and Spain had the highest and lowest adjusted RSV-associated hospitalisation rate (408/100000, 95% CI: 319-516; and 176/100000, 137-226) in >60 years, which was about 2.4 times the unadjusted estimate. The alternative method with 5 more studies added had similar estimates for the five countries; another country (Norway) was added and it had the highest adjusted hospitalisation rate (742/100000). RSV-associated hospitalisation rate increased with increasing age across all countries.

Conclusions: With RSV vaccines now approved for use in older adults, our findings help inform the need for country-level RSV prevention.

Abstract category: Evolution & Epidemiology

Conflict of Interest: TZ, SM, YM and SS: None declared; HH: Grants to institution from: Icosavax, Innovative Medicines Initiative, Pfizer; Consulting fees to institution from Bill and Melinda Gates Foundation, Pfizer, Sanofi, WHO; Payment or honoraria to institution from AbbVie; Meeting travel support from Sanofi; Data Safety Monitoring Board or Advisory Board participation from: GSK, Icosavax, Janssen, Merck, Novavax, Pfizer, Resvnet, Sanofi, WHO; MIF: Employee and stock holder of GSK; RMF: Employee of GSK; XW: Funding to institution from GSK; Grants or contracts from WHO, Wellcome Trust; Consulting fees from Pfizer, WHO; Payment or honoraria from Pfizer; Meeting travel support from Pfizer.

THE IMPACT OF COVID-19 ON RESPIRATORY SYNCTYIAL VIRUS ACUTE LOWER RESPIRATORY INFECTIONS IN CHILDREN UNDER TWO YEARS: A CROATIAN SINGLE-CENTER EXPERIENCE

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Presenting author: Josko Markic

Introduction: Acute lower respiratory infections (ARI) caused by respiratory syncytial virus (RSV) are imposing a significant burden on the healthcare system. The aim of this study was to present characteristics of children under two years of age hospitalised due to all ARI and RSV-associated ALRI at the University Hospital of Split, Croatia.


Results: A total of 1,112 ALRI cases were hospitalized in observed period, out of which 364 cases (32.7%) tested positive for RSV. Changes in the seasonality were noted like reduced infection rate during the spring and summer of 2021. Age-related differences were observed, with a higher proportion of RSV-associated and all-cause ALRI cases in infants <28 days during the COVID-19 period compared to the other periods. In addition, a higher proportion of children experienced severe all-cause ALRI and RSV-associated ALRI requiring supplemental oxygen during the COVID-19 and post-COVID-19 periods compared to the pre-pandemic period. No difference was observed in intensive care unit admissions. The median length of hospitalization was shortest during the pre-COVID-19 period.

Conclusions: With RSV vaccines now approved for use in older adults, our findings help inform the need for country-level RSV prevention.

Abstract category: Evolution & Epidemiology

Conflict of Interest: TZ, SM, YM and SS: None declared; HH: Grants to institution from: Icosavax, Innovative Medicines Initiative, Pfizer; Consulting fees to institution from Bill and Melinda Gates Foundation, Pfizer, Sanofi, WHO; Payment or honoraria to institution from AbbVie; Meeting travel support from Sanofi; Data Safety Monitoring Board or Advisory Board participation from: GSK, Icosavax, Innovative Medicines Initiative, Pfizer; Consulting fees to institution from Bill and Melinda Gates Foundation, Pfizer, Sanofi, WHO; Payment or honoraria from Pfizer, Resvinet, Sanofi, WHO; MIF: Employee and stock holder of GSK; RMF: Employee of GSK; XW: Funding to institution from GSK; Grants or contracts from WHO, Wellcome Trust; Consulting fees from Pfizer, WHO; Payment or honoraria from Pfizer; Meeting travel support from Pfizer.
Conclusion: This study presented our local change in both the incidence and clinical severity of hospitalized ALRI cases. Understanding the impact of COVID-19 pandemic, including non-pharmaceutical Interventions on the transmission dynamics of respiratory viruses is significant in the light of the potential future epidemics.

Abstract category: Evolution & Epidemiology

Keywords: Acute Lower Respiratory Infections; Respiratory Syncytial Virus; COVID-19; Children

Conflict of Interest: None declared.

REPRODUCTIVE SYNCYTIAL VIRUS INFECTION AMONG PREGNANT WOMEN IN RURAL AREA SOUTHERN MOZAMBIQUE: A PROSPECTIVE OBSERVATIONAL STUDY.

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Presenting author: Sérgio Massora

Background & Aims: Knowledge gaps exist regarding the burden of Respiratory syncytial virus (RSV) infection in pregnancy. We aimed to determine the incidence of RSV infection among pregnant women and risk factors associated to RSV illness in rural area southern of Mozambique.

Methods: A health facility-based prospective observational study was conducted in pregnant women who attended Antenatal care (ANC) and outpatient services at two rural health centers in Southern Mozambique presenting with clinical signs/symptoms of acute upper respiratory infection (AURI) or acute lower respiratory infection (ALRI) within the past 7 days. Clinical and demographic data was collected. A nasopharyngeal swab (NP) was obtained from all pregnant women. Respiratory samples were analyzed for RSV detection by molecular methods (TaqMan Array).

Results: A total of 599 pregnant women were recruited from October 2019 to April 2022. Mean age of pregnant women was 24.6 years (SD=6), and mean gestational age was 25 weeks (SD=7). HIV prevalence in study women was 23%. AURI was the most common clinical presentation of respiratory illness. Most commonly reported respiratory signs/symptoms included cough 94% (566/599) and rhinorrhea 58% (349/599). Among 101 NP tested RSV associated acute respiratory infection (ARI) was 5.9% (6/101). Final analyses of clinical and microbiological data are currently ongoing, and will be presented at the RSVVV 24 meeting.

Conclusion: RSV maternal immunization strategy is being considered for RSV prevention in young infants. Generating data on RSV in African pregnant women is relevant to understand their potential benefit from maternal vaccination.

Abstract category: Evolution & Epidemiology

Keywords: Pregnant Women, RSV, Respiratory Infections

Conflict of Interest: None declared.

EVALUATION OF PEDIATRIC CASE DEFINITIONS FOR RESPIRATORY SYNCYTIAL VIRUS (RSV) BEFORE AND DURING THE COVID-19 PANDEMIC, NEW VACCINE SURVEILLANCE NETWORK, 2016–2023

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Background: Case definitions for influenza and other respiratory viral illnesses may be less sensitive for RSV and may underestimate RSV burden.

Methods: We enrolled children aged <2 years hospitalized with acute respiratory illness (ARI) at 7 U.S. hospitals during December 2016 to March 2020 (pre-pandemic) and January 2021 to June 2023 (pandemic). ARI was defined as ≥1 of the following: fever, cough, earache, nasal congestion, runny nose, sore throat, post-tussive emesis, shortness of breath, wheezing, or apnea. Respiratory specimens were collected and tested by reverse transcription polymerase chain reaction. We assessed sensitivity and specificity of three variations of the severe acute respiratory illness (SARI) case definition, to detect laboratory-confirmed RSV in hospitalized children. The three variations of SARI were defined as cough plus 1) no fever requirement, 2) any parent-reported fever, or 3) parent-reported fever ≥38.0°C.
Results: Among 3,605 hospitalized children aged <2 years with laboratory-confirmed RSV in the pre-pandemic period, sensitivity (95% CI) and specificity (95% CI) were 60% (58–61%) and 52% (51–54%) for SARI with parent-reported fever ≥38.0°C; 68% (66–69%) and 45% (44–46%) for SARI with any parent-reported fever; and 99% (99–99%) and 11% (10–12%) for SARI without fever. Both SARI case definitions requiring fever were poorly sensitive in infants aged 0–2 months. Age-based sensitivities and specificities were similar to pre-pandemic estimates during the pandemic period.

Conclusion: During both the pre-pandemic and pandemic periods, SARI case definitions requiring fever were less sensitive and may underestimate RSV burden in hospitalized children, particularly among infants 0–2 months of age.

Abstract category: Evolution & Epidemiology

Keywords: RSV, Sensitivity, Specificity, SARI, Acute Respiratory Illness

Conflict of Interest: None declared.

Presenting author: Heidi Moline

MODELLING THE AGE-SPECIFIC RISK OF HOSPITALISATION DUE TO RSV INFECTION

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Presenting author: Hannah Moore

The recent licensure of RSV therapeutics has driven the need for strategic decisions on the implementation of RSV immunisation programs. Data driven approaches, considering the local RSV epidemiology, are critical to advise on the optimal use of these therapeutics for effective RSV control. We are developing an RSV dynamic transmission model to characterise RSV epidemiology and measure the differential impact of potential immunisation scenarios on population subgroups at a higher risk of severe RSV infection (e.g., infants born preterm).

A key input to these models is the risk of RSV-related hospitalisation, once infected. We developed an age-to-risk function to incorporate into our dynamic models. We used linked administrative data from Western Australia to provide RSV hospitalisations categorised by age and stratified by preterm status at birth. Fitting our model to these time series provided estimates of the risk of hospitalisation, given RSV infection, by age and preterm status. We estimate that the risk of hospitalisation given infection for term infants declines to below 10% of the risk by the age of 7 months. For preterm infants, where the risk of hospitalisation given infection is higher at birth than for term-born infants, the risk of hospitalisation declines to below 10% of the risk at birth by the age of 9 months. The dynamic model will be used for assessing potential immunisation strategies, especially if at-risk infants may be considered for additional monoclonal antibody schedules. Furthermore, the age-to-risk function has wider relevance to the epidemiological characterisation of RSV.

Abstract category: Evolution & Epidemiology

Conflict of Interest: HCM has received institutional honoraria for participation in advisory group meetings on RSV epidemiology from Merck Sharp and Dohme, Pfizer and Evolvehealth. HCM and KG are in receipt of research funds from an Investigator Initiated Studies Program of Merck Sharp & Dohme (Australia) Pty Ltd (not related to this study) and HCM is in receipt of research funds from Sanofi-Aventis (Australia) (not related to this study). ABH was previously engaged by Pfizer Inc to advise on modelling RSV vaccination strategies for which she received no financial compensation.

FACTORS PREDICTING SECONDARY RESPIRATORY MORBIDITY FOLLOWING EARLY-LIFE RSV INFECTIONS

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Presenting author: Hannah Moore

Introduction: The association between early-life respiratory syncytial virus (RSV) infections and later respiratory morbidity is well-established but evidence on factors that influence this risk is limited. We examined socio-demographic and perinatal factors associated with later childhood respiratory morbidity requiring secondary care following exposure to laboratory-confirmed RSV in the first two years.

Methods: We used a probabilistically linked whole-of-population-based birth cohort including 252,287 children born in WA between 2000 and 2009 with follow-up to end 2012. Cox proportional-hazards models estimated adjusted hazard ratios (aHR) of the association of various risk factors with the first respiratory episode for asthma, wheezing and unspecified acute lower respiratory infection >2 years of age.

Results: The analytic cohort included 4,151 RSV-positive children born before age 2 years. The incidence of subsequent respiratory morbidity following early-life RSV infection decreased with child age at outcome (highest in 2–4-year-olds: 41.8/1000 child-years [95% CI 37.5–46.6]), increased with age at RSV infection (highest in 6–12-month-olds: 23.6/1000 child-years [95% CI 19.9–27.8]), and decreasing gestational age (50.8/1000 child-years [95% CI 33.5–77.2] for children born extremely preterm <28 weeks gestation). Risk factors included age at first RSV episode [6–12 months aHR: 1.42 [95%CI 1.06–1.90], extreme prematurity [<28 weeks aHR: 2.22 [95% CI 1.40–3.53]), maternal history of asthma (aHR:1.33 [95% CI 1.04–1.70]), and low socio-economic index (aHR:1.76 [95% CI 1.03–3.00]).

Discussion: Our results suggest that in addition to preterm and young infants, children aged 12–24 months could also be potential target groups for RSV prevention to reduce the burden of later respiratory morbidities associated with RSV.

Abstract category: Evolution & Epidemiology

Keywords: Age at RSV Infection; Asthma; Linked Data; Respiratory Morbidity; Respiratory Syncytial Virus; Wheeze.

Conflict of Interest: H.C.M. has received institutional honoraria for participation in advisory committees sponsored by Merck Sharpe & Dohme (Australia) Pty Ltd, Pfizer, and Sanofi for other work unrelated to this analysis. H.C.M. also receives funding from Sanofi in the form of an externally sponsored collaboration agreement...
for other work unrelated to this analysis. P.R. has received institutional honoraria from advisory committees sponsored by GSK, Pfizer, Merck, AstraZeneca, and Novavax. P.R. also receives funding from Merck Sharpe & Dohme (Australia) Pty Ltd. and GSK. H.C.M. and M.S. have received travel funding from Seqirus (unrelated to the work presented here). All other authors report no potential conflicts.

**IMPACT OF COVID-19 ON RESPIRATORY VIRUS DETECTION AT A TERTIARY CARE HOSPITAL IN INDIA (SOUTH)**

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Globally, acute lower respiratory infections cause 336 million episodes and 1.1 million deaths annually. India accounted for a third of the global burden and highest mortality. Viruses transmitted by respiratory routes spread through land and airline networks. Community-level mitigation measures for COVID-19 resulted in a dramatic reduction in virus transmission. Scaling back of measures led to a resurgence of virus transmission and caused local epidemics. We examined the trend of respiratory virus detection at a tertiary care hospital from over 3 periods - pre-pandemic (2017-2019), pandemic (2020-2021) and post-pandemic (2022-2023).

We sequenced respiratory syncytial virus (RSV) genomes by NGS and reconstructed the phylogeny of glycoprotein and fusion genes of RSV using ML methods.

**Results:** Of 8264 samples received, virus positivity was seen in 3373 (41%) with 80% mono-infections. RSV was detected in 483 (5.8%) with 73% mono-infections. RSV detection rates were highest in the children <5 years (63%) as were rates of other pathogens. Detection rates did not change across periods. All age groups showed a rebound in positivity, except the >50 year age group. Sequencing revealed multiple genotypes circulating in Vellore during the period for both RSV group A and group B with contraction in genetic diversity and geographical restriction. Viruses from India interspersed with viruses from diverse geographic regions suggesting a global transmission network.

**Conclusions:** The SARS CoV-2 pandemic resulted in reduced detection of seasonal respiratory viruses with contracted genetic diversity. Routine sequencing of respiratory viruses should be carried out to monitor emergence of newer lineages.

**Abstract category:** Evolution & Epidemiology

**Keywords:** RSV, Genotype, Phylogeny

**Conflict of Interest:** None declared

**RSPIRATORY SYNCYTIAL VIRUS IN ADULTS WITH MILD AND SEVERE ILLNESS SOUTH AFRICA 2009-2019**

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**Presenting author:** Jocelyn Moyes

Introduction: Data on Respiratory Syncytial Virus (RSV) infection in adults is limited in Africa. Describing factors associated with severe RSV is this setting may inform targeted vaccine introduction.

**Methods:** We conducted sentinel surveillance for influenza-like illness (ILI) in outpatient clinics and severe respiratory illness (SRI) in hospitals in South Africa from 2009 through 2019. We enrolled consenting adults (age ≥18 years). Dedicated nurses collected demographic data, medical history, in-hospital treatment, outcome data, and nasopharyngeal swabs for RSV testing by polymerase chain reaction. We compared characteristics of RSV-positive patients with SRI to RSV-positive patients with ILI (comparison group) using logistic regression.

**Results:** Of 25,438 adults with RSV results, 25% (n=6258) were classified as ILI and 75% (n=19,180) as SRI. RSV detection rate was 2% in both the ILI and SRI groups. ILI (n=125) and SRI (n=364). Median age was 35 years (interquartile range (IQR) 27-47) for RSV-associated-ILI and 40 years (IQR 32-52) for RSV-associated SRI. The case fatality ratio among all SRI patients was 9% (1724/18,931) and 12% (42/364) for RSV-associated SRI. On multivariable analysis comparing RSV-associated SRI to ILI, age 40-59 years [adjusted odds ratio (aOR) 1.8 (95% confidence interval (CI) 1.1-3.0)] and >75 years [aOR 16.5 (95% CI 1.9-145.5)] compared to age 18-39 years, HIV infection [aOR 4.3 (95% CI 2.1-13.4)] and any underlying illness [aOR 5.3 (95% CI 2.5-7.5)] were associated with SRI.

**Conclusion:** In South Africa, older adults, some groups of younger adults, adults with underlying illnesses, and those living with HIV may benefit most from RSV vaccination.

**Abstract category:** Evolution & Epidemiology

**Keywords:** RSV Adults Severe Illness HIV

**Conflict of Interest:** None declared for this time period.
METAGENOMIC SEQUENCE ANALYSIS OF RESPIRATORY SAMPLES DURING SEVERE ACUTE RESPIRATORY INFECTIONS OF RSV-A AMONG ABORIGINAL NICOBARESE TRIBAL CHILDREN IN CAR NICOBAR ISLAND IN INDIA.

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Presenting author: Muruganandam Nagarajan

Introduction: Almost all people have had RSV infection during infancy. Car Nicobar Island is home to an aboriginal tribe called the Nicobarese. An upsurge of RSV-A infections was reported during October–November 2021 among Nicobarese children. Understanding the bacterial flora during RSV associated severe acute respiratory infections (SARI) is important.

Method: Throat and nasal swabs were collected from the Nicobarese children suffering from RSV-A. The children with SARI were treated at the inpatient department (IPD). Metagenomic (mNGS) analysis for the V3 and V4 16S rRNA regions was performed to understand the changes in the bacterial flora.

Result: In the IPD gender-based cohort, Actinobacteria, Bacilli, Betaproteobacteria, and Gammaproteobacteria were identified as dominant bacterial classes at the phylum level, displayed dominance of Firmicutes, Proteobacteria, and Actinobacteria. The number of detected Operational Taxonomic Units (OTUs) was generally higher in female samples, indicating greater bacterial diversity. In the IPD age-based cohort, Actinobacteria, Bacilli, and Gammaproteobacteria were identified as dominant bacterial classes, and at the phylum level, Proteobacteria, Firmicutes, and Actinobacteria. The number of detected OTUs was generally higher in infants, indicating increased bacterial diversity.

Conclusions: Metagenomic analysis revealed that Actinobacteria, Bacilli, and Gammaproteobacteria were the dominant bacterial classes in both gender and age-based analyses. However, the number of detected OTUs was generally higher in infants. Outcome of the study and further understandings may be helpful in the future for changing the treatment modality to reduce the severity of the secondary bacterial infections during the RSV-A infections among children.

Abstract category: Evolution & Epidemiology

Keywords: Metagenomics Sequence Analysis, Severe Acute Respiratory Infections, RSV-A, Aboriginal Tribe, Nicobarese, Car Nicobar Island.

Conflict of Interest: None declared.

INCIDENCE OF RESPIRATORY Syncytial Virus Infection AMONG CONFIRMED COVID-19 CASES IN GHANA

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Presenting author: Evangeline Obodai

Respiratory Syncytial Virus (RSV) causes a substantial burden of acute lower respiratory infection in children and elderly persons, particularly in low-middle-income countries. However, little is known about the burden of RSV–related acute respiratory infection (ARI) in patients with suspected SARS-CoV-2 infection. We aimed to determine the incidence of RSV-positive ARI during the COVID-19 pandemic.

Oro-nasopharyngeal swabs collected from suspected COVID-19 cases with ARI from January to October 2022 were submitted to the National COVID-19 testing laboratory at the Noguchi Memorial Institute for Medical Research for SAR-CoV-2 testing. Respiratory samples were further investigated for RSV using specific real time multiplex RT-PCR assay. A comparative assessment of RSV-positive outcomes and disease burden was also performed.

In this study, 104 respiratory samples of COVID-19 patients were analyzed for SARS-CoV-2 and RSV; of them 3 (2.9%) tested positive for RSV. The median (range) age of study participants was 46.5 (2-89) years, 51% were male and majority (80%) resided within the capital city, Accra. All three patients infected with RSV were older adults above age 60 years. Two of the RSV-positive cases were identified at the peak (in October) of the RSV season in Ghana, while the third case was identified during non-RSV season (in January). Genotypic analysis revealed RSV genotype B as the circulating strain.

The study data suggests a significant impact of RSV infection among COVID-19 patients during the pandemic period. Public health interventions leading to substantial reduction of the disease burden in the elderly and high-risk groups will be cost-effective.

Abstract category: Evolution & Epidemiology

Keywords: RSV, Acute Respiratory Infections, COVID-19 Cases, Older Adults, Ghana

Conflict of Interest: None declared

UNRAVELING THE IMPACT OF CASE DEFINITIONS FOR RSV DETECTION IN OLDER ADULTS IN THE VALENCIA REGION, SPAIN

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Background: There is an ongoing debate whether influenza surveillance networks could be leveraged for RSV monitoring. Here we evaluate the influenza-like illness (ILI) case definition’s impact on detecting RSV hospitalizations in older adults using a hospital network setup for influenza monitoring.

Methods: Multicentre prospective observational study in the Valencia Region of Spain during seasons 2018/19, 2021/2022 and 2022/23 in adults ≥ 65 (4 hospitals per season). Seasons were restricted to RSV circulation for analyses. All hospitalizations with respiratory symptoms were screened. We analysed the proportion of included screened hospitalizations and laboratory-confirmed RSV hospitalizations that met ECDC ILI (at least, one systemic symptom and, at least, one
respiratory symptom with an onset in the 7 days prior to admission), WHO SARI (fever and cough with an onset in the 10 days prior to admission) and WHO SARI-extended (cough with an onset in the 10 days prior to admission), definitions.

Results: From the 5,590 included patients, 62%, 52%, and 35% met WHO-SARI-extended, ILI, and WHO-SARI criteria, respectively. Among RSV+ patients (n=232), 96%, 76% and 53% met WHO SARI-extended, ILI and WHO SARI criteria, respectively. Data per season and age group is shown in Figure 1.

Compared to WHO SARI-extended, ILI criteria leads to a 26% reduction in the number of included patients and a 21% reduction of RSV positive cases, and WHO-SARI 42% and 45%, respectively.

Conclusions: ILI definition may result in an underestimation of RSV burden of at least 21% in older adults. Fever requirement (WHO-SARI) seems inappropriate for RSV detection.

Abstract category: Evolution & Epidemiology

Keywords: RSV, Case Definition, Adults, Burden of Disease

Conflict of Interest: This research has been funded by the Chair of Catholic University of Valencia and Moderna. The opinions expressed here are those of the authors and do not necessarily represent those of Moderna.

RESPIRATORY SYNCTIAL VIRUS-ASSOCIATED HOSPITALISATION RATES IN OLDER ADULTS WITH COMORBIDITIES USING A TIME-SERIES ANALYSIS APPROACH IN TWO EUROPEAN COUNTRIES

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Presenting author: Richard Osei-Yeboah

Background: Adults with chronic medical conditions are at higher risk of respiratory syncytial virus (RSV) infection complications. Using health registries, we estimated RSV-associated respiratory tract infection (RTI) hospitalisation rates in adults aged ≥45 years with comorbidities in Denmark and Scotland.

Methods: Using routine health records from 2010-2018, we used time-series linear regression models to estimate the rates and episodes of RSV-associated RTI hospitalisations by age group and seven selected comorbidities.

Results: In Denmark, annual RSV-RTI hospitalisation rates ranged from 3.1 (95% confidence interval: 2.6–3.6) per 1000 adults with asthma to 19.4 (18.9–25.7) per 1000 adults with chronic kidney disease (CKD). For each of the conditions except diabetes, RSV rates increased with age. In Scotland, annual RSV-RTI hospitalisation rates ranged from 3.1 (2.6–3.6) per 1000 adults with asthma to 9.0 (7.7–10.4) per 1000 adults with chronic obstructive pulmonary disease (COPD). Compared to the overall populations in both countries we found a rate ratio (RR) increase in adults with – CKD (7-fold in Denmark; 3-fold in Scotland), COPD (4-fold; 6-fold), IHD (4-fold; 4-fold), diabetes (2-fold; 2-fold), stroke (2-fold; 3-fold) and asthma (1.5-fold; 3-fold), and 2-fold for adults with CLD in Scotland. In Scotland, the RR estimates for RSV-RTI hospitalisations were generally similar to those for influenza-RTI across comorbidities.

Conclusion: Our findings show that RSV causes substantial hospitalisations in adults with comorbidities and the risk of severe RSV illness varies by type of comorbidity. These findings are essential for identifying risk groups and assisting authorities in prioritising healthcare settings and vaccination policies.

Abstract category: Evolution & Epidemiology

Keywords: Respiratory Syncytial Virus, Adults, Chronic Medical Conditions, Hospitalisation

Conflict of Interest: JP declares unrestricted grants from Sanofi to Nivel for research on RSV, influenza and SARS-CoV-2. Nivel received a research grant from the University of Edinburgh for the submitted work. XK reports grants from GlaxoSmithKline and consultancy fees from Pfizer, outside the submitted work. HC reports grants, personal fees, and nonfinancial support from World Health Organization. Grants and personal fees from Sanofi Pasteur. Grants from Bill and Melinda Gates Foundation. All payments were made via the University of Edinburgh. HC is a shareholder in the Journal of Global Health Ltd. HN reports grants from Pfizer, Bill and Melinda Gates Foundation and National Institute of Health and Social Care Research outside submitted work. HN reports personal fees from Pfizer, GSK, Sanofi, Novavax and Merck. All other authors report no potential conflicts. All authors report no potential conflicts.
SIGNATURES OF POSITIVE SELECTION WITHIN AND ACROSS THE ANTIGENIC SITES OF THE RESPIRATORY SYNCTIAL VIRUS (RSV) FUSION PROTEIN

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Presenting author: Brittany Petros

Respiratory Syncytial Virus (RSV) is a leading cause of morbidity and mortality, particularly in infants and the elderly. Advances in RSV structural biology and immunology and subsequent structure-guided vaccine design have resulted in the development and approval of vaccines that target the fusion (F) protein. The efficacy of these vaccines hinders on (i) the existing circulating diversity of RSV, and (ii) the ability of RSV to develop non-lethal mutations in its antigenic sites (i.e., a fitness tradeoff between immune evasion and F protein function). At the whole-gene level, the F protein is undergoing negative selection. However, we hypothesize that this finding paints an incomplete picture of its evolution, which likely contains a few regions under positive selection (e.g., known antigenic sites, subject to selective pressure from the human immune system) among a background of functionally important regions under negative selection.

Here, we analyze >7,000 F gene sequences from a global set of samples collected between 1956 and early 2023 to quantify pre-existing (i.e., existing prior to the availability of RSV vaccines) epitope-specific evolutionary selective pressures. We compare the rates of nonsynonymous to synonymous substitutions across antigenic sites ð – V, uncover signatures of parallel evolution across the F proteins of RSV subtypes A and B, and identify epistatic interactions between residues that constrain RSV evolution. Finally, we introduce a framework for integrating experimental protein structural data with viral genome sequences to conduct structure-informed evolutionary hypothesis testing.

Abstract category: Evolution & Epidemiology
Keywords: RSV genomics; RSV evolution; antigenic sites; epistasis

Conflict of Interest: Dr. Sabeti is a co-founder and consultant at Sherlock Biosciences Inc. and Delve Bio, and is a Board Member of Danaher Corporation; she holds equity in all three companies. She has several patents related to diagnostics, genome sequencing, and informatics, including two patents licensed to Sherlock Biosciences.

PEDIATRIC RESPIRATORY SYNCTIAL VIRUS: SHIFTING EPIDEMIOLOGY OR SHIFTING SURVEILLANCE?

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Presenting author: Brittany Petros

The incidence of respiratory syncytial virus (RSV) dropped drastically with the emergence of SARS-CoV-2 but was followed by a surge in RSV cases with the relaxation of pandemic mitigation measures. A prevailing hypothesis is that the RSV-naïve pediatric population increased during the period of low transmission, colloquially referred to as the “immunity debt” hypothesis. However, changing respiratory viral testing practices may also contribute to the heightened case counts.

We conducted a multicenter, retrospective analysis of 342,530 RSV clinical encounters and 980,546 RSV diagnostic tests occurring at 32 United States pediatric hospitals in 2013–2023. Test volume increased by a factor of 18.93 (95% CI: 14.99, 23.90) in 2021–2023 relative to the pre-pandemic period and was accompanied by a 2.42-fold increase (95% CI: 1.68, 3.46) in patient volume. Diagnosed patients were older than in the pre-pandemic period, though a substantial fraction of the apparent shift in age can be attributed to increased testing of older children. Hospitalization, intensive care, and mechanical ventilation rates were significantly lower in 2021-2023, declining by 14.9% (95% CI: -19.6%, -10.1%), 16.0% (95% CI: -19.9%, -12.1%) and 10.3% (95% CI: -14.1%, -6.5%), respectively. These declining measures of clinical acuity were observed across patient age strata. These findings are consistent with increased testing, particularly of older children with more mild illness, as the main driver of the increase in RSV case counts following the emergence of SARS-CoV-2.

Abstract category: Evolution & Epidemiology
Keywords: RSV Genomics; RSV Evolution; Antigenic Sites; Epistasis

Conflict of Interest: Dr. Sabeti is a co-founder and consultant at Sherlock Biosciences Inc. and Delve Bio, and is a Board Member of Danaher Corporation; she holds equity in all three companies. She has several patents related to diagnostics, genome sequencing, and informatics, including two patents licensed to Sherlock Biosciences.
WHOLE GENOME SEQUENCING AND MOLECULAR CHARACTERIZATION OF CIRCULATING RESPIRATORY SYNCYTIAL VIRUS (RSV) 2019-2023 STRAINS USING A NEXT GENERATION SEQUENCING PLATFORM

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Presenting author: Varsha Potdar

Background: Respiratory syncytial virus (RSV) significantly affects respiratory infections, especially in young children, elderly adults with health issues, and immunocompromised individuals. Its higher prevalence during winter and monsoon can cause severe bronchiolitis and pneumonia. Though deaths are uncommon, it can lead to long-term asthma. To develop effective treatments and preventive vaccines, understanding its molecular characterization is vital.

Methods: - we utilized amplicon-based whole genome sequencing using next-generation sequencing platform and analyze RSV strains in Pune from 2019 to 2023.

The RSV positive clinical of less than 25 Ct value were processed for whole genome sequencing. Briefly post RNA extraction and cDNA creation, cDNA libraries were prepared for Illumina-MiSeq sequencing. Bioinformatic analyses assembled the RSV genome, with molecular characterization achieved via Maximum likelihood-based phylogenetic analysis. We pinpointed non-synonymous mutations with MEGA11 software.

Results: - We obtained the whole genomes of 5 RSV-A and 15 RSV-B samples. Our results showed 99% genome sequence coverage for both RSV-A and RSV-B strains, with 100% identity to 2022’s circulating strains. Phylogenetically, RSV-A samples were ON1 genotype and RSV-B samples BA-CCB genotype. We explored amino acid changes in the G and F glycoproteins, essential for current vaccine research.

In conclusion, our sequencing revealed RSV’s genetic diversity in varying age groups. The RSV fusion protein (F) stands as a promising vaccine target, facilitating comparisons with global sequences for local vaccine creation. This study underscores the potential of next-generation sequencing in molecular studies, with implications for shaping molecular epidemiology strategies against respiratory infections, aiming to lessen public health impacts.

Keywords: - Fusion (F) glycoprotein, Respiratory syncytial virus (RSV), Molecular characterization, Next-generation sequencing.

HEALTHCARE RESOURCE USE AND COSTS ASSOCIATED WITH RESPIRATORY SYNCYTIAL VIRUS INFECTIONS IN INDIVIDUALS AGED 60 YEARS OR OLDER IN ITALY: A RETROSPECTIVE OBSERVATIONAL STUDY

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Background: Respiratory syncytial virus (RSV) is a highly contagious, respiratory virus that can have a substantial impact on the health of older adults. This retrospective observational study aimed to estimate healthcare resource utilisation (HCRU) and direct healthcare costs associated with RSV in Italy.

Methods: Data were collected from an integrated Italian administrative database, covering approximately 20% of the Italian population. Patients aged ≥60 years, with ≥1 hospitalisation discharge diagnosis ICD-9-CM code for RSV were follow-up at one year. Patient characteristics, HCRU and direct healthcare costs were extracted.

Results: In total, 289 RSV-hospitalised patients (average baseline age: 67.6 years) were evaluated, with 201 (69.5%) aged ≥60 years. Of those aged ≥60 years, most had Charlson Comorbidity Index scores of 1–2 (n=117 [58.2%]) or 3–4 (n=41 [20.4%]); 40.3%, 23.9% and 17.4% had chronic-obstructive pulmonary disorder, diabetes, and heart failure, respectively. Preliminary results at the 1 year follow up indicate that direct healthcare costs associated with the management of RSV hospitalised patients aged ≥60 years in Italy averaged €11,599, and were mainly caused by hospitalisation costs (78.9% of total costs), followed by prescription costs (16.2%) and outpatient services (4.9%).

Conclusions: Although RSV-specific codes were likely underused, this preliminary, real-world analysis indicates that RSV infections in adults aged ≥60 years generate a considerable clinical and economic burden in Italy. The possibility of case ascertainment bias should be considered when interpreting these data.

Acknowledgements: GSK sponsored the study and purchased the study report from ClIcon S.r.l. Società Benefit that is the basis for this abstract.

Abstract category: Evolution & Epidemiology

Keywords: Respiratory syncytial virus, healthcare resource utilisation, healthcare costs, elderly, Italy

Conflict of Interest: GSK sponsored the study and purchased the study report from ClIcon S.r.l. Società Benefit that is the basis for this abstract. AP: employee and stock owner of GSK; MJF: employee and stock owner of GSK and has received support for attending meetings and/or travel from GSK as an employee; MD, CV, LDE: no conflicts of interest to declare. AD: received consulting fees from CSL Seqirus and VIHTALI; and payment or honoraria from SD Biosensor and CSL Seqirus; GEC: received grants or contracts, consulting fees, and payment or honoraria from GSK; participated on a Data Safety Monitoring Board or Advisory Board for GSK; Director of VIHTALI, a spin-off of Università Cattolica del Sacro Cuore, Rome, Italy; CR: received payment or honoraria from AstraZeneca, GSK, MSD, CSL Seqirus, and Sanofi.
THE ECONOMIC BURDEN OF RSV-ASSOCIATED ILLNESS IN CHILDREN <2 YEARS OF AGE IN 4 LMICS

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Presenting author: Neele Rave

Background: Respiratory syncytial virus (RSV) imposes a substantial burden, particularly in low- and lower-middle-income countries (LMICs). Intervention strategies for RSV, such as monoclonal antibodies (mAb) and maternal immunization (MI), have shown positive results. However, economic burden data are sparse, especially in LMICs.

Aim: This study aims to provide valuable insights into the costs of managing respiratory infections, specifically RSV, in four LMICs.

Methods: In this ongoing study, data are being collected in four LMICs (Mozambique, Nigeria, Ghana and Nepal) during one RSV season. Total outpatient and inpatient cost per illness episode, including direct medical, direct non-medical and indirect costs have been collected through caregiver interviews and through the analysis of patient charts and hospital expenditures.

Results: To date, 2,147 children (1,027 inpatient) have been recruited at four study sites, of which 38% were positive for RSV. The median age at testing was 3 months. Overall RSV positivity was higher among inpatients (49%) compared to outpatients (22%). Based on initial data analysis, average total cost incurred per case was US$ 40,48 (95% CI 4,26 – 85,32), US$ 73,24 (95% CI 60,06 – 86,43), US$ 156,79 (95% CI 98,60 – 214,83) and US$ 186,75 (95% CI 107,69 – 265,83), respectively in Mozambique, Nigeria, Ghana and Nepal.

Conclusion: RSV illness cause a high economic burden on the health care system as well as families in Mozambique, Nigeria, Ghana and Nepal. Generating comprehensive data on health care resource use and costs associated with RSV will help to guide prevention strategies against RSV in LMICs.

This study was funded by PATH.

Abstract category: Evolution & Epidemiology

Keywords: Burden, Cost, Respiratory Syncytial Virus, Children, Respiratory Illness

Conflict of Interest: LB has regular interaction with pharmaceutical and other industrial partners. He has not received personal fees or other personal benefits. UMCU has received funding for the RSV GOLD III – Health Economics study from PATH.

THE ReSViNET DASHBOARD OF GLOBAL RSV INFECTION

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Introduction: Respiratory Syncytial Virus (RSV) is associated with a substantial burden of disease globally. Children under 5 years of age, older adults, and those with underlying comorbidities are at higher risk of severe RSV disease. Understanding the seasonal pattern of RSV is crucial for optimizing and evaluating future immunization programs especially in view of the changes in RSV seasonality due to the COVID19 pandemic. The objective of this study is to compile global RSV surveillance data in an online, publicly accessible dashboard.

Materials and Methods: The ReSViNET dashboard is a longitudinal observational study of RSV epidemiology based on aggregated secondary data from existing surveillance reports. Countries that consistently report the weekly number of laboratory-confirmed RSV cases are included in the study. The weekly number of new RSV-positive cases, the total number of specimens or cases tested, and the proportion of RSV-positive cases, were collected from January 2022 onwards.

Results: The ReSViNET dashboard currently reports RSV surveillance data from 29 countries, and 15 additional countries have been identified. More than 1,300 users from 70 different countries are using the dashboard totaling more than 2,900 views since May 2023.

Discussion and conclusion: This dashboard allows RSV circulation trends to be assessed and to compared between countries. Despite an active search for new countries and the goal of geographic diversity, African and Asian countries are underrepresented. This knowledge gap likely to reflect a disparity in resources available for surveillance. Overall, the ReSViNET dashboard is a powerful tool for disseminating information and raising awareness.

Abstract category: Evolution & Epidemiology

Keywords: ReSViNET Dashboard, RSV surveillance

Conflict of Interest: None declared
COMPARISON OF MATERNAL AND INFANT RSV TITERS AT BIRTH OVER A MULTI-YEAR PERIOD

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Background: Maternal RSV vaccines have been developed to elicit transfer of more RSV-specific IgG across the placenta to provide infants protection against RSV. Birth timing related to RSV seasonality may have important implications for quantity or efficiency of maternal IgG transfer.

Methods: We collected sera from 184 maternal-infant pairs (n=368) at delivery between 2017 and 2021 and measured RSV F IgG using an electrochemiluminescence assay. We performed descriptive statistics to show the distribution of births and IgG results by quarter and term/preterm gestation, evaluating maternal and cord IgG titers using Pearson Correlation Coefficients (PCC). Linear regressions were run to determine the association between maternal and cord IgG titers.

Results: Maternal and cord IgG titers were 99450±63736 BAU/ml and 158575±113007 BAU/ml, respectively, and similar across annual quarters. Only 24 pairs had cord:maternal antibody transfer ratio of less than 1; 12 of these infants were born in quarter 1 (January–March) and 10 of these infants were preterm. Maternal and cord titers were moderately correlated (PCC= 0.734, p<0.001), with maternal titers producing a beta estimate of 1.30 (95% CI: 1.13, 1.46; p<0.001) when predicting cord titers adjusting for gestational age.

Conclusions: Maternal and infant RSV antibody levels are positively correlated. However, lower cord:maternal IgG ratios occurred most frequently in preterm infants born between January and March. This may indicate a greater need for maternal RSV vaccination in this group of mothers. Since there is no agreed upon protective threshold for infant RSV IgG concentrations, vaccination schedules should take expected birth date into consideration.

Abstract category: Evolution & Epidemiology

Keywords: antibody, IgG, vaccination, maternal, infant

Conflict of Interest: None declared

UNDER-RECOGNIZED RSV INFECTIONS AMONG CHILDREN WITH ACUTE RESPIRATORY ILLNESS IN EMERGENCY DEPARTMENTS AT SEVEN US CHILDREN’S HOSPITALS, NEW VACCINE SURVEILLANCE NETWORK, 2016–2021

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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 clinical testing results may underestimate RSV burden without adjustment for limited testing and coding.

Methods: We conducted prospective, year-round, active surveillance with laboratory confirmation of RSV infection (“surveillance-based RSV testing” [SB]) in children aged <18 years seen in emergency departments (ED) with ARI at seven pediatric sites during 2016–2021. Medical chart review for ICD-10 codes (ARI codes J06, J11, J12, J18, J20, J21, J22) for RSV infection. RSV detection rates also were compared between clinical and SB RSV testing.

Results: Among 21,235 children enrolled in an ED with a SB RSV test, 3,352 (15.8%) children tested RSV-positive; detections were more frequent in children aged <6 months (29.7%) than in children aged 6 months to 2 years (13.5%) (p<0.001). Clinical RSV testing was performed in 3,419 (16.1%) children with SB and detected 862 (25.7%) of SB RSV-positives.

Conclusion: Both RSV/ARI ICD-10 codes and clinical testing underestimated total RSV infections in children with ARI seen in an ED. Active surveillance with SB testing could improve estimation of RSV rates in children to support vaccine and prophylaxis efforts.

Abstract category: Evolution & Epidemiology

Keywords: RSV, Surveillance, ICD-10 codes, Epidemiology, Children, Laboratory Test

Conflict of Interest: None declared

DEPARTMENTS AT SEVEN US CHILDREN’S HOSPITALS, NEW VACCINE SURVEILLANCE NETWORK, 2016–2021
PREVALENCE AND PREDICTORS OF RESPIRATORY SYNCYTIAL VIRUS AMONG CHILDREN PRESENTING WITH ACUTE RESPIRATORY INFECTIONS ON THE ALONG KENYA-UGANDA BORDER

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Presenting author: Nathan Shaviya

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, the study sought to determine predictors of RSV in the cross border population residing within the study site. 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.

Abstract category: Evolution & Epidemiology
Conflict of Interest: None Declared

MALNUTRITION STATUS PRE AND POST SEVERE OR VERY SEVERE RSV LRTI IN INDIAN CHILDREN: A COHORT STUDY IN MELGHAT INDIA

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Presenting author: Eric Simões

Background: RSV is the single most important cause of severe lower respiratory tract infection (LRTI) globally. There are no studies which have examined prospectively the nutritional status of children before during and after an episode of RSV LRTI.

Methods: Active surveillance of infants and children younger than 2 years, for detection of acute LRTI, was conducted in 93 villages of Melghat, from August 2016 to December 2020. Nasopharyngeal swabs were collected from subjects with severe, or very severe LRTIs and tested for RSV by PCR. Periodic anthropometry measurements of the entire cohort were done from birth to 24 months, including at the time of any LRTI: Z-scores of weight-for-age (WFA), length-for-age (LFA) and weight-for-length (WFL) were obtained using WHO standards. Fitted curves (with 95% CI) were derived all anthropometric measurements for uninfected controls and all RSV LRTI cases before, during and after infection.

Results: 480 RSV cases were compared to 6,307 controls. Anthropometry was available for 256/480 (53.3%) pre infection, 480/480(100%) at infection and 301/480 (62.7%) post infection. Those <15 months of age had higher and older children had a lower WFA compared to controls before the infection; for all it declined during infection and dropping significantly post infection compared to controls (Figure 1) The proportion of children with RSV LRTI and severe acute malnutrition increased from 12.1% pre infection to 72.3% post infection.

Conclusions: In rural Indian children severe RSV LRTI, precipitates severe acute malnutrition in almost ¾ of these marginally nourished subjects.

Abstract category: Evolution & Epidemiology
Keywords: RSV LRTI; Malnutrition; Children < 2 years; Nutritional status pre and post infection
Conflict of Interest: EAFS discloses the following conflicts of interest; grants and consulting fees to the institution from Merck & Co. Pfizer Inc and Icosavax; grants to the institution from AstraZeneca Inc. Roche Pharmaceuticals and Johnson and Johnson; and honoraria to the institution for consulting, and/or lectures from Sanofi Pasteur, Cidara Therapeutics, Adiago Therapeutics and Nuance Pharmaceuticals; manuscript editorial writing support and support for attending a meeting and from Pfizer Inc and Astra Zeneca Inc; and participation on a DSMB from Abbvie Inc, GlaxoSmithKline plc, Moderna Inc and Bill and Melinda Gates Foundation.
MODELED BURDEN OF RSV IN ADULTS AGED 50-59 YEARS WITH CHRONIC CARDIOPULMONARY DISEASES IN THE UNITED STATES

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Presenting author: David Singer

BACKGROUND: Adults with chronic cardiopulmonary conditions are at increased risk of severe respiratory syncytial virus (RSV) disease. This study estimated the burden of RSV in adults 50-59 years of age (YOA) with chronic cardiopulmonary diseases in the United States (US).

METHODS: A multichort Markov model was used to separately estimate annual RSV burden in adults 50-59 YOA in the US with chronic obstructive pulmonary disease (COPD) (n=3,299,241), heart failure (HF) (n=712,959), coronary artery disease (CAD) (n=2,865,359), and asthma (n=3,439,066). Discounted life-years (LY) and quality-adjusted life years (QALY) lost due to RSV-related death were estimated over the remaining lifetime. Model inputs included RSV epidemiology and healthcare resource use (HRU) patterns. Inputs were sourced from scientific literature and public data. Model outcomes included RSV acute respiratory illnesses (ARI), lower respiratory tract disease (LRTD), HRU, deaths, LYs, and QALYs lost.

RESULTS: The model estimated annual RSI-ARI cases of 184,459 (population with COPD), 39,740 (HF), 150,926 (CAD), and 192,385 (asthma), with 57% of cases being LRTD. These RSV-ARI cases were estimated to result in 10,281, 3,842, 6,947 and 5,191 hospitalizations annually, respectively for COPD, HF, CAD, and asthma populations. RSV-related deaths in these populations ranged from 296 for HF to 723 for COPD. Discounted QALY losses ranged from 4,129 to 12,106 for the HF and COPD populations, respectively, due to RSV-related morbidity and mortality. See Table 1 for results.

CONCLUSIONS: Adults 50-59 YOA with cardiopulmonary diseases experience significant RSV burden and this population may benefit from RSV prevention measures.

FUNDING: GlaxoSmithKline Biologicals SA (VEO-00056)

Abstract category: Evolution & Epidemiology

Keywords: Respiratory syncytial virus; burden of disease; COPD; heart failure; coronary artery disease; asthma

Conflict of Interest: David Singer, Elizabeth La, Sara Poston and Daniel Molnar are employed by and hold shares in GSK. Jonathan Graham and Mei Grace are full-time employees of RTI Health Solutions, an independent nonprofit research organization, which received funding from GSK for this study. Their compensation is unconnected to the studies on which they work. The authors declare no other financial and non-financial relationships and activities.

RESPIRATORY SYNCYTIAL VIRUS IN CHILDREN PRESENTING TO HOSPITALS IN FOUR PROVINCES IN LAO P.D.R. IN 2022

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Presenting author: Manila Souksavanh

Respiratory Syncytial Virus (RSV) is the leading cause of viral pneumonia in young children in low income countries with an estimated 3.2 million hospitalizations and 118,000 deaths in 2015. In Laos limited data are available on the burden and epidemiology of RSV infection in children, especially in rural areas. We conducted a study on hospitalized children with acute respiratory infection (ARI) in four provinces in Laos from January to December 2022. RSV was tested by RT-PCR in upper respiratory tract sample from all recruited patients. In Vientiane capital, 101/258 (39.2%) children less than 5 years old were positive for RSV. 62/233 (27%), 63/354 (18%) and 21/137 (15%) children less than 15 years old were positive for RSV, in southern, northern and central provinces respectively. In all provinces, RSV epidemic was observed during rainy season. However, timing differences were observed. Whereas 97% of RSV infections were detected between April and July in the northern province, 90% of infections occurred between July to October in the southern and central provinces. The epidemic lasted longer in the southern province, from May to September, with few cases detected until December. Both groups, A and B, were detected, however distribution differences between north and south were observed. Only RSVB was identified in the northern province, whereas mainly RSVB was identified in the southern and central provinces. In Vientiane capital, 63% were RSVB and 37% RSVA, with sequential circulation, RSVA appearing to replace RSVB over time. Whole genome sequencing will allow the characterization of circulating RSVA and RSVB strains.

Abstract category: Evolution & Epidemiology

Keywords: Respiratory Syncytial Infection, Molecular Epidemiology, Laos, Rural Areas

Conflict of Interest: None declared
EPIEMIOLOGY OF RESPIRATORY SYNCYTIAL VIRUS INFECTIONS IN A TERTIARY CARE CENTRE IN KERELA, SOUTH INDIA

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Presenting author: Asha Sudheer

Background: In the wake of new vaccines against RSV infections, a study was done to assess the prevalence as well as severity of RSV in our paediatric population. This has implications in the design of future vaccines as well as timing for vaccine delivery among the different age groups for the Indian population.

Method: We conducted a prospective viral surveillance study of the paediatric population admitted to a tertiary care hospital in Kochi, Kerala, from the time period of January 2019 to Nov 2023. Subtyping was done for RSV isolates using G primers.

Results: Out of the 279 positive RSV cases year wise distribution of the subtypes were done. PreCOVID and PostCOVID data shows a gradual shift in the subtype peaks seasonally from 2019-2023. RSV peaks are independent and have specific seasonality. In totality RSV A cases(n=108) are more than RSVB(n=79) though the predominant serotype changed every year. Among the different age groups, the frequency of RSV was predictably higher in the <1 year age group with RSV A cases >RSVB. RSVB had more cases in the 2-5 age group. RSV B was associated with more coinfections than A. Human rhinovirus followed by Bocavirus was the most common coinfection with both subtypes. RSV B was associated with more ICU admissions and more comorbid conditions than RSVB.

Conclusion: Data suggests that since the peak season has changed there might be a requirement of vaccination of the preschool age groups of 2-5 and that too before rainy season

Abstract category: Evolution & Epidemiology

Keywords: RSV Epidemiology, Kerala, Subtypes, Severity, Coinfections

Conflict of Interest: None declared

EPIEMIOLOGY AND CLINICAL FEATURES OF RESPIRATORY SYNCYTIAL VIRUS (RSV) IN HOSPITALIZED CHILDREN DURING COVID19 IN GORGAN, IRAN

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Presenting author: Alireza Tahamtan

RSV infection can cause a variety of respiratory illnesses in infants and young children. As the circulation of respiratory viruses changed during the COVID-19 pandemic, here we aimed to evaluate the epidemiology and clinical features of RSV in hospitalized children during the pandemic in Gorgan, north of Iran.

Overall, 411 respiratory swab samples from children under five hospitalized from October to March 2021-2022, were collected. The incidence of RSV and the virus subgroups and genotypes were checked by PCR methods. All samples were also tested for SARS-CoV-2 and influenza viruses and the data obtained from the demographic and clinical information of patients were analyzed by SPSS software.

The frequency of RSV, SARS-CoV-2, and influenza was found to be 27%, 16.5%, and 4.1%, respectively. Subgroup A was dominant and seems to cause more severe clinical symptoms; circulating genotypes were ON1 and BA9.

It was found that despite the prevalence of the SARS-CoV-2 in the population and the relative decrease of respiratory viruses compared to before the pandemic, the frequency of RSV is higher in children; also, investigating the epidemiology of the virus and determining the circulating strains can be helpful to infection control and treatment.

Abstract category: Evolution & Epidemiology

Keywords: Respiratory Syncytial Virus, RT-PCR, Molecular Epidemiology, COVID-19, Hospital-Acquired Pneumonia

Conflict of Interest: There is no conflict of interest.
child-years) and increased thereafter, but increased in non-metropolitan areas (e.g., Goldfields: 344 vs 663.43 per 1,000 child-years). The strongest predictors of testing were age <12 months (adjusted odds ratio [aOR] = 2.15, 95% CI 2.10–2.20), preterm birth (<32 weeks; aOR = 3.18, 95% CI 2.61–3.96), and remote residence (aOR = 0.77, 95% CI 0.73–0.82).

Conclusions: Higher RSV testing rates suggest an underlying high disease burden, whereas declining rates in metropolitan regions may indicate increases in private sector testing. These current testing rates highlight the potential underestimation of RSV-hospitalizations by routine surveillance, and the need for estimation of the true burden of RSV.

Disclosure: This study was funded by Sanofi.

**Abstract category:** Evolution & Epidemiology

**Keywords:** Respiratory Syncytial Virus, Testing, Geographical Location, Trend, Australia

**Conflict of Interest:** None declared

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**RISK FACTORS FOR POOR OUTCOMES IN CHILDREN HOSPITALIZED WITH VIRUS-ASSOCIATED ACUTE LOWER RESPIRATORY INFECTIONS: A SYSTEMATIC REVIEW AND META-ANALYSIS**

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**Background:** Acute lower respiratory infection (ALRI) caused by respiratory viruses is among the most common causes of hospitalization and mortality in children. We aimed to identify risk factors for poor outcomes in children <5 years old hospitalized with ALRI caused by influenza, SARS-CoV-2, and respiratory syncytial virus (RSV).

**Methods:** We searched Medline, Embase and Global Health databases and included observational studies reporting risk factors for poor outcomes (defined as use of supplemental oxygen, mechanical ventilation, intensive care unit admission, prolonged hospital stay, and mortality) published between January 2011 and January 2023. Two authors independently extracted data on study characteristics, outcomes, and risk factors. Meta-analyses were conducted using the random effects model.

**Results:** We included 30 studies. For influenza related ALRI, chronic conditions and age 6-24 months were identified as risk factors for poor outcomes. Cardiovascular disease, immunosuppression, chronic kidney disease, diabetes, and high blood pressure were reported as risk factors for mortality due to SARS-CoV-2 associated ALRI. For RSV related ALRI, significant risk factors based on meta-analyses were: neurological disease (odds ratio [OR] 6.14; 95% confidence intervals [95% CIs] 2.39-15.77), Down’s syndrome (5.43; 3.02-9.76), chronic lung disease (3.64; 1.31-10.09), immunocompromised status (3.41; 1.85-6.29), prematurity (2.98; 1.93-4.59), congenital heart disease (2.80; 1.84-4.24), underlying disease (2.45; 1.94-3.09), age <2 months (2.29; 1.78-2.94), age <6 months (2.08; 1.81-2.39), viral coinfection (2.01; 1.27-3.19), low birth weight (1.88; 1.19-2.95), being underweight (1.80; 1.38-2.35).

**Conclusions:** These findings might contribute to the development of guidelines for prophylaxis and management of ALRI caused by influenza, SARS-CoV-2, and RSV.

**Abstract category:** Evolution & Epidemiology

**Keywords:** Risk Factor, Poor Outcome, ALRI, RSV, SARS-CoV-2, Influenza

**Conflict of Interest:** None declared
CHARACTERISING DISPARITIES IN GLOBAL PAEDIATIC RESPIRATORY SYNCYTIAL VIRUS-RELATED MORTALITY: INSIGHTS FROM THE RSV GOLD STUDY ACROSS INCOME GROUPS

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Presenting author: Femke Vernooij

Background: Although respiratory syncytial virus (RSV) is the second leading paediatric cause of mortality globally, granular insight into this burden is lacking. Characterising the clinical profile of children dying with RSV infection from different income groups is important for estimating and extrapolating vaccine impact, guiding decision-making on vaccination programmes.

Methods: RSV Global Online Mortality Database (RSV GOLD) is a combined retrospective/prospective case series collecting global data on under-five mortality with laboratory-confirmed RSV infection. We included community-acquired and in-hospital deaths from January 1, 1995 until August 28, 2023.

Results: We included 1523 community-acquired in-hospital deaths from 76 countries. 464 (30.5%) children were from low- and lower-middle-income countries (LMICs), 460 (30.2%) from upper-middle-income countries (UMICs), and 599 (39.3%) from high-income countries (HICs). Most children from LMICs and UMICs died under the age of six months. Death under six months occurred 1.9 and 1.6 times more often in children from LMICs and UMICs compared to children from HICs. Although most children had a comorbidity, comorbidity was 1.6 and 2.5 times more often reported in HICs compared to LMICs and UMICs. Healthy term and preterm children died at a younger age compared to children with comorbidities.

Conclusions: This is the largest study reporting on clinical characteristics of under-five RSV-related deaths per income group to date. We expect major vaccine impact on RSV-related mortality in LMICs and UMICs.

Funding: This study was funded by the Bill and Melinda Gates Foundation.

Abstract category: Evolution & Epidemiology

Keywords: Respiratory Syncytial Virus, Paediatric Mortality, Disease Burden

Conflict of Interest: None declared

ACUTE LOWER RESPIRATORY TRACT INFECTIONS BY RSV: CORRELATION BETWEEN THE VIRAL GENOMIC FEATURES AND CLINICAL EVOLUTION, A PILOT ANALYSIS IN A PEDIATRIC HOSPITAL DURING 2022

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Global genomic surveillance of RSV is an emerging area that has gained significant attention due to the worldwide implementation of vaccines shortly. The objective of this study was to describe the clinical-epidemiological profile of hospitalized patients under 12 months due to ALRI with positive RSV diagnosis, without coinfections and comorbidities during the 2022 outbreak. Besides correlate genetic lineages with patient evolution and perform evolutionary studies with complete genomes.

The analysis included 51 patients, 6 had coinfections. Most patients were males (76%), averaging 5 months old. Comorbid children were absent in 93% of patients at admission. Most cases (86%) occurred during epidemiological weeks 26-35. Seven percent were premature, and 31% had asthmatic parents. Bronchiolitis was diagnosed in 71% of patients, while 29% had pneumonia. Mechanical ventilation was required for 7%, and 52% received high-flow nasal cannula support. Of the hospitalized patients, 83% were discharged without complications after an average stay of 10 days.

Genome sequencing was successful in 86% of cases (n=45), with 91.5% belonging to subgroup A. Among sequenced cases, 44.1% were A.D.1 lineage, 25.6% A.D.3, 20.9% A.D.5.2 and 9.3% B.D.5.2.1.1, which cocirculated throughout the year. Interestingly, complications occurred in only 3/19 of A.D.1 lineage patients, compared to 3/11 in A.D.3.

The evolutionary analysis indicated that the circulating lineages in 2022 were reintroductions closely related to Brazilian sequences from 2022, alongside ongoing circulation of genetic clusters introduced in 2021.

Performing molecular surveillance and burden of disease of RSV will be crucial for characterizing circulating strains globally in the pre- and post-vaccine era.

Abstract category: Evolution & Epidemiology

Keywords: RSV; Genomic Surveillance; Hospitalized Children; Clinical Epidemiological Profile; Genetic Lineages; Circulating Lineages; Evolutionary Analyses

Conflict of Interest: None declared
ESTIMATING THE POTENTIAL PUBLIC HEALTH IMPACT OF THE RSVPREF3 OA VACCINE AGAINST RESPIRATORY SYNCYTIAL VIRUS FOR ADULTS ≥ 60 YEARS IN GERMANY

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Background: RSVPREF3 older adults (OA) vaccine against the respiratory syncytial virus (RSV), recently approved for individuals ≥ 60 years is a preventive intervention against RSV disease. This study aimed at estimating the potential public health impact of the RSVPREF3 OA vaccination in Germany.

Methods: A static cohort-based Markov model was developed to estimate the impact of the vaccine on OA ≥ 60 years (3-year time horizon, flu-like vaccination coverage). We compared the outcomes of medically attended RSV cases, deaths, and healthcare resource use for a scenario with and without one-dose of RSVPREF3 OA vaccine given at the start of the simulation.

Due to uncertainties in the RSV hospitalization rate, we evaluated two different scenarios involving a less (1) and a more (2) conservative estimation of this parameter. The RSV-associated mortality rate in-hospital (a) and in-hospital plus 30 days after discharge (b) were analysed, resulting in four scenarios.

Results: Preliminary results indicate that RSVPREF3 OA has the potential to prevent 10,053 medically attended upper and 199,789 lower respiratory tract diseases, 58,577 hospitalizations and 6,112 deaths, according to our base case scenario (scenario 1a).

The number needed to vaccinate to prevent one medically attended RSV case, one hospitalisation or one death in the base case scenario is 55, 197 or 1,884, respectively (table 1).

Conclusion: These findings suggest that RSVPREF3 OA vaccine has the potential to substantially reduce RSV burden in the German OA population. Further research is needed to obtain more robust estimates of incidence and mortality.

Funding: GlaxoSmithKline Biologicals SA (220838)

Abstract category: Evolution & Epidemiology

Keywords: RSV, Model, Older Adults, Vaccination, Burden Of Disease, Public Health

THE CLINICAL SPECTRUM OF INFLUENZA VIRUS AND RESPIRATORY SYNCYTIAL VIRUS INFECTION: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Presenting author: Xin Wang

Background: Understanding the clinical spectrum of influenza virus and respiratory syncytial virus (RSV) is crucial to planning control measures, and parameterising cost-effectiveness and epidemic models. We conducted a systematic review and meta-analysis to investigate the clinical spectrum of influenza virus and RSV.

Methods: We searched PubMed and Web of Science for studies published from Jan 2000 to Oct 2022 that reported data on the full clinical spectrum of influenza and RSV, including asymptomatic and symptomatic infection, and more severe clinical outcomes. Meta-analysis was conducted using a generalized linear mixed-effect model when three or more studies were identified.

Results: We included 32 studies. We estimated that 61% (95%CI 48%-72%) of influenza infection and 75% (95%CI 57%-88%) of RSV infection were symptomatic. The proportion of symptomatic influenza infection was 68% (95%CI 58%-78%) and 36% (95%CI 22%-53%) for pediatric and adults, and 62% (95%CI 45%-76%), 81% (95%CI 31%-98%) and 84% (95CI 31%-98%) for H1N1pdm09, H3N2 and seasonal H1N1. One study reported full severity pyramid, including asymptomatic, ALRI and hospitalised RSV infection, among young children by subtype A and B.

Conclusions: Sixty percent of influenza infections and three quarters of RSV infection were symptomatic. Differences in symptomaticity of influenza were found between age and virus subtype groups. Asymptomatic and mild RSV infection might have an considerable contribution to RSV transmission. More data are needed to improve estimates on the proportion of asymptomatic RSV infection and understanding of their impact to RSV transmission.
Abstract category: Evolution & Epidemiology

Keywords: RSV; Influenza; Clinical Spectrum; Symptomatic; Asymptomatic

Conflict of Interest: XW receives research grants from GlaxoSmithKline and consultancy fees from Pfizer, outside the submitted work. All other authors report no conflict of interests.
A GENERIC, SALIVA-BASED PCR TEST FOR THE DETECTION OF RSV OFFERS A LOW-BURDEN APPROACH FOR SUSTAINABLE SURVEILLANCE OF RSV

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Introduction. With the introduction of RSV vaccines, large-scale surveillance is crucial for monitoring their safety, performance, and impact on reducing the global burden of RSV infection. Saliva, being non-invasive, offers a low burden approach to support surveillance efforts.

Methods. We modified our saliva-based, RNA-extraction-free test (originally developed for SARS-CoV-2) for the detection of RSV. To facilitate broad implementation, we validated the assay using numerous reagents and PCR instruments from different suppliers. To determine the feasibility of using simple, laboratory plastic tubes for sample collection, we assessed the stability of RSV detection in raw saliva. Additionally, we developed a full genome sequencing protocol for RSV, based on the Oxford Nanopore SARS-CoV-2 sequencing workflow.

Results. We achieved an assay limit of detection of 4 copies/µl. RSV remained detectable for 24 hours at 40°C, ≥7 days at +4°C, 19°C and 30°C, ≥8 weeks in a ‘frost-free’ freezer (-20°C), and through cold-chain-free postal conditions. Sequencing RSV from saliva yielded 80-95% genome coverage with minimal adjustments to the SARS-CoV-2 protocol.

Conclusion. Saliva, due to its non-invasive nature and low resource requirements, is ideal for large-scale surveillance. Combined with an open-source, extraction-free PCR test, this significantly reduces costs, ensuring ongoing assessment of vaccination programs and incidence of RSV. The ability to sequence RSV from saliva further enhances surveillance capacity and monitoring of seasonal epidemics. Importantly, we have demonstrated that this RSV test can be expanded to simultaneously screen for SARS-CoV-2 and influenza A/B. This multiplexing capability offers the potential for a cost-effective, all-in-one diagnostic solution.

Abstract category: Evolution & Epidemiology

Keywords: saliva, qPCR, surveillance, diagnostics

Conflict of Interest: None declared

CHARACTERISTICS OF IN-SEASON AND OFF-SEASON RSV CASES — U.S., 2016–2020

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Presenting author: Kari Yacisin

Background. In temperate climates, RSV outbreaks typically occur during the fall/winter/spring, but cases also occur outside a typical season (i.e., “off-season”). We sought to describe the characteristics of RSV cases occurring in-season and off-season.

Methods. Using the Premier Healthcare Database, we identified U.S. RSV cases from Jan2017–Mar2020. An RSV case was defined as a medical encounter with an ICD-10-CM code for RSV illness. In-season was narrowly defined as Dec–Feb and off-season as Jun–Aug; cases in Sep–Nov and Mar–May were excluded to avoid misclassification because of variability in season onset/offset. We analyzed case demographic, baseline clinical, and visit characteristics using descriptive statistics.

Results. We identified 141,427 in-season cases and 3,756 off-season cases among children (<18 years) and 41,735 in-season and 1,243 off-season cases among adults. Most pediatric cases were among infants (<1 year) both in-season (60%) and off-season (59%). Black and Hispanic pediatric patients contributed to a larger proportion of off- vs. in-season cases (Black: 22% vs 15%, and Hispanic 30% vs 19%, respectively; p<0.0001). Trends were similar for adult cases. A higher proportion of off-season vs in-season inpatient pediatric cases received antibiotics (54% vs 45%, respectively; p<0.0001). Preexisting medical conditions frequency and readmission rates were similar off- and in-season for children and adults.

Conclusions. RSV cases were observed off-season, despite likely under-detection. Racial and ethnic disparities in off-season RSV cases may exist. Further analysis of possible confounders (e.g., region, socioeconomic status, residential density) is needed to understand potential disparities and ensure equitable access to RSV prevention.

Abstract category: Evolution & Epidemiology

Conflict of Interest: All authors are employees of Pfizer and may hold stock/stock options in Pfizer Inc.

CRITICAL COVID-19 ILLNESS AMONG INFANTS LESS THAN SIX MONTHS OF AGE WITH AND WITHOUT RSV CODETECTION

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Background: Respiratory syncytial virus (RSV) and COVID-19 infections can be critical in infancy. Infants with RSV and COVID-19 codetection may have more severe illness than infants with COVID-19 alone. Our objective was to describe critical COVID-19 illness among infants with RSV and COVID-19 codetection.

Methods: Infants aged <6 months hospitalized 5 May 2022–31 October 2023 for acute COVID-19 with a positive COVID-19 test enrolled in a case-control study of COVID-19 vaccine effectiveness at one of 27 U.S. pediatric hospitals were included. Critical illness was illness requiring invasive or noninvasive mechanical ventilation, vasopressors, or extracorporeal membrane oxygenation, or in-hospital death. Demographic and clinical characteristics were compared between infants with and without RSV codetection.
Results: Of 1,327 infants hospitalized for COVID-19, 558 had RSV testing. RSV was detected in 74 (13.3%) infants. Infants with RSV codetection were older (median age: 2.8 vs. 1.9 months) and fewer had underlying medical conditions (12.2% vs. 58.0%) and shortness of breath (72.9% vs. 45.1%) were more common, and fewer less common (41.0% vs. 74.6%). Infants with COVID-19 and RSV versus without RSV had more intensive care unit admissions (51.4% vs. 17.4%), critical illness (27.0% vs. 11.6%), and longer hospitalizations (3 vs. 2 days).

Conclusions: Hospitalized infants aged <6 months with COVID-19 and RSV codetection were older and had more severe outcomes compared to infants with COVID-19 alone. Preventative measures for both viruses in young infants, such as maternal vaccination, are important.

Abstract category: Evolution & Epidemiology

Keywords: Respiratory Syncytial Virus, Infants, COVID-19, Codetection

Conflict of Interest: Margaret M. Newhams, Amber O. Orzel-Lockwood, and Adrienne G. Randolph report research funding to their institution from CDC. Natasha B. Halasa reports past grant support from Quidel and Sanofi, and current grant support from Merck. Regina M. Simeone reports past stock holdings in Pfizer.

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Presenting author: Chenkai Zhao

Background: The COVID-19 pandemic and its relevant control measures have reportedly interrupted the circulation of common human respiratory viruses. With the relaxation of strict control measures, these viruses started to re-circulate albeit with varied timing. We aimed to characterise the variations in the timing of re-circulation of human respiratory viruses.

Methods: We analysed data of human respiratory viral infections identified from published literatures (through a systematic literature search), public databases, and unpublished data shared by international collaborators. We defined virus-specific onset and peak of each epidemic wave per study site, and synthesised the time intervals between the last wave before the COVID-19 pandemic and subsequent waves after the onset of the pandemic, separately for onset and peak across study sites.

Results: We included 33 study sites providing data for 1244 epidemic waves. Rhinovirus and influenza B virus had the earliest and latest resurgence, with the onset-onset time interval of 368 days (95% CI: 276–491) and 1059 days (936–1197), respectively; respiratory syncytial virus had a relatively earlier reurgence, with the onset-onset time interval of 639 days (584–698). From the second epidemic wave onwards, there was a decreasing trend in the onset-onset time interval between two sequent epidemic waves. Analysis of the peak-peak time interval yielded broadly similar results. (Figure)

Conclusions: Substantial between-virus variations exist in the timing of re-circulation following the onset of the COVID-19 pandemic, which might be a result of virus-virus interaction and transmission advantaage of certain viruses.

Abstract category: Evolution & Epidemiology

Keywords: Respiratory viruses, Re-circulation, Seasonality, Virus-virus interaction, COVID-19 pandemic

Conflict of Interest: None declared

RESPIRATORY SYNCYTIAL VIRUS-ASSOCIATED HOSPITALISATIONS BY DEPRIVATION LEVEL IN SCOTLAND

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Background: Socioeconomic deprivation is associated with an increased risk of respiratory infection and worse clinical outcomes. We aimed to estimate RSV-associated hospitalisations across deprivation levels in Scottish population.

Methods: Using national hospital and virological databases, we utilised two approaches, i.e., a multiple linear regression model with spline function and a direct measurement using ICD-10 codes, to estimate annual average number and rate of RSV-associated hospitalisations by five quintiles of deprivation according to Scottish Index of Multiple Deprivation (SIMD) and by age. We estimated rate ratios (RRs) of RSV-associated hospitalisation and 95% uncertainty ranges (URs) between SIMD levels, by sampling from a log-normal distribution of rate estimates.

Results: Using the model-based approach, estimates of RSV-associated hospitalisation rates increased with higher deprivation levels. The annual average rate ranged from 0.47 (95% CI: 0.46–0.49) for individuals of all ages in the least deprived group (5th quintile by SIMD) to 1.51 (1.03–1.79) for the most deprived group (1st quintile), with a RR of 1.96 (1.23–3.25), 1.6 (1.00–2.66), 1.35 (0.85–2.25) and

![Figure 1. Ratio of RSV-RTI hospitalisation rates between SIMD levels, by age.](https://via.placeholder.com/150)
1.12 (0.70-1.85) for the 1st to 4th quintile relative to the 5th quintile. By age, the pattern of RSV-associated hospitalisation rates with SIMD was most pronounced in children aged two years and below (Figure). ICD-10 based approach produced much lower rates than the model-based approach, but yielded similar RR estimates between SIMD.

Conclusion: Scottish population of higher deprivation are at increased risk of RSV hospitalisation. The differences between deprivation levels are most pronounced in infants and young children.

Abstract category: Evolution & Epidemiology

Keywords: Respiratory syncytial virus, hospitalisation, deprivation, children, adults

Conflict of Interest: HC reports grants, personal fees, and nonfinancial support from World Health Organization. Grants and personal fees from Sanofi Pasteur. Grants from Bill and Melinda Gates Foundation. All payments were made via the University of Edinburgh. HC is a shareholder in the Journal of Global Health Ltd. XW reports grants from GlaxoSmithKline and consultancy fees from Pfizer, outside this submitted work. All other authors report no potential conflicts.
VACCINES, THERAPIES & TREATMENTS
PRELIMINARY ASSESSMENT OF THE IMPACT ON RSV HOSPITALIZATION OF THE FIRST 2 MONTHS OF UNIVERSAL PROPHYLAXIS WITH NIRSIVIMAB IN INFANTS IN GALICIA (SPAIN): NIRSE-GAL STUDY (WWW.NIRSEGAL.ES)

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Background: Galicia (Spain) was the first place in the world to announce the implementation of universal prophylaxis against RSV with nirsevimab in infants as part of the regional immunization program. The NIRSE-GAL study* aims to evaluate its results. We report here the impact data in the first 2 months since the start of the campaign.

Methods: The 2023/24 immunisation campaign against RSV in Galicia with nirsevimab started on 25-September-2023 (week 39) and will conclude on 31-March-2024, including seasonal, rescue-cohort (6 months) and high-risk infants (www.nirsegal.es).

Weekly RSV hospitalizations for four observation groups—rescue-cohort, infants under 2 months, under 6 months, and infants in their second RSV season (non-nirsevimab group)—were compared with data from previous seasons spanning from 2017 to 2023, excluding those affected by COVID-19 (2020-2022).

Results: The hospitalization rates/100,000 at week 46 for the 2023-24 season, compared to the median of previous seasons (in brackets), were as follows: 27.9 [262.6] rescue-cohort, 39.3 [257.4] under 2 months, 39.7 [196.6] under 6 months, and 82.9 [42.8] second RSV season, respectively (figure 1). RSV season started in week 44 with a positivity rate above 3%. In the group without nirsevimab (second RSV season), weekly hospitalization rate was similar to that of the 2017-18 season. Lower hospitalization rates were observed for groups included in the nirsevimab campaign—at birth, under 2 months, and under 6 months—compared to previous seasons.

Conclusions: The current early results, although preliminary, suggest a significant reduction in RSV hospitalizations attributable to the nirsevimab campaign.

Abstract category: Vaccines, Therapies & Treatments

Keywords: nirsevimab, immunization campaign, hospitalization rates, Spain

Conflict of Interest: *The NIRSE-GAL study (CEIC 2023–377) is funded by Sanofi Pasteur/AstraZeneca through a research grant to the Healthcare Research Institute of Santiago.

UNIVERSAL PROPHYLAXIS WITH NIRSIVIMAB AS ROUTINE INFANT IMMUNIZATION IN GALICIA (SPAIN), 2023/2024: STRATEGY AND COVERAGE; THE NIRSE-GAL STUDY

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Presenting author: Maria Sonia Ares Gómez

Background: Galicia (Spain) was the first place in the world to announce the implementation of universal prophylaxis against RSV with nirsevimab in infants as part of the regional immunization program. The NIRSE-GAL study aims to evaluate its results.

Methods: The 2023/24 immunisation campaign against RSV in Galicia with nirsevimab started on 25-September-2023 and will conclude on 31-March-2024, structured around three immunisation groups: seasonal, catch-up and high-risk (Table). The campaign was preceded by informative and educational activities for healthcare professionals, and dissemination materials to the general population. Nirsevimab administration occurs through Galicia’s network of hospitals. Children in the high-risk and catch-up groups received individual flexible electronic appointments over a 3-week period (25–30 September/high-risk group; 1–15 October/catch-up group) including weekends. Infants born during season receive the nirsevimab dose in the hospital in the first 24 h of life, except when there is a medical contraindication.

Results: As of November 19th, the overall immunization coverage at birth reached 92.8%. Health area-specific coverage varied from 90.4% to 95.9% (Figure 1A). Catch-up immunization coverage was 85.7% (ranging 82.6% to 87.8% (Figure 1B). 100% uptake was achieved in the high-risk group. No severe adverse effects have been reported so far after 8,909 administered doses.

Conclusions: The success in the implementation phase of nirsevimab in Galicia is based on a robust information and education campaign and a hospital-based roll-out, enabling rapid immunisation of the target population before the start of RSV circulation. Galicia’s experience implementing nirsevimab may aid policymakers in developing an RSV immunisation prevention strategy.

Abstract category: Vaccines, Therapies & Treatments
Keywords: nirsevimab, immunisation campaign, Strategy and coverage,
Conflict of Interest: the NIRSE-GAL study (CEIC 2023–377) is funded by Sanofi Pasteur/AstraZeneca through a research grant to the Healthcare Research Institute of Santiago.

TRANSPLACENTAL TRANSFER OF NATURALLY ACQUIRED RSV MATERNAL ANTIBODIES AMONG >600 PRETERM AND FULL-TERM INFANTS: USA, THE NETHERLANDS, SWITZERLAND AND GUATEMALA

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Presenting author: Jessica Atwell

BACKGROUND: Maternal immunization (MI) confers protection to infants via transplacental transfer (TPT) of maternal antibodies. While full-term infants (≥37
weeks gestational age (wGA)) are generally born with RSV cord to maternal titer ratios (CMRs) >1.0, preterm infants are expected to have lower CMRs, and are also at increased risk of severe RSV. Data on RSV antibody TPT by wGA are needed to assess the potential for efficient vaccine-induced antibody transfer in preterm infants and multiples.

METHODS: Via a collaborative multi-site seroepidemiology project in the USA, the Netherlands, Switzerland and Guatemala, TPT of naturally acquired RSV-A and B neutralizing antibody titers were assessed by wGA at birth among mother/infant dyads born 2021-2023.

RESULTS: 628 mother/infant pairs (including 66 sets of twins) born across a range of wGA (≤27: 5%, 28-30: 7%, 31-33: 17%, 34-36: 37%, ≥37: 35%) were enrolled. Geometric mean (GM) RSV-A CMRs by category of wGA at birth were: <27wGA: 0.64, 28-30wGA: 0.80, 31-33wGA: 0.91, 34-36wGA: 1.07, and ≥37wGA: 1.21. GM CMRs for RSV-B were similar. Analysis of TPT among multiples is ongoing.

CONCLUSION: TPT of naturally acquired RSV antibody increases with increasing wGA at birth. GM CMR among infants born 34-36 wGA surpasses 1.0 and is therefore in range with that of full-term infants. These data can inform the potential for maternal RSV vaccination to protect infants born preterm. Further study of vaccine-induced antibody transfer and effectiveness by wGA at both vaccination and birth (including assessment of time between vaccination and birth) is needed.

Abstract category: Vaccines, Therapies & Treatments

Keywords: RSV, Maternal Immunization, Transplacental Transfer, Antibodies

Conflict of Interest:

None declared

ADVANCING PUBLIC HEALTH WITH DATA: FORECASTING THE IMPACT OF THE ROLLOUT OF RSV PROPHYLACTICS IN 2023/2024

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Presenting author: Louise Blair

Recent advancements in the Respiratory Syncytial Virus (RSV) prophylactic market, including the 2023 approval of nirsevimab, the first new treatment since palivizumab in 1998, offer enhanced protection against a virus known for high morbidity in infants. The competitive nature of this market necessitates projections of prophylactic uptake and evaluation of potential impact across countries. To project country-specific uptake patterns and peak uptake values for nirsevimab, a two-staged mixed-effects model was used. The first stage modelled uptake trajectories, adjusting for healthcare expenditure, eligibility and disease burden. A second stage used the same predictors to estimate the maximum uptake, which were used to scale the uptake trajectories. These values were then used to forecast potential reduction of disease burden per country. Future incidence rates of hospitalisations were predicted using ARIMA models, with the reduction in burden calculated by multiplying predicted uptake with established prophylactic efficacy rates. Prediction of nirsevimab uptake (0-1 years in the United States following 1 year of product introduction) was 65% [95% CI: 52%, 78%], a figure that mirrors the reported high demand for nirsevimab. When combined with reported efficacy, our model forecasts a potential reduction in hospitalisations of 49.3% [39.5%, 59.2%] for this season (2023-2024), compared to expected burden, underscoring the significant impact of prophylactic deployment (Fig.1). This approach offers a robust, data-driven approach to estimating the impact of emerging RSV prophylactics. With use of this tool, public health organisations can better estimate trends related to uptake and the potential impact on health outcomes.

Abstract category: Vaccines, Therapies & Treatments

Keywords: nirsevimab, uptake, prophylaxis impact, forecasting

Conflict of Interest: None declared
EQUITY CONSIDERATIONS IN THE U.S. RSV VACCINE SHARED CLINICAL DECISION-MAKING RECOMMENDATION FOR ADULTS AGED 60 YEARS AND OLDER

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1. Coronavirus and Other Respiratory Viruses Division – National Center for Immunization and Respiratory Diseases – U.S. Centers for Disease Control and Prevention

Presenting author: Amadea Britton

Intro: In June 2023 the U.S. Advisory Committee on Immunization Practices (ACIP) voted to recommend adults aged ≥60 years receive a single dose of RSV vaccine, using shared clinical decision-making (SCDM). In their deliberations, ACIP considered the recommendation’s impact on health equity among U.S. racial and ethnic minority groups.

Background: Equity, defined by WHO as the absence of unfair, avoidable or remediability differences, is a core consideration of ACIP. For older adult RSV vaccines, impact on equity was considered in both the recommendation type (SCDM) and age-threshold.

Methods: The ACIP Adult RSV Work Group reviewed evidence on disparities in RSV disease by race, ethnicity and age and summarized the potential impact of a recommendation including adults aged 60–64 years via SCDM.

Results: U.S. Non-Hispanic Black, Hispanic, and American Indian/Alaska Native adults have higher prevalence of chronic medical conditions that increase risk of severe RSV disease at younger ages. The Work Group concluded that a recommendation including adults aged 60–64 years had the potential to increase equity by ensuring vaccine access for adults at increased risk before age 65, disproportionately from racial and ethnic minority groups. However, prior U.S. experience with SCDM vaccine recommendations suggests SCDM’s impact on equity is mixed and may not achieve increased uptake among those at greatest risk.

Conclusion: ACIP concluded that a recommendation including adults aged 60–64 years was important to address equity even if the impact of SCDM was unclear. Monitoring impacts on health equity will be critical to the U.S. RSV vaccination program.

Abstract category: Vaccines, Therapies & Treatments

Keywords: RSV vaccines, shared clinical decision-making, equity, vaccine policy

Conflict of Interest: None declared.

A COMPREHENSIVE STUDY ON THE IMPACT AND COST-EFFECTIVENESS OF RESPIRATORY SYNCYTIAL VIRUS PREVENTION STRATEGIES IN ARGENTINA

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Presenting author: Mauricio Caballero

Objective: The objective of this study was to evaluate the potential impact and cost-effectiveness of two strategies designed to prevent RSV infection in young children in Argentina.

Methods: Using a static cohort model with a finely disaggregated age structure (individuals under the age of 5 years), we calculated the burden of respiratory syncytial virus (RSV) disease in Argentina with and without the use of maternal vaccine (RSVpreF, Pfizer) or monoclonal antibody (Nirsevimab, Sanofi, Astra Zeneca). We compared each strategy to no intervention and to each other, assuming year-round administration for a 10-year period. The primary outcome measure was the cost per disability-adjusted life year (DALY) averted from a societal perspective, and we conducted both probabilistic and deterministic uncertainty analyses.

Results: Using central assumptions for the maternal vaccine ($50/dose, 81% efficacy, 6 months protection) and Nirsevimab ($50/dose, 77% efficacy, 5 months protection), Nirsevimab was found to be more cost-effective ($5215 per DALY averted compared to $8545 per DALY averted for the maternal vaccine) when compared to no pharmaceutical intervention. Despite having a lower net discounted cost ($195 million versus $273 million for Nirsevimab), the maternal vaccine prevented fewer RSV deaths (32.9% versus 19.9%). Our findings were highly sensitive to assumptions regarding dose price, efficacy, and duration of protection. At $50/dose and a willingness-to-pay threshold of 0.9 times the national GDP per capita, Nirsevimab and the maternal vaccine have a high and intermediate probability of being cost-effective, respectively.

Conclusion: Maternal vaccine and Nirsevimab may be cost-effective if their prices are set appropriately.

Abstract category: Vaccines, Therapies & Treatments

Keywords: RSV vaccines, shared clinical decision-making, equity, vaccine policy

Conflict of Interest: none declared

Table 1. Input parameters. Cost-effectiveness of RSV prevention strategies in Argentina for 10 birth cohorts. Period 2025–2034

<table>
<thead>
<tr>
<th>Input parameter</th>
<th>Value</th>
<th>Uncertainty range</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>RSV disease case rate per 100,000 per year (%)</td>
<td>1.29%</td>
<td>1.17% – 1.40%</td>
<td>Argentina’s do</td>
</tr>
<tr>
<td>RSV vaccine sensitivity</td>
<td>85%</td>
<td>82% – 87%</td>
<td>Argentina’s do</td>
</tr>
<tr>
<td>Maternal vaccine coverage</td>
<td>64%</td>
<td>60% – 68%</td>
<td>Argentina’s do</td>
</tr>
<tr>
<td>Nirsevimab coverage</td>
<td>65%</td>
<td>62% – 68%</td>
<td>Argentina’s do</td>
</tr>
<tr>
<td>Nirsevimab efficacy</td>
<td>61.1%</td>
<td>58% – 64%</td>
<td>Argentina’s do</td>
</tr>
<tr>
<td>Nirsevimab duration of protection</td>
<td>6 months</td>
<td>5 – 7 months</td>
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<tr>
<td>Nirsevimab dose price</td>
<td>$50/dose</td>
<td>$40 – $60/dose</td>
<td>Argentina’s do</td>
</tr>
<tr>
<td>Nirsevimab administration cost</td>
<td>$650</td>
<td>$500 – $750</td>
<td>Argentina’s do</td>
</tr>
<tr>
<td>Nirsevimab cost per DALY averted</td>
<td>$7500</td>
<td>$6500 – $8500</td>
<td>Argentina’s do</td>
</tr>
<tr>
<td>Nirsevimab effectiveness</td>
<td>77%</td>
<td>74% – 80%</td>
<td>Argentina’s do</td>
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<tr>
<td>Nirsevimab duration of protection</td>
<td>5 months</td>
<td>4 – 6 months</td>
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COST-EFFECTIVENESS OF STRATEGIES TO PREVENT RESPIRATORY SYNCYTIAL VIRUS IN YOUNG CHILDREN IN MOZAMBIQUE

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Presenting author: Assucênio Chissaque

Introduction: Respiratory syncytial virus (RSV) is an important cause of severe acute lower respiratory disease in infants. A maternal vaccine (Abrysvo) and a monoclonal antibody (Nirsevimab) have recently become available, but their prices are yet to be determined in low- and middle-income countries.

Methods: We used a static proportionate outcomes model to estimate the potential health impact and cost-effectiveness of year-round administration of Abrysvo and Nirsevimab over the period 2025-2034 in Mozambique. We compared each RSV prevention strategy to the current status quo (no pharmaceutical RSV prevention strategy) and to each other. The primary outcome measure was the cost (2022 US$) per disability-adjusted life year (DALY) averted from a government health perspective. We ran a range of deterministic and probabilistic uncertainty analyses and estimated the probability that each intervention would be cost-effective over a range of willingness-to-pay thresholds (WTPT).

Results: Administration of Abrysvo (US$10/ dose, 69% efficacy, 87% coverage) over the period 2025-2034 could cost US$121 million and prevent around 2,400 RSV deaths and 59,400 DALYs. Over the same period, Nirsevimab (US$120/ dose, 77% efficacy, 94% coverage) could cost US$124 million and prevent 3,500 RSV deaths and 85,700 DALYs. Compared to the current status quo, the cost per DALY averted was US$ 1,199 for Abrysvo and US$ 709 for Nirsevimab. Both products would need to be priced below US$4/ dose to achieve >90% probability of being cost-effective at a WTPT of 35% (US$190) the national GDP per capita.

Conclusion: Abrysvo and Nirsevimab have the potential to be impactful and cost-effective in Mozambique if appropriately priced.

Abstract category: Vaccines, Therapies & Treatments
Keywords: Maternal Vaccine (Abrysvo), mAb (Nirsevimab), Acute Respiratory Tract Infection Vaccination, Modelling, UNIVAC, Cost-Effectiveness, Mozambique.
Conflict of Interest: There is no conflict of interest.

THE ANTI-RESPIRATORY SYNCYTIAL VIRUS ACTIVITY OF PIPER GUINEENSE DRIED FRUIT EXTRACT IN VITRO

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Presenting author: Chinenyenwa Chukwuuekwe

According to the results of numerous studies, Respiratory Syncytial Virus (RSV) infection is still the most frequent cause of viral lower respiratory tract infection in infants and young children worldwide. RSV infections persist into adulthood as a result of the immune system's ineffective protective response to the infection. Compounds derived from phytomedicine have previously been shown to be potential sources for the development of Anti-RSV medicines, which in this study, Piper guineense (PG) dried fruit extract is used to evaluate this plant's Anti-RSV property.

In this current study, Hep-2 and Vero cells from African green monkey were used to examine the Anti-RSV and cell cytotoxicity properties of the dried fruit extract of Piper guineense using viral plaque reduction and corresponding cell viability assays. The usual procedure of thiazolyl blue tetrazolium bromide (MTT) reduction in Hep-2 cells was used in the associated setup for studies of PG extract on cell viability.

The extract of PG was found to have Anti-RSV properties, with an IC50 of 69.81 ± 11.98 µg/ml for RSV inhibition, and a TC50 of 53.39 ± 19.11 µg/ml for cell cytotoxicity in Hep2 cells.

Our results demonstrate that the dried fruit extract of PG has Anti-RSV activity and has a moderate effect on recipient host cell survival, suggesting that target chemical compounds against RSV can be developed from the extract.

Abstract category: Vaccines, Therapies & Treatments
Keywords: Respiratory Syncytial Virus (RSV), Antiviral, Cytotoxicity, Anti-RSV, Viral Inhibition, Cell Viability
Conflict of Interest: None declared

ANTI-RESPIRATORY SYNCYTIAL VIRUS ACTIVITY OF MORINGA OLEIFERA LEAF EXTRACT IN HEP 2 CELLS

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Presenting author: Akuoma Ekeh

Aim: Respiratory syncytial virus (RSV) causes respiratory viral infection of a global proportion. There is currently no approved, safe and effective antiviral drug against it. Natural products hold potential for discovery of anti-RSV agents. The present study assessed the anti-RSV activity of Moringa oleifera (MO) Method: Antiviral activity of MO leaf extracts was evaluated by a modified viral plaque reduction assay. Parallel assays for effect of the antiviral agents on cell viability was carried out on Hep 2 cells using the 3-(4,5-dimethylthiazolyl)-2,5-diphenyltetrazolium bromide (MTT) reduction assays. Results: Extracts of MO showed anti-RSV activity with IC50 = 50.22 ± 4.941 µg/ml while the cell cytotoxic effect of extract was CC50 = 23.83 ± 6.913 µg/ml. Conclusion: MO extract has exhibited notable anti-RSV activity warranting its further chemical and biomedical development for possible clinical utility against RSV.

Abstract category: Vaccines, Therapies & Treatments
Keywords: RSV, Moringa Oleifera, Antiviral, Viral Plaque Reduction, Cell Viability
Conflict of Interest: None declared
KNOWLEDGE AND ATTITUDES ABOUT RESPIRATORY SYNCYTIAL VIRUS (RSV), RSV VACCINATION DURING PREGNANCY, AND INFANT MONOCLONAL ANTIBODIES FOR RSV

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Presenting author: Leora Feldstein

BACKGROUND: Respiratory Syncytial Virus (RSV) is the leading cause of hospitalization among infants in the U.S. Monoclonal antibodies (mAb) for infants and vaccines for pregnant people may reduce risk of severe RSV.

METHODS: In April-May 2023, we surveyed participants aged 18-49 years from a community-based cohort study in Oregon and Washington about RSV awareness, trust in RSV prevention information sources, and perceptions of RSV prevention products.

RESULTS: Of the 1,177 respondents, mean age was 41.4 years, most were female (66%), non-Hispanic white (77%), had a bachelor’s or higher degree (86%), and a household income >$100,000 (73%). Among those with children (92.3%, n=1,087), 40% thought their child would have mild symptoms if they had RSV and 22% felt their child would need to go to a doctor or urgent care. Most respondents agreed that public health officials and physicians as information sources suggest their importance in promoting RSV vaccination during pregnancy and infant mAb was high, with 70% and 68% responding very likely, respectively. When asked about potential side effects, 37% and 41% expressed concern about potential side effects of vaccine or mAb, respectively.

CONCLUSION: Most respondents within a highly-educated and upper middle-class cohort reported that they or their partner would likely get an RSV vaccine during pregnancy or RSV mAb for their infant. The high level of trust in public health officials and physicians as information sources suggest their importance in promoting RSV vaccination.

Abstract category: Vaccines, Therapies & Treatments
Keywords: RSV, Vaccination, Monoclonal Antibodies, Knowledge, Attitudes
Conflict of Interest: None

VACCINATION DURING PREGNANCY: TARGETED REVIEW OF TEMPORAL AND CLINICAL FACTORS INFLUENCING ESTIMATES OF VACCINE EFFICACY/EFFECTIVENESS AGAINST INFANT RESPIRATORY ILLNESS

Deshayne B. Fell (1), Jennifer Deese (1), Bradford D. Gessner (1), Jessica E. Atwell (1)

1. Pfizer Inc.

Presenting author: Deshayne Fell

Vaccination during pregnancy can passively protect infants via transplacental transfer (TPT) of maternal antibodies. Numerous studies have demonstrated vaccine efficacy/effectiveness (VE) of maternal vaccination to prevent infant illness; however, potential influences of temporal and clinical factors—known to impact TPT—on VE estimates are unclear. We performed a targeted literature search through November 2023 including publications presenting VE among infants following
maternal vaccination with pertussis-containing, influenza, or COVID-19 vaccines. We extracted results by: (a) GA at vaccination, (b) time from vaccination to birth, (c) clinical subgroups (preterm infants, immunocompromised pregnant individuals). Among 21 pertussis studies, 3 of 8 providing VE estimates stratified by GA at vaccination reported higher VE at <2 months (m) of age following 3rd vs. 1st/2nd trimester vaccination. Pertussis VE <3m (3 studies) and <6m (1 study) was similar by time from vaccination to birth. Among 28 influenza publications, 4 stratified by GA at vaccination—1 reported higher VE against influenza hospitalization at age <6m following 3rd vs. 2nd trimester vaccination; however, estimates from the other 3 studies were similar across GA groups. Among 7 COVID-19 studies, 3 of 4 found qualitatively higher VE following 3rd trimester vaccination. VE estimates were similar among preterm/term infants in 2 studies (1 study each against influenza and COVID-19). A single influenza study showed lower VE among infants born to immunocompromised mothers. Few studies of vaccination during pregnancy have evaluated whether temporal and clinical factors impact VE among infants. Understanding these factors will be critical for optimal implementation of maternal RSV vaccines.

Abstract category: Vaccines, Therapies & Treatments
Keywords: Maternal Immunization, Vaccine Efficacy, Vaccine Effectiveness
Conflict of Interest: This work was sponsored by Pfizer Inc. and all authors are employees of Pfizer Inc.

THE COST-EFFECTIVENESS OF PREVENTIVE INTERVENTIONS FOR PAEDIATRIC RESPIRATORY SYNCYTIAL VIRUS INFECTION IN CAMEROON
Authors listed in alphabetical order: Louis Bont (1), Andrew Clark (2), Frédéric Debellet (3), Norbert Fuhungwa (4), Henshaw Mandi (4), Clint Pecenka (3), Neele Rave (1), Farina Leonie Shaaban (1)
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2. Department of Health Services Research and Policy, London School of Hygiene & Tropical Medicine, London, UK.
3. Center for Vaccine Innovation and Access, PATH, Seattle, WA, USA
4. Triangle Research Foundation Douala, Cameroon
Presenting author: Norbert Fuhungwa
Background: Pharmaceutical Respiratory Syncytial Virus (RSV) prevention strategies are emerging, but their cost-effectiveness in low- and middle-income countries (LMICs) remains under-researched. We aimed to model the health impact and cost-effectiveness of a maternal vaccine (bivalent preF RSV vaccine) and long-acting infant monoclonal antibody (Nirsevimab) for RSV prevention in children aged <5 years in Cameroon.

Methods: Using a static proportionate outcomes model we estimated the impact and cost-effectiveness of the bivalent preF RSV vaccine and Nirsevimab compared to no pharmaceutical intervention and each other for the period 2024-2033. We assumed year-round administration and equal prices (range: $3.5-$25). The primary outcome was the incremental cost per disability-adjusted life year (DALY) averted from a government perspective. To assess effects of uncertainties in parameters, sensitivity analyses were conducted and cost-effectiveness was explored over a range of willingness to pay thresholds expressed as proportions of GDP per capita.

Results: Over the period 2024-2033, the bivalent preF RSV vaccine (assuming 69% efficacy; 6 months protection) was estimated to avert 55,194 DALYs and 2,215 (26.8%) RSV-related deaths, while Nirsevimab (assuming 77% efficacy; 5 months protection) was estimated to avert 65,657 DALYs and 2,635 (31.9%) RSV-related deaths, in preliminary analyses. At $3.5 per dose the bivalent preF RSV vaccine and Nirsevimab were both cost-effective when compared separately to the status quo (no pharmaceutical intervention). Cost-effectiveness of both interventions depended strongly on the price per dose.

Conclusion: Depending on pricing and Gavi support, maternal vaccination and long-acting infant monoclonal antibodies are likely impactful and cost-effective in Cameroon.

Abstract category: Vaccines, Therapies & Treatments
Keywords: mAb (Nirsevimab), Maternal Vaccine (Bivalent pref RSV Vaccine), UNIVAC Model, Cost-Effectiveness, Respiratory Syncytial Virus, Cameroon
Conflict of Interest: Nothing to declare

IMMUNOGENICITY OF mRNA-1345: RESULTS FROM THE RSV PHASE 3 PIVOTAL TRIAL IN ADULTS AGED ≥60 YEARS
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Presenting author: Jaya Goswami
Background: The mRNA-1345 vaccine demonstrated efficacy in preventing RSV-associated disease in adults (≥60 years) in the phase 2/3 ConquerRSV trial, with no evident safety concerns. We present humoral immunogenicity of mRNA-1345 in a subset of study participants; safety data are presented separately.

Methods: In this ongoing phase 2/3, multi-country, double-blind, placebo-controlled study (NCT05127434; EudraCT:2021-005026-20), adults (≥60 years) were randomized (1:1) to receive 1 dose of mRNA-1345 (50 μg) or placebo. RSV-A and RSV-B neutralizing antibody (nAb) geometric mean titers (GMTs) and binding antibody (bAb) geometric mean concentrations (GMcs) were assessed at baseline and Day 29 (D29) and seroresponse rates calculated in the randomly-selected per-protocol immunogenicity set (n=1848; mRNA-1345, n=1515; placebo, n=333).

Results: mRNA-1345 increased nAb GMTs (95% CI) from 2552.8 (95% CI, 2414.3-2699.4) and 1425.4 (95% CI, 1352.7-1501.9) IU/mL at baseline to 21,475.4 (95% CI, 20,273-22,748.1) and 7246.0 (95% CI, 6864.8-7648.4) IU/mL at D29 against RSV-A and RSV-B, respectively [geometric mean fold rise [GMFR]: RSV-A=8.4; RSV-B=5.1; Figure]. Seroresponse rates for mRNA-1345 (4-fold rise from baseline) were 74.2% and 56.5% against RSV-A and RSV-B, respectively; participants meeting seroresponse criteria had lower baseline GMTs than those who did not. Similar pattern of response was observed for pref bAb GMC (mRNA-1345 GMFR: 7.7). D29 nAb and bAb responses across demographic and risk subgroups were generally consistent with the general study population.

Conclusion: mRNA-1345 boosted nAb (RSV-A and RSV-B) and bAb levels in adults (≥60 years), including in those at higher risk for severe disease. Results are consistent with previously demonstrated efficacy against RSV disease.
Efficacy and Safety of mRNA-1345, an RSV Vaccine, in Older Adults: Results Through ≥6 Months of Follow-Up

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4. Spotlight Research Center, LLC, Miami, FL, USA

Presenting author: Jaya Goswami

Background: In the phase 3 trial primary analysis, mRNA-1345 was efficacious against RSV-associated lower respiratory tract disease (RSVLRTD) in adults ≥60 years, with no evident safety concerns. We present findings from additional analyses performed when >90% of participants completed ≥6-month follow-up.

Methods: This ongoing phase 3, multi-country, double-blind, placebo-controlled study (NCT05127434) randomized (1:1) adults ≥60 years to receive 1 dose of mRNA-1345 (50 μg) or placebo. Primary objectives included safety and tolerability evaluation and vaccine efficacy (VE) of prevention of a first episode of RSV-LRTD with ≥2 or ≥3 symptoms between 14 days and 12 months postinjection, respectively; key secondary efficacy objectives included prevention of RSV-associated acute respiratory disease (RSV-ARD). Efficacy against RSV-LRTD with shortness of breath (SOB) was assessed as a surrogate measure of more severe disease.

Results: The analysis included 36,157 participants (mRNA-1345, n=18,112; placebo, n=18,045). mRNA-1345 was well-tolerated; no safety concerns were identified. At a median follow-up of 8.6 months, mRNA-1345 VE was 63.3%, 63.0%, and 53.9% against RSV-LRTD with ≥2 and ≥3 symptoms and RSV-ARD, respectively. Lower bound of the 95% CI exceeded prespecified success criteria of 20% for all endpoints (Figure). VE was evident across RSV-A and RSV-B subtypes and was generally consistent across demographic and risk subgroups. VE was 74.6% (95% CI, 50.7-86.9) against RSV-LRTD with ≥2 symptoms, including SOB.

Conclusion: A single dose of mRNA-1345 was well-tolerated, with no safety concerns identified, and continued to demonstrate efficacy for the prevention of RSV disease through 26 months among adults ≥60 years.
CONTENT ANALYSIS OF RSV-RELATED NEWS IN THE DIGITAL MEDIA

Rhythm Hora (1), Arindam Ray (2), Rashmi Mehra (1), Syed F Quadri (1), Amrita Kumari (1), Seema Singh Koshal (1), Amanjot Kaur (1), Arup Deb Roy (1)

1. John Snow India Private Limited
2. Bill and Melinda Gates Foundation

Presenting author: Rhythm Hora

Background: Respiratory syncytial virus (RSV) is identified as a leading cause of lower respiratory tract infections in children under the age of 5 years. Introduction of a vaccine against RSV will potentially reduce the burden of the disease. Since media has been known to play a pivotal role in shaping public perception of a new vaccine, the present study aims to explore the landscape of online RSV news coverage in India.

Materials and Methods: Media content analysis was retrospectively conducted by an online search for news stories in the four most visited newspapers (Hindustan Times, The Hindu, The Indian Express and The Times of India) and three news sites (India Today, NDTV news and News 18). A total of 58 news pieces appearing over a period of 1 year (November 1, 2022 - October 31, 2023) were retrieved after entering selected “keywords” ("RSV" and "RSV vaccine"). Inclusion criteria encompassed English language news pieces with RSV-specific content. Two reviewers searched online resources, compiled, reliably coded and analyzed the news pieces using NVIVO.

Results: The preliminary findings suggest that RSV vaccine introduction in the routine immunization programme is a possible solution to combating RSV related comorbidities in India. Detailed analysis is under process.

Conclusion: Initial findings suggest that majority of the retrieved articles are centered around the disease burden and RSV vaccine in India. A potential limitation of this study was the exclusion of online news articles in regional languages.

Abstract category: Vaccines, Therapies & Treatments
Keywords: RSV, RSV vaccine

Conflict of Interest: The authors present no conflict of interest

LIVE-ATTENUATED RESPIRATORY SYNCYTIAL VIRUS VACCINE FOR THE PREVENTION OF RSV DISEASE IS SAFE AND IMMUNOGENIC IN 6- TO 18-MONTH-OLD NORTH AND SOUTH AMERICAN CHILDREN

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Presenting author: Olubukola Idoko

Background: Despite decades of research and recent success with passive immunization, a pediatric vaccine for RSV the primary cause of pediatric hospitalizations in infants is not available. Early trials with live attenuated candidates suggest promise for pediatric vaccination.

Methods: The Sanofi-sponsored Phase I/II trial (NCT04491877) evaluated a live-attenuated RSV candidate (RSVt), co-developed in collaboration with NIH, in 6-18mo olds. Safety, reactogenicity, immunogenicity and infectivity of the intranasally administered vaccine at 2 dose levels [low dose (LD) and high dose (HD)] or placebo were evaluated. One or two administrations (two months apart) were assessed in sequential cohorts allowing safety review prior to increased dosage/number of doses. Participants (N=259) provided blood samples at baseline and at least 5 months post the vaccine to assess immunogenicity. Vaccine viral shedding was assessed 7 days post each vaccine. Safety was assessed up to at least 5 months post last vaccine.

Results: There were no safety concerns after one or two vaccines at either dose level. No related SAEs or deaths were reported. Around 70% of RSV-naive vaccine recipients attained a ≥4-fold rise in serum neutralizing antibody post one or two vaccinations. Vaccine viral shedding decreased markedly following the second vaccine administration when compared to the first (57% vs 11% HD seroresponders) suggesting protective potential. Geometric Mean Concentrations (GMCs) post season or 5 months post second vaccine were comparable to 28 days post vaccination two GMCs.

Conclusion: The current results suggest a promising safety, infectivity, and immunogenicity profile for RSVt vaccines and support the future development.

Abstract category: Vaccines, Therapies & Treatments
Keywords: Live-attenuated, RSV, Safe, Immunogenic, Children

Conflict of Interest: CV and SJ are consultants for Moderna, Inc. PAD has no conflicts to disclose. GPM has received a research grant from Merck and conducts clinical trials for Pfizer, Merck, GSK, Medicago and Moderna, Inc. GI is an employee of Spotlight Research Center, LLC.
ASSESSING THE IMPACT OF PHARMACIST INITIATED VACCINATION AGAINST RESPIRATORY SYNCYTIAL VIRUS (RSV) IN OLDER ADULTS

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Presenting author: Ajit Johal

Since 2009, pharmacists in British Columbia, Canada have had the expanded scope of practice to administer all approved vaccinations as schedule 2 products. Thereby negating the requirement to obtain a prescription from a medical doctor to administer recommended vaccinations. To assess the impact of independent pharmacist vaccine assessment and administration a pilot study was conducted at community pharmacy locations in Vancouver, British Columbia. The vaccine assessed was the recently approved Respiratory Syncytial Virus (RSV) (recombinant, AS01E adjuvanted) vaccine for adults aged 60 and older. This was the first RSV vaccine approved in Canada for the older adult population. From September 12th - December 1st, 2023, a total of 107 (RSV) (recombinant, AS01E adjuvanted) vaccines were administered at three community pharmacy locations in Vancouver, British Columbia Canada. Of the total 107 doses given, a total of 86 (80%) were initiated by pharmacists at the location. Illustrating the current and future impact on older adult vaccination rates in jurisdictions where pharmacists can independently assess and administer recommended vaccinations.

Abstract category: Vaccines, Therapies & Treatments
Keywords: Vaccines, RSV, Older Adults
Conflict of Interest: Speaker Honorarium from GSK, Pfizer, Valneva, Merck.

MONOCLONAL ANTIBODIES TARGETING SITES IN RSV ATTACHMENT G PROTEIN PROVIDE CROSS-PROTECTION AGAINST RSV A AND RSV B

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Presenting author: Surender Khurana

Currently, only Palivizumab and Nirsevimab targeting the RSV fusion protein are licensed for pre-treatment of high-risk infants. Glycoprotein-targeting antibodies may also provide protection against RSV. In this study, monoclonal antibodies were generated from mice immunized with recombinant non-glycosylated G proteins from either RSV-A2 strain or RSV-B1 strain. Mapping of the MAbs binding sites using different G proteins and peptides identified five unique antigenic classes (G0-G5). None of the anti-G MAbs neutralize RSV-A2 or RSV-B1 in vitro. The protective efficacy of these MAbs was determined in mice challenged with either RSV-A2 line 19F expressing firefly luciferase or RSV-B1 expressing firefly luciferase, one day after treatment with anti-G MAbs. Infectious RSV titers, viral dissemination and pathology were measured in lungs on day 5 post challenge. All MAbs significantly reduced lung infectious viral titers by more than 2 logs on day 5 post-RSV challenge. The majority of mice receiving anti-G MAbs prior to RSV-A2 or RSV-B1 challenge showed reduced lung pathology compared with lung pathology observed in the mock- treated animals. RSV dissemination in the lungs (determined by whole body live imaging) was variable and correlated with lung pathology following viral challenge. Together, our data demonstrated that new anti-G MAbs targeting multiple sites including conformation-dependent class G0 Mab 77D2, CCD-specific class G1 Mab 40D8, and carboxy terminus of CCD class G5 Mab 7H11, showed cross-reactive protection following challenge with either RSV-A or B subtypes. These findings may support further development of G-targeting cross-protective monoclonal antibodies against RSV.

Abstract category: Vaccines, Therapies & Treatments
Keywords: RSV-G, THERAPUETICS, MONOCLONAL ANTIBODIES, PREVENTION, TREATMENT
Conflict of Interest: None declared

POTENTIAL STRATEGIES FOR COMBATING RESPIRATORY SYNCYTIAL VIRUS (RSV) DISEASE IN INDIA: A NARRATIVE REVIEW

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1: John Snow India Private Limited
2: Bill and Melinda Gates Foundation

Presenting author: Seema Singh Koshal

Background: Respiratory syncytial virus (RSV) has been identified as a leading cause of lower respiratory tract infections in young children and elderly. In 2020, the RSV-associated disease burden among children in 72 low-income and lower-middle-income countries was estimated at an average of 20.8 million cases, 1.8 million hospital admissions, 40,000 deaths, and 1.2 million discounted disability-adjusted life years (DALYs). As per the 2019 report of the National Health Portal of India, 41,996,260 cases and 3,740 deaths from respiratory infections were recorded across India in 2018. The present study aims to provide an overview of the available measures for combating Respiratory Syncytial Virus (RSV) disease in India.

Methods: A literature review of existing studies, research reports, and epidemiological data was conducted to gather information on RSV and RSV preventative measures in India. The safety, efficacy, and accessibility of preventive products, including vaccines and antiviral medications, were reviewed and included.

Results: The study reveals a substantial RSV disease burden in India, with high prevalence leading to significant hospitalization and mortality rates. Evaluation of preventive products indicates promising avenues for reducing the impact of RSV, emphasizing the potential breakthroughs offered by vaccines and antiviral medications.

Conclusion: The study maps out the available measures along with their potential to reduce the burden of RSV in India. A cross-disciplinary approach involving collaboration amongst different stakeholders is imperative to devise comprehensive strategies for effectively tackling RSV in the Indian context.

Abstract category: Vaccines, Therapies & Treatments
Keywords: RSV, Vaccine, strategies, India
Conflict of Interest: None declared
CLINICAL AND PRECLINICAL DATA SUPPORTING INHALED DELIVERY OF ‘MUCO-TRAPPING’ ANTIBODIES FOR AT HOME TREATMENT OF RSV INFECTIONS

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3. Eshelman School of Pharmacy, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA.

Presenting author: Sam Lai

Background: There are no approved RSV treatments. Antiviral monoclonal antibodies (mAbs) offer an outstanding safety profile and possess an unrecognized effector function in mucus: mAbs with suitable Fc-mucin affinity can effectively trap viruses in mucus (“muco-trapping”). Widespread use of intravenous administration is not practical for cost and logistical reasons.

Rationale: Convenient at-home inhalation delivery that doses mAb directly to the sites of infection when symptoms first emerge should prevent hospitalization. We are advancing a platform of inhalable, muco-trapping mAbs that quickly clear viruses from Airways.

Results: We engineered a muco-trapping anti-F mAb that traps RSV in both adult and pediatric airway mucus. We evaluated the mAb in lambs with established lower respiratory tract RSV infections at peak viral titers, dosed daily via nebulization starting 3 days post-infection. Within 3 days, viral titers were reduced by 4- to 5- log in both BALF and lung tissues; bronchilitis, neutrophil infiltration, and epithelial damage also decreased to near background levels (Table 1).

In human clinical trials, inhaled mAb delivery achieved therapeutic concentrations throughout the respiratory tract. Levels were significantly higher than IV delivery, despite 6-fold lower dose used. Nebulized mAb dosing was safe and well tolerated, with fewer AEs than IV.

Conclusions: Inhaled delivery achieves therapeutic mAb concentrations in the entire human respiratory tract. Nebulized treatment of RSV infected lambs confirmed the efficacy of inhaled delivery. Inhaled treatment offers a promising safe intervention that should effectively halt RSV disease progression and alleviate symptoms.

Acknowledgements: USAMRIID (MTEC award W81XWH-20-9-0008), NIH, and the Packard Foundation.

Abstract category: Vaccines, Therapies & Treatments

Keywords: Antibody, inhaled treatment, mucus, nebulize

Conflict of Interest: S.K.L is founder of Mucommune, LLC and currently serves as its interim CEO. S.K.L is also founder of Inhalon Biopharma, Inc, and currently serves as its CSO, Board of Director, and Scientific Advisory Board. S.K.L has equity interests in both Mucommune and Inhalon Biopharma; S.K.L’s relationships with Mucommune and Inhalon are subject to certain restrictions under University policy. The terms of these arrangements are managed by UNC-CH in accordance with its conflict of interest policies. Other co-authors may have equity interests in Inhalon Biopharma.

Table 1: RSV Infected Neonatal Lamb Study Summary

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Viral Load (Log10 PFU/ml)</th>
<th>% of Lung with Gross Lesions</th>
<th>Bronchilitis Score</th>
<th>Cumulative Histo-Score</th>
<th>Neutrophil Infiltrate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saline (nebulized)</td>
<td>3.9 ± 1.8</td>
<td>45 ± 1.6</td>
<td>33.1 ± 17.4</td>
<td>1.9 ± 0.9</td>
<td>12.0 ± 4.7</td>
</tr>
<tr>
<td>Nebulized muco-trapping mAb</td>
<td>0.0 ± 0.0</td>
<td>0.5 ± 0.9</td>
<td>5.5 ± 3.5</td>
<td>0.3 ± 0.4</td>
<td>3.2 ± 2.8</td>
</tr>
<tr>
<td>Synagis (IV)</td>
<td>0.5 ± 1.1</td>
<td>1.7 ± 1.5</td>
<td>23.7 ± 19.2</td>
<td>0.8 ± 1.7</td>
<td>5.7 ± 4.7</td>
</tr>
</tbody>
</table>

Conflict of Interest: S.K.L is founder of Mucommune, LLC and currently serves as its interim CEO. S.K.L is also founder of Inhalon Biopharma, Inc, and currently serves as its CSO, Board of Director, and Scientific Advisory Board. S.K.L has equity interests in both Mucommune and Inhalon Biopharma; S.K.L’s relationships with Mucommune and Inhalon are subject to certain restrictions under University policy. The terms of these arrangements are managed by UNC-CH in accordance with its conflict of interest policies. Other co-authors may have equity interests in Inhalon Biopharma.
RESPIRATORY SYNCYTIAL VIRUS AMONG INFANTS IN ARGENTINA

Anneli Kaufmann, Lucila Rey, Elizabeth Ferreira, Angela Waterval-Overbeek, W. Law, 1, and 2

Abstract

Background: Respiratory syncytial virus (RSV) is a leading cause of infant hospitalisation and mortality globally. Given that the incidence of severe RSV infection peaks during the first months of life, a key strategy would involve maternal immunisation. This strategy has demonstrated success in national immunisation programmes in the Netherlands, with maternal vaccine coverage for pertussis reaching 72%. Recently, the first maternal vaccine for RSV has been approved by the EMA. Until now, limited data are available regarding the factors that influence its acceptance. Our study seeks to explore attitudes towards routine implementation of maternal RSV immunisation.

Methods: A multi-method study was conducted in the Netherlands (April-July 2021) in pregnant women without age or pregnancy duration restrictions. Questionnaires, distributed via posters in healthcare facilities frequently visited by pregnant women and on social media, covered sociodemographic characteristics, vaccination history, willingness to receive RSV vaccination, and RSV awareness. A subgroup of women participated in semi-structured interviews.

Results: A total of 76 women participated in the study. Maternal RSV vaccine acceptance increased from 40.3% in research to 82.3% post-licensure health council recommendation. Influencing factors included university education (OR; 5.6, 95%CI: 0.005-31.236), non-first pregnancies (OR; 7.2, 95%CI: 30.310), pertussis vaccine awareness (OR; 36.8, 95%CI: 0.005-30.310). Interviews highlighted the importance of vaccine knowledge, emphasizing active involvement from healthcare workers (GPs/midwives) and partner influence.

Conclusion: Overall, pregnant women expressed willingness to receive the RSV vaccine. Our findings contribute valuable insights into the rationale behind decision-making, emphasizing educational background, pregnancy history, RSV awareness, and the influence of healthcare workers and partners.

Abstract category: Vaccines, Therapies & Treatments

Conflict of Interest: Anneli Kaufmann and Angela Waterval-Overbeek are Pfizer employees.

BUDGET IMPACT OF RSVpreF MATERNAL VACCINE AMONG PREGNANT PEOPLE FOR PREVENTION OF RESPIRATORY SYNCYTIAL VIRUS AMONG INFANTS IN THE US

Ahuva Averin (1), Amy Law (2), Erin Quinn (1), Emily Kutrieb (1), Mark Atwood (1)

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Abstract

Background: Respiratory syncytial virus (RSV) is a leading cause of lower respiratory tract illnesses (LRTI) among young children in the United States (US). Given the recent US Advisory Committee on Immunization Practices recommendation for use of Pfizer's RSVpreF vaccine during pregnancy to prevent RSV-LRTI among infants, we estimated 5-year budgetary impact of RSVpreF for a fictional payer with 10M beneficiaries.

Methods: Using a deterministic cohort model depicting clinical outcomes and economic costs of RSV-LRTI among infants from birth to age 1 year, we estimated the value of RSVpreF use during pregnancy. Model parameter values were estimated principally based on published sources. Model outcomes, including cases of disease, disease-attributable deaths, and costs of disease and vaccination, were projected during the first year of life for five annual birth cohorts.

Results: Over 5 years, RSVpreF among pregnant persons prevented 1,397 RSV-LRTI hospitalizations, 2,015 RSV-LRTI emergency department episodes, and 5,831 RSV-LRTI outpatient clinic episodes among infants (Table). With medical care costs projected to be reduced by $51.7M and cost of vaccination projected to be $47.2M, total costs were reduced by $4.5M overall and nearly $0.01 PMPM.

Conclusions: Findings from this analysis show that use of RSVpreF among pregnant people—in lieu of no vaccination—would yield substantive reductions in cases of RSV-LRTI among infants, and that increased vaccination costs would be fully offset by reductions in disease-related medical costs.

Abstract category: Vaccines, Therapies & Treatments

Keywords: Budget impact; respiratory syncytial virus; maternal vaccination; infant

Conflict of Interest: Funding for this study was provided by Pfizer Inc. to Avalere Health. Lucila Rey-Ares, Nadia Zuccarino, Celina Guadalupe Vega, and Amy Law are employed by and may hold stock in Pfizer Inc. Ahuva Averin, Derek Weycker, Mark Atwood, Erin Quinn, and Emily Kutrieb are employed by Avalere Health.

COST-EFFECTIVENESS OF MATERNAL RSVpreF VACCINE DURING PREGNANCY FOR PREVENTION OF RESPIRATORY SYNCYTIAL VIRUS AMONG INFANTS IN ARGENTINA

Lucila Rey-Ares (1), Ahuva Averin (2), Nadia Zuccarino (1), Celina Guadalupe Vega (1), Emily Kutrieb (2), Erin Quinn (2), Mark Atwood (2), Derek Weycker (2), Amy W. Law (3)

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2. Avalere Health, Boston, MA, USA
3. Pfizer Inc., New York, NY, USA

Abstract

Background. Respiratory syncytial virus (RSV) lower respiratory tract illness (LRTI) is common among young children in Argentina. We estimated the value-based
price (VBP) of Pfizer’s novel RSVpreF vaccine for use among pregnant people for prevention of RSV-LRTI among infants aged <1 year.

Methods. Clinical outcomes and economic costs of RSV-LRTI during infancy and expected impact of RSVpreF vaccination during pregnancy on outcomes and costs among infants were projected using a population-based cohort model. Model inputs (i.e., population characteristics, disease/fatality rates, costs) were based on local and global data. Vaccine effectiveness was based on efficacy data from Pfizer’s Phase III clinical trial ("MATISSE"). Base case and sensitivity analyses (i.e., for RSVpreF vs. no vaccine) were conducted from healthcare system perspective. Willingness-to-pay ranged from $10,636-31,908 per quality-adjusted life-year (QALY; i.e., 1-3x gross domestic product per capita). Costs are reported in US$.

Results. RSVpreF administered to 342,110 pregnant persons provided protection to 330,079 infants at birth and prevented 3,915 RSV hospitalizations, 6,399 RSV cases requiring emergency department care, 6,182 RSV cases requiring a physician office visit, and 67 disease-related deaths (Table). Direct costs were projected to be reduced by $3.5 million. With 2,061 QALYs gained, VBP of RSVpreF was estimated to range from $74.46-202.62 per dose. In sensitivity analyses, results were robust to changes in key parameter values.

Conclusions. RSVpreF among pregnant persons would significantly reduce the clinical and economic burden of RSV-LRTI among infants in Argentina and would be considered a cost-effective intervention over a wide range of prices.

Abstract category: Vaccines, Therapies & Treatments

Keywords: Cost-effectiveness; respiratory syncytial virus; vaccination; maternal; infant

Conflict of Interest: Funding for this study was provided by Pfizer Inc. to Avalere Health. Lucila Rey-Ares, Nadia Zuccarino, Celina Guadalupe Vega, and Amy Law are employed by and may hold stock in Pfizer Inc. Ahuva Averin, Derek Weycker, Mark Atwood, Erin Quinn, and Emily Kutrieb are employed by Avalere Health.

RECOMMENDATIONS OR GUIDELINES FOR RESPIRATORY SYNCYTIAL VIRUS (RSV) VACCINATION IN OLDER ADULTS AND SUPPORTIVE PHASE 3 DATA: AN OVERVIEW

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Presenting author: Nicolas Lecrenier

Background: There are currently 2 RSV vaccines approved in the USA and most of Europe for the prevention of RSV-related lower respiratory tract disease (LRTD) in older adults (OA; ≥60 years of age [YOA]): RSVPreF3 OA (GSK) and RSVpreF (Pfizer), both licensed in 2023. A single dose of the RSV vaccines administered in OA demonstrated efficacy in preventing RSV-LRTD with an acceptable safety profile. To accurately contextualize the national recommendations/guidelines on RSV vaccination in OA, we reviewed the available recommendations/guidelines and the supportive clinical data.

Methods: We searched the national health authority’s and/or vaccination committee’s websites of countries where RSV vaccines are authorized, and supportive clinical data published in PubMed/Embase/grey literature, in November 2023. Topics of interest included target population, age group, special population recommendations, and related vaccine efficacy, safety/reactogenicity.

Results: From 8 available national recommendations, 5 were in adults ≥60 YOA, 2 in ≥75 YOA, and 1 in ≥18 YOA with underlying conditions/comorbidities. Six recommendations mentioned at-risk populations (Table 1). Regarding supportive data, differences were identified between vaccines (in efficacy analysis endpoints, special and target populations, follow-up time, case definitions [Table 1, Table 2 – next page]). Clinically acceptable safety/reactogenicity profiles were observed for both vaccines.

Conclusions: Several countries already provided national vaccination recommendations against RSV disease, for varying target ages and comorbidities. RSVPreF3 OA and RSVpreF have demonstrated efficacy against RSV disease in OA and other at-risk populations. Efficacy figures cannot be directly compared between the 2 vaccines due to differences in statistical methods and endpoint definitions.

Funding: GlaxoSmithKline Biologicals SA
Abstract category: Vaccines, Therapies & Treatments

Keywords: RSV vaccines, recommendations in older adults, phase 3 supportive clinical data, overview.

Conflict of Interest: NL, NJ, ND, YAM, MVW, and YS are GSK employees. NL, NJ, ND, MVW, and YS also have stock options or shares from GSK. NL declares having patents planned, issued, or pending for HPV vaccine, Zoster vaccine, Staphylococcus. ND has stock options or shares from Haleon and declares patents Vaccination Against RSV, filing numbers 2218080.6 and 2303002.6, filed in the UK Intellectual Property Office. MVW is a co-applicant on a pending patent filed by GSK.

PERSPECTIVES OF PREGNANT AND LACTATING WOMEN, COMMUNITY MEMBERS, HEALTHCARE WORKERS, AND POLICYMAKERS IN KENYA TO INFORM DEMAND GENERATION FOR MATERNAL RSV VACCINES

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2. Jhpiego Kenya, Nairobi, Kenya

Presenting author: Rupali Limaye

Background: RSV is responsible for ~40% of all hospital admissions of infants <1 year in low- and middle-income countries. An RSV vaccine for pregnant persons is imminent. We identified factors to inform maternal RSV vaccine demand generation strategies in Kenya.

Methodology: We conducted 60 in-depth interviews with pregnant people, lactating people, community members, healthcare workers, and policymakers and administered a survey to pregnant and lactating people (n=400). Participants were recruited from one rural and one urban county.

Results: Participants were shown a 10-second video of a baby with characteristic RSV wheezing, which was essential for disease recognition. Participants elucidated terms used for RSV, their beliefs in what causes RSV, and RSV risk perception. Related to the COVID-19 vaccine rollout among pregnant people, we found that healthcare providers and community leaders should be educated about RSV disease and vaccines and mobilized to gain the trust of communities. Related to maternal RSV vaccine hesitancy, people who were experiencing their first pregnancy and those who did not have a network that was supportive of RSV vaccine acceptance were more than 3 times and 2 times likely, respectively, to be characterized as having higher vaccine hesitancy compared to those not in their first pregnancy or those that had supportive networks related to RSV vaccine acceptance.

Discussion: Maternal RSV vaccine demand generation efforts should consider the population’s disease awareness and risk perception, capitalize on lessons learned related to the COVID-19 vaccine rollout, and address vaccine hesitancy concerns before a vaccine is available.

Abstract category: Vaccines, Therapies & Treatments

Conflict of Interest: None declared
EVALUATION OF DUAL CHIMERIC PATTERN RECOGNITION RECEPTOR LIGANDS AGONISTS AS ADJUVANTS FOR PREFUSOGENIC BASED RSV VIRUS-LIKE PARTICLE VACCINE CANDIDATE

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Presenting author: Ahmedali Mandviwala

Respiratory syncytial virus (RSV) is a major cause of severe respiratory disease in infants and young children worldwide. Recent studies have shown that a partially cleaved, fusion-inactive F protein, termed prefusogenic-F (prefg) is stable and elicits neutralizing antibodies. Along with fusion protein, glycoprotein (G) is also shown to induce neutralizing antibodies and matrix protein (M) plays a central role in viral assembly. Therefore, we have developed RSV virus-like particles (RSV-VLP) using baculovirus with sequence of preFg, G and M proteins, characterized them and evaluated their immunogenicity in mice. Our in vivo immunization studies showed induction of neutralizing antibody and potent binding antibody response against all the three proteins without enhanced respiratory disease (ERD) after challenge. Use of two separate pathogen recognition receptor (PRR) agonists as adjuvants in vaccine formulations has shown to enhance the immune response against the antigen. Therefore, we further explored whether chimeric adjuvants CL413 and CL429 can enhance RSV specific immune response compared to MPLA, an FDA approved adjuvant. Our in vivo studies in mice showed that intramuscular administration of VLPs supplemented with either CL413 or CL429 induces higher binding and neutralizing antibodies compared to the MPLA adjuvanted VLP. The IgG2a subtype response was also significantly increased. The chimeric adjuvants promoted enhanced secretion of IFNγ and IL4 from stimulated splenocytes. Adjuvanted formulations also inhibited development of ERD in immunized mice after RSV challenge. These results highlight the significance of use of chimeric PRR ligands with RSV-VLP and their administration by the i.m route.

Abstract category: Vaccines, Therapies & Treatments

Keywords: virus-like particles, chimeric adjuvants

Conflict of Interest: None declared

RISK ANALYSIS FOR EXPERIMENTAL RSV INFECTION IN THE OUTPATIENT SETTING- A SYSTEMATIC REVIEW


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5. Centre for Inflammation Research, University of Edinburgh, United Kingdom
7. Department of Clinical Sciences, Liverpool School of Tropical Medicine, Liverpool, United Kingdom
8. Division of infectious Diseases and International Health, University of Virginia, School of Medicine, Charlottesville, VA, USA
9. The Wellcome Trust Research Laboratory, Christian Medical College, Vellore, India
10. National Heart and Lung Institute, Imperial College London, London
11. Mahidol Vivax Research Unit, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand
12. Faculty of Medicine and Institute for Life Sciences, University of Southampton, Southampton, UK
13. Department of Hygiene and Infection Control, University Medical Center Utrecht, The Netherlands
14. Infectious Diseases Research, Lee Kong Chian School of Medicine, Singapore
15. Respiratory Syncytial Virus Network (ReSViNET) Utrecht, The Netherlands

Presenting author: Natalie Mazur

Background: Controlled human infection models (CHIM) have emerged as a promising tool for an affordable clinical development pathway. The costs of CHIM are driven by quarantine facilities and may be significantly reduced by performing CHIM in the outpatient setting. We aim to provide a framework for future RSV outpatient CHIM as a tool for the development of affordable RSV therapeutics.

Methods: A systematic review was conducted to search for outpatient CHIM using respiratory pathogens and data was extracted on safety (transmission, AEs, SAEs, PPE, and emergency care), logistic (inoculation, patient monitoring, sample collection) and ethical (patient burden and ethical review) aspects. Corresponding authors were asked to fill in a questionnaire or conduct a teleconference to collect additional data. PPE adequacy to prevent transmission via fomites was measured in an inpatient RSV CHIM.

Results: We analyzed sixty outpatient CHIM using four respiratory pathogens (influenza, RSV, streptococcus pneumoniae, and rhinovirus). One transmission event resulting in a mild cold was recorded. Hygiene instructions, minimal PPE usage and exclusion of at-risk household members mitigated the risk of transmission. Standard droplet and isolation measures prevented RSV transmission via fomites. Recruitment was enhanced, study costs were decreased, and sample collection mainly occurred at the study site. Ethical advantages included reduced patient burden, increased generalizability of study results, and contribution to global equity.

Conclusion: We conclude that safety, logistical and ethical risks are minimal for outpatient RSV CHIM. Our results provide guidance for researchers and ethics committees for future RSV outpatient CHIM enhancing affordable RSV vaccine development.

Abstract category: Vaccines, Therapies & Treatments

Keywords: Vaccines, Controlled Human Infection Model, Clinical Development Pathway

Conflict of Interest: UMCU has received fees for invited lectures from Abbvie, Merck and Sanofi
Background: Respiratory syncytial virus (RSV) is a leading cause of lower respiratory tract illness (LRTI) among infants in Brazil. Specific treatments are lacking, and the use of a prophylactic passive immunisation intervention is limited to children with high-risk conditions; thus most infants remain unprotected. Novel RSVpreF vaccine is expected to be licensed soon in Brazil for use among pregnant women for prevention of RSV in infants. The burden of RSV-LRTI from birth to 1 year of age, and the expected impact of RSVpreF maternal vaccination on outcomes among infants from birth. Publicly available data were used to parameterise the model and the model output included the number of medically attended RSV cases and RSV-related deaths, as well as direct costs of RSV and costs of caregiver productivity loss.

Results: Year-round RSVpreF maternal vaccination with 70% uptake would protect per year over 148,000 infants from birth. RSVpreF would prevent over 20,000 RSV medically attended cases annually, including 3,800 hospitalised cases. RSVpreF would substantially reduce healthcare resource use and reduce direct and indirect costs associated with RSV by several million US dollars. Considering median pharmacist pay of $61.8/hour, the labor cost for administering PFS is $0.82 and $1.64 for VRR in Belgium, and $3.56 and $6.23, respectively, in Malaysia. PFS was the preferred formulation, with main reasons being ease of administration and reduced immunization errors (47 VRR errors vs 10 for PFS; 57 errors/192 preparations).

Conclusion: Compared with VRR, PFS vaccines require roughly half the administration time and mean cost in labor and are associated with a reduced number of errors. PFS formulations have the potential for significant savings due to reduced labor and error-related costs.
on the latest publicly available data, including data from DATASUS, the numbers of medically attended RSV-LRTI cases (by care setting) and associated deaths, as well as RSV-LRTI-related costs were projected. Sensitivity analysis on vaccine uptake was conducted. Costs are reported in US dollars.

Results: Year-round RSVPref vaccination among pregnant women in Brazil would prevent >39,500 medically attended RSV-LRTI cases, including 9,400 RSV-LRTI hospitalisations and 370 RSV-related deaths. RSVPref would reduce direct medical costs alone by $6 million. If uptake of RSVPref is similar to recent uptake of pertussis maternal vaccination (70%) or even higher (up to 100%), maternal vaccination would prevent 58,900-84,000 medically attended cases, including 14,000-20,000 hospitalisations, and 560-800 deaths; reducing medical care costs by $9-12 million annually, respectively.

Conclusion: Maternal RSVPref would significantly reduce the clinical and economic burden of RSV among infants in Brazil.

Abstract category: Vaccines, Therapies & Treatments

Keywords: Respiratory Syncytial Virus Vaccines, Public Health, mathematical model, Brazil

Conflict of Interest: The research described herein was supported by Pfizer. AR, DP and DM are employees and shareholders of Pfizer. AA and MA are employees of Avalere Health, which received financial support from Pfizer Inc. for this study. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter apart from those disclosed.

PUBLIC HEALTH IMPACT AND COST-EFFECTIVENESS OF THE ADJUVANTED RSVPREF3 VACCINE AMONG ADULTS AGED >60 YEARS IN THE UNITED STATES

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Abstract category: Vaccines, Therapies & Treatments

Keywords: respiratory syncytial virus, adjuvanted RSVPref3 vaccine, public health impact, cost-effectiveness, older adults, vaccination

Conflict of Interest: Elizabeth La, Frederik Verelst, Desmond Curran, Sara Poston and Daniel Molnar are employed by and hold shares in GSK. Jonathan Graham is a full-time employee of RTI Health Solutions, an independent nonprofit research organization, which received funding for this study.

OUTCOMES OF BIRTH INCLUDING PREMATURITY IN A GLOBAL MATERNAL IMMUNIZATION TRIAL FOR PREVENTION OF RSV DISEASE IN INFANTS

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Abstract category: Vaccines, Therapies & Treatments

Keywords: Respiratory Syncytial Virus Vaccines, Public Health, mathematical model, Brazil

Conflict of Interest: The research described herein was supported by Pfizer. AR, DP and DM are employees and shareholders of Pfizer. AA and MA are employees of Avalere Health, which received financial support from Pfizer Inc. for this study. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter apart from those disclosed.

Table 1: Pregnancy Outcomes - Maternal Participants - Safety Population

<table>
<thead>
<tr>
<th>Vaccine Group (as Administered)</th>
<th>RSVPref 120 μg (N=300)</th>
<th>Placebo (N=300)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days between vaccination and delivery</td>
<td>2680</td>
<td>2657</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>57.8 (23.96)</td>
<td>57.8 (24.14)</td>
</tr>
<tr>
<td>Median (Range)</td>
<td>44.0 (2, 121)</td>
<td>55.0 (1, 132)</td>
</tr>
<tr>
<td>Gestational age at delivery (weeks)</td>
<td>3658</td>
<td>3643</td>
</tr>
<tr>
<td>Median (SD)</td>
<td>38.11 (4.44)</td>
<td>38.13 (3.56)</td>
</tr>
<tr>
<td>Median (Range)</td>
<td>38.14 (27.4, 43.0)</td>
<td>38.14 (27.9, 44.1)</td>
</tr>
<tr>
<td>Outcome at delivery</td>
<td>3549 (99.7)</td>
<td>3548 (99.8)</td>
</tr>
<tr>
<td>Stillbirth</td>
<td>10 (0.2)</td>
<td>9 (0.2)</td>
</tr>
<tr>
<td>Induced elective abortion</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Unusuals</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Note: Days between vaccination and delivery = date of delivery - vaccination date.

Table 1: Pregnancy Outcomes - Maternal Participants - Safety Population

- **Note**: Days between vaccination and delivery = date of delivery - vaccination date.
- **Note**: Induced Elective Abortion.
- **Note**: a = number of participants in the specified category.

CONCLUSIONS: Results indicate that the adjuvanted RSVPref3 vaccine is a cost-effective option for the prevention of RSV in US adults aged ≥60 years, with the potential to substantially reduce RSV burden.
RESULTS: Birth outcomes, including GA at birth, Aggar scores & birthweight (BW) were similar in both groups (Table 1, Table 2). Most infants were born full term (93%) in both groups & had a normal BW. An imbalance in the number of total premature infants (5.7%) in RSVpreF vs (4.7%) in placebo was not statistically significant (RR 1.2) was noted within a small number of upper-middle-income countries. There were 3 deaths in preterm infants (1 RSVpreF & 2 placebo). The majority of preterm infants were born late preterm, between 34–36 weeks. When birth outcomes were analyzed by the timing of maternal vaccination, there were no consistent trends across GAs. There were 19 stillbirths (10 RSVpreF, 9 placebo) & 22 infant deaths (8 RSVpreF, 14 placebo).

CONCLUSIONS: Birth outcomes were similar in RSVpreF vs placebo groups and no meaningful differences were detected.

Abstract category: Vaccines, Therapies & Treatments

Keywords: birth outcomes, bivalent RSV prefusion F vaccine, maternal immunization

Conflict of Interest: 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, Merckx. Beate Kampmann, PhD COI: Institution received funding from Pfizer for conduct of study. Eric A. F. Simões, MD COI: Institution received funding from Pfizer for conduct of study. In addition grants and consulting fees to the company from Merck & Co. and Pfizer Inc; grants to the institution from Astra Zeneca Inc. Roche Pharmaceuticals and Johnson and Johnson; & honoraria to the institution for consulting, and/or lectures from sanofi paseur, Cidara Therapeutics, Adlgo Therapeutics and Nuance Pharmaceuticals; manuscript editorial writing support and support for attending a meeting and from Pfizer Inc and Astra Zeneca Inc, and participation on a DSMB from Abbvive Inc, GlaxoSmithKline plc, Moderna Inc and Bill and Melinda Gates Foundation, all outside the submitted work. 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. Uzma Sarwar, MD COI: Employee of Pfizer and holder of Pfizer stock and stock options. James Baber MBChB, MPH COI: Employee of Pfizer and holder of Pfizer stock and stock options. Maria Maddalena Lino, MD,PhD COI Employee of Pfizer and holder of Pfizer stock and stock options. Philip Zachariah MD MSc MA COI: Employee of Pfizer and holder of Pfizer stock and stock and stock options. Annalesa S. Anderson, PhD COI Employee of Pfizer and holder of Pfizer stock and stock options. Kena A. Swanson, PhD COI: Employee of Pfizer and Sharholder of Pfizer stock. Alejandro Gurman, MD, COI: Employee of Pfizer and Sharholder of Pfizer stock and stock options.

PREVENTION OF INFANT RSV ILLNESS WITH A BIVALENT RSV PREFUSION F VACCINE ADMINISTERED DURING PREGNANCY: EFFICACY RESULTS FROM A PHASE 3 GLOBAL CLINICAL TRIAL

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3. MRC Vaccines and Infectious Diseases Analytics Research Unit, Johannesburg, South Africa
4. Medical Research Council Unit The Gambia at the London School of Hygiene & Tropical Medicine, Fajara, The Gambia
5. Vaccine Research and Development, Pfizer Inc, Hurley, UK
6. Vaccine Research and Development, Pfizer Australia, NSW, Australia

Presenting author: Iona Munjal

Introduction: End of study results of a global, phase 3, randomized, double-blind, placebo-controlled study in pregnant participants between 24–36 weeks' gestation randomized 1:1 to receive a bivalent RSVpreF vaccine or placebo are presented here.

Methods: Vaccine efficacy (VE) was assessed against infant RSV-positive medically-attended severe lower respiratory tract illness (RSV-MA-LRTI) and RSV-positive medically-attended LRTI (RSV-MA-LRTI) occurring within 6 months after birth. The study was conducted in 18 countries, including approximately one-third enrolled in low-middle income countries (LMICs), over 4 RSV seasons.

Results: Overall, 7385 maternal participants (3698 RSVpreF: 3687 placebo) were vaccinated; 7305 infants (3659 RSVpreF: 3646 placebo) were enrolled. VE against RSV-MA LRTI in the final analysis (Table 1) is consistent with results from the primary analysis with 82.4% (95% CI: 75.7, 88.9%) in infants within 90 days after birth and 70.0% (95% CI: 50.6, 82.5%) within 180 days. Cumulative VE through 24 months was 36.4% (14.4, 53.1), largely driven by efficacy less than 6 months. RSVpreF was 57.6% (95% CI: 31.3, 74.6%) and 49.2% (95% CI: 31.4, 62.8%) efficacious in reducing the incidence of RSV-MA-LRTI within 90 and 180 days after birth respectively (Table 2 – next page).
RSVpreF was safe and well tolerated in maternal participants, with no safety signals detected in infants through 24-months after birth; adverse event incidences were similar in vaccine and placebo groups for mothers and infants.

Conclusions: The end of study analysis confirms that maternal vaccination with RSVpreF was efficacious at preventing MA-LRTI due to RSV in infants through 6 months of age.

Abstract category: Vaccines, Therapies & Treatments

Keywords: RSV; Maternal Vaccine; Infant Efficacy

Efficacy of a Bivalent RSVpreF Vaccine in Older Adults Beyond a First RSV Season

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(3) Diablo Clinical Research, United States

Presenting author: Iona Munjal

In a global, 2-year, phase 3, randomized, double-blind, placebo-controlled study evaluating vaccine efficacy (VE) to prevent RSV lower respiratory tract illness (LRTI) in adults ≥60 years of age, a primary analysis conducted during the first RSV season showed that bivalent RSVpreF is highly efficacious against RSV-LRTI. Observed VEs were 85.7% for RSV-LRTI with ≥3 symptoms and 66.7% for RSV-LRTI with ≥2 symptoms. Further analyses of VE, including VE by age group, were conducted at the end of season 1 (EoS1) and season 2 after the second epidemiological RSV season in the USA (mid-S2) for an understanding of VE persistence.

The EoS1 analysis included participants from both the northern and southern hemispheres (N=36,127), with an average acute respiratory illness (ARI) surveillance period of 7.05 months. The mid-S2 analysis included northern hemisphere participants only (n=20,019). The average duration from vaccination through the mid-S2 analysis cutoff was 13.9 months.

For RSV-LRTI with ≥3 symptoms, VE was 88.9% and 78.6% for EoS1 and within mid-S2, respectively, resulting in VE across 2 seasons of 84.4%. For RSV-LRTI with ≥2 symptoms, VE was 65.1% and 48.9% for EoS1 and within mid-S2, respectively, resulting in VE across 2 seasons of 56.8%.

Table 1. Vaccine efficacy of RSVpreF at the end of season 1, mid-season 2, and across 2 seasons

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>End of Season 1</th>
<th>Mid-season 2</th>
<th>Across Seasons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccine</td>
<td>85.7% (95% CI: 78.8-90.5)</td>
<td>78.6% (95% CI: 71.8-84.6)</td>
<td>84.4% (95% CI: 78.6-89.5)</td>
</tr>
</tbody>
</table>

- **RSV-LRTI with ≥3 symptoms**: 100% reduction in RSV-LRTI with ≥3 symptoms for EoS1 and mid-S2, respectively, resulting in VE across 2 seasons of 84.4%.
- **RSV-LRTI with ≥2 symptoms**: 65.1% reduction in RSV-LRTI with ≥2 symptoms for EoS1 and mid-S2, respectively, resulting in VE across 2 seasons of 56.8%.


d.csv
Pfizer’s bivalent respiratory syncytial virus prefusion F subunit vaccine (RSVpreF [ABRYSVO™]) was approved in the United States and Europe for prevention of lower respiratory tract disease caused by RSV in individuals ≥60 years. RENOIR is an ongoing global, phase 3, placebo-controlled study, where ≥ 60 years old participants were randomized 1:1 to receive RSVpreF or placebo. Here, we report updated safety data through end of season 1 (EOS1), including an additional three months of follow up after the primary analysis, for participants representing both northern and southern hemispheres (N=37045).

In addition to overall safety, subgroup analyses by gender, race, and chronic conditions were conducted (Table 1). The incidence of any local reaction (LR) was 12.3% in those that received RSVpreF and 6.7% in those that received placebo. Among those that received RSVpreF, incidence of LRs was higher among 60-69 years old (14.1%), females (16.0%) and participants with chronic cardiopulmonary conditions (CCP) (18.5%). (Table 1)

The incidence of any systemic reaction was similar among RSVpreF (27.7%) and placebo (26.3%). (Table 2). Through EOS1, similar rates of adverse events (AEs) were reported among both groups (16.8% vs 16.5%) (Table 3). The Reported AE rate through one month was similar among both groups (10.6% RSVpreF vs 10.3% placebo), with overall higher incidence among females, those with CCP, and octogenarians (Table 4 – next page).

In conclusion, RSVpreF maintains its favorable safety profile after an updated analysis of the safety population through EOS1 overall and by subgroups.

Table 1: Local Reaction a, Any b Within 7 Days After Vaccination by Age Group, Sex, Race and Prespecified Significant Conditions: E - Diary Substudy Safety Population

<table>
<thead>
<tr>
<th>Subgroup Safety Population</th>
<th>RSVpreF n(%)</th>
<th>Placebo n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>1004 / 3627 (27.7)</td>
<td>907 / 3446 (26.3)</td>
</tr>
<tr>
<td>Age Group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>60-69 yr</td>
<td>664 / 2151 (30.3)</td>
<td>588 / 2091 (28.1)</td>
</tr>
<tr>
<td>70-79 yr</td>
<td>298 / 1255 (23.4)</td>
<td>285 / 1147 (24.8)</td>
</tr>
<tr>
<td>≥ 80 yr</td>
<td>42 / 221 (19.0)</td>
<td>34 / 228 (15.3)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>435 / 1910 (22.8)</td>
<td>389 / 1794 (22.2)</td>
</tr>
<tr>
<td>Female</td>
<td>569 / 1717 (32.3)</td>
<td>538 / 1692 (30.6)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>780 / 2703 (28.3)</td>
<td>704 / 2375 (25.2)</td>
</tr>
<tr>
<td>Black</td>
<td>151 / 495 (21.7)</td>
<td>145 / 460 (25.0)</td>
</tr>
<tr>
<td>Asian</td>
<td>55 / 285 (19.3)</td>
<td>46 / 288 (16.2)</td>
</tr>
<tr>
<td>Other/unknown</td>
<td>18 / 91 (9.5)</td>
<td>12 / 55 (22.7)</td>
</tr>
<tr>
<td>Prespecified Significant Condition: 1, b</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>439 / 1724 (24.7)</td>
<td>428 / 1744 (24.5)</td>
</tr>
<tr>
<td>≥ 1 Significant Condition</td>
<td>565 / 1855 (30.0)</td>
<td>479 / 1702 (28.1)</td>
</tr>
<tr>
<td>≥ 1 Chronic pulmonary</td>
<td>178 / 448 (39.7)</td>
<td>150 / 423 (35.5)</td>
</tr>
</tbody>
</table>

a. Local reactions were collected in the e-diary from Day 1 to Day 7 after vaccination for a subset of study participants from selected sites. Any reactogenicity represented as related adverse events within 7 days of vaccination from the e-diary subset safety population are included in this table.
b. Sex refers to the sex of the participant at the time of vaccination.

c. Significant conditions include current tobacco use, diabetes, lung disease (including COPD and asthma), heart disease (including congestive heart failure), liver disease, and renal disease.

d. This category included asthma, COPD, and congestive heart failure.

Table 2: Systemic Reaction a, Any b Within 7 Days After Vaccination by Age Group, Sex, Race and Prespecified Significant Conditions: E - Diary Substudy Safety Population

<table>
<thead>
<tr>
<th>Subgroup Safety Population</th>
<th>RSVpreF n(%)</th>
<th>Placebo n(%)</th>
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<tbody>
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</tr>
<tr>
<td>60-69 yr</td>
<td>664 / 2151 (30.3)</td>
<td>588 / 2091 (28.1)</td>
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<tr>
<td>70-79 yr</td>
<td>298 / 1255 (23.4)</td>
<td>285 / 1147 (24.8)</td>
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<tr>
<td>≥ 80 yr</td>
<td>42 / 221 (19.0)</td>
<td>34 / 228 (15.3)</td>
</tr>
<tr>
<td>Sex</td>
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</tr>
<tr>
<td>Male</td>
<td>435 / 1910 (22.8)</td>
<td>389 / 1794 (22.2)</td>
</tr>
<tr>
<td>Female</td>
<td>569 / 1717 (32.3)</td>
<td>538 / 1692 (30.6)</td>
</tr>
<tr>
<td>Race</td>
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<tr>
<td>White</td>
<td>780 / 2703 (28.3)</td>
<td>704 / 2375 (25.2)</td>
</tr>
<tr>
<td>Black</td>
<td>151 / 495 (21.7)</td>
<td>145 / 460 (25.0)</td>
</tr>
<tr>
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<td>55 / 285 (19.3)</td>
<td>46 / 288 (16.2)</td>
</tr>
<tr>
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<td>18 / 91 (9.5)</td>
<td>12 / 55 (22.7)</td>
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<tr>
<td>Prespecified Significant Condition: 1, b</td>
<td></td>
<td></td>
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<tr>
<td>None</td>
<td>439 / 1724 (24.7)</td>
<td>428 / 1744 (24.5)</td>
</tr>
<tr>
<td>≥ 1 Significant Condition</td>
<td>565 / 1855 (30.0)</td>
<td>479 / 1702 (28.1)</td>
</tr>
<tr>
<td>≥ 1 Chronic pulmonary</td>
<td>178 / 448 (39.7)</td>
<td>150 / 423 (35.5)</td>
</tr>
</tbody>
</table>

a. Systemic reactions were collected in the e-diary from Day 1 to Day 7 after vaccination for a subset of study participants from selected sites. Any reactogenicity represented as related adverse events within 7 days of vaccination from the e-diary subset safety population are included in this table.
b. Systemic reactions were collected in the e-diary from Day 1 to Day 7 after vaccination for a subset of study participants from selected sites. Any reactogenicity represented as related adverse events within 7 days of vaccination from the e-diary subset safety population are included in this table.

c. Significant conditions include current tobacco use, diabetes, lung disease (including COPD and asthma), heart disease (including congestive heart failure), liver disease, and renal disease.

d. This category included asthma, COPD, and congestive heart failure.
ANTI-RESPIRATORY SYNCYTIAL VIRUS COMPOUNDS DERIVED FROM ALCHONEA CORDIFOLIA LEAF EXTRACT

Damian C. Odimegwu (1,2), Festus Basden C. Okoye (3), Charles C. Esimone (4)

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2.Department of Molecular and Medical Virology, Ruhr University Bochum, Germany
3.Department of Pharmaceutical Chemistry, Nnamdi Azikiwe University Awka, Nigeria
4.Department of Pharmaceutical Microbiology and Biotechnology, Nnamdi Azikiwe University Awka, Nigeria

Presenting author: Damian Odimegwu

Background: Analyses of Alchonea cordifolia (AC) leaf extract sourced from Southeast Nigeria lead to the generation of three (3) fractions; Methanol, Water, and ethylacetate fractions of appreciable anti-RSV activities.

Methods: Antiviral activities were evaluated by a modified viral plaque reduction assay using the recombinant strain rgrRSV expressing the green fluorescent protein (gfp) as a reporter gene. Parallel assays for effect of the antiviral agents on cell viabilities were carried out using the 3-(4,5-dimethylthiazolyl-2)-2,5-diphenyltetrazolium bromide (MTT) reduction assays. Mechanism of antiviral activity of the fractions were performed using time-of-addition assay.

Results: Results showed anti-RSV activities with IC50 = 28.19, 38.42, and 11.33µg/ml for Methanol, Water, and ethylacetate fractions respectively. Corresponding assays for the cytotoxic effect of fractions on utilized cell line gave CC50 = 111.2, > Limit, and 63.86µg/ml respectively. Further chemical purification of the ethylacetate fraction led to identification of sub-fractions 1 – 22 with varying activity profiles against RSV. Sub-fraction 10 and 11 both recorded IC50 < 20µg/ml and improved activity/selectivity indices (13.29 and 32.71 respectively) and were further subjected to a time-of-addition study for elucidation of mechanism of action. Results further showed that both sub-fractions seem to interfere with some undefined early and late viral protein activities with IC50 < 20µg/ml.

Conclusion: The investigated fractions from AC show promising outcomes for further advanced development against RSV infection.

Abstract category: Vaccines, Therapies & Treatments

Keywords: Respiratory syncytial virus (RSV), respiratory tract infections, anti-RSV fractions, viral inhibition, cell viability

Conflict of Interest: None declared

EARLY EFFECTIVENESS OF NIRSEVIMAB AGAINST HOSPITAL ADMISSIONS FOR RESPIRATORY SYNCYTIAL VIRUS LOWER RESPIRATORY TRACT INFECTIONS IN INFANTS IN SPAIN

Mónica López-Lacort1, Cintia Muñoz-Quiles1, Ainara Mira-Iglesias 1, 1 F Xavier López-Labrador 1 1, Beatrix Menguial-Chuliá 1, Carlos Fernández-García 1, Mario Carballido-Fernández 2, Ana Pineda-Capilliure 3, Juan Mollar-Maseres 4, Maruan Shahali Benavent 5, Matilde Zornoza-Moreno 6, Jaime Jesús Pérez-Martín 6, Santiago Alfayate-Miguezue 6, Ana Isabel Menasalva_ruz 6, Ivan Sanz-Muñoz 7, José María Eiros 7, Vanesa Matías Del Pozo 7, Marina Toquero_Asenso 7, VÀHNSI group 1, Eliseo Pastor-Villalla B, José Antonio Lluch-Rodríguez B, Javier Díez-Domingo 1; Alejandro Orrico-Sánchez1

1. Vaccine Research Department, Fisablo-Public Health, Valencia (Spain)
2. Hospital General Universitario de Castellón (Spain)
3. Hospital Universitario Dr. Peset, Valencia (Spain)
4. Hospital Universitario La Fe, Valencia (Spain)
5. Hospital Marina Baixa, Alicante (Spain)
6. Murcia Health Council, Murcia (Spain)
7. National Influenza Centre, Valladolid (Spain)
8. Dirección General de Salud Pública, Valencia (Spain)

Presenting author: Alejandro Orrico-Sánchez

Background: Nirsevimab has shown efficacy against lower respiratory tract infections (LRTI) in clinical trials. In October 2023, Spain introduced universal RSV prophylaxis with Nirsevimab. Here we assess its effectiveness against hospital admissions for RSV- LRTI in infants in Spain. 

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Methods: A multicentre study including 9 hospitals in 3 Regions (5 in Valencia, 3 in Murcia and 1 in Valladolid) where respiratory admissions are routinely tested by RT-PCR. Study population (15,676 children) included all children eligible for Nirsevimab immunization (born from April 1st, 2023). Study period lasted from October 1st, 2023 to December 31st–January 10th, depending on the hospital. The immunization coverage data were obtained from the regional vaccination registries. Effectiveness against RSV-LRTI admissions was estimated by screening method (using Bayesian binomial regression of random effects) and test-negative design (TND; using a Bayesian logistic regression considering hospital as random effect). LRTI-hospitalized children negative for RSV were used as sensitivity analysis. 95% credible intervals (CI) were also showed.

Results: Nirsevimab coverage ranged between 78.7% and 98.6%. 182 admissions for LRTI were included. Of them, 97 were positive for RSV. Among RSV cases, 58 (60%) had been immunized. By Region, Nirsevimab effectiveness ranged between 69% and 96%. Pooled data showed 83.8 (95% CI 75.6-89.6) and 74.8 (95% CI 50.5-89.2) effectiveness using screening and TND, respectively. Among the 23 negative controls, 19 (83%) had been immunized. Nirsevimab was not effective against RSV-negative LRTI.

Conclusions: During the first 3 months of program, Nirsevimab showed high effectiveness against RSV LRTI-hospitalizations.

Abstract category: Vaccines, Therapies & Treatments

Keywords: Nirsevimab, RSV, Low respiratory tract infection, effectiveness

Conflict of Interest: None declared

POTENTIAL IMPACT OF NIRSEVIMAB AND BIVALENT MATERNAL VACCINE AGAINST RSV BRONCHIOLITIS IN INFANTS: A POPULATION-BASED MODELLING STUDY

Mónica López-Lacort1,3, Ana Corberán-Vallet2, Francisco J. Santonja2, Cintia Muñoz-Quiles1,3,*, Javier Díez-Domingo1,3,4, Alejandro Orrico-Sánchez1,3,4.

1 Vaccine Research Unit, Fisabio-Public Health, Spain
2 Statistics and Operational Research Department, University of Valencia, Spain.
3 CIBER ESP, Madrid, Spain.
4 Universidad Católica de Valencia, Spain.

Presenting author: Alejandro Orrico-Sánchez

A new monoclonal antibody (nirsevimab; Beyfortus®) and a bivalent prefusion RSV vaccine (Abrysvo®) for maternal immunization have been approved recently. This is a modelling study to estimate the potential impact of different immunization programs with these products on RSV-bronchiolitis. Population-based real-world data from primary care and hospitalizations were considered. RSV bronchiolitis dynamics in absence of these immunization scenarios were explained by a multivariate age-structured Bayesian model. Then, the potential impact was simulated under different assumptions including the most recent clinical trial data. Differences in endpoints, populations, and timeframes between trials make the two products’ efficacy difficult to compare. Our results suggest that each strategy would effectively reduce RSV-bronchiolitis. A seasonal with catch-up program with nirsevimab would prevent up to 9,210 RSV bronchiolitis and up to 1,755 RSV hospitalizations per 100,000 infants-year. A year-round maternal immunization program would prevent up to 5,837 RSV bronchiolitis and up to 1,282 RSV-hospitalizations per 100,000 infants-year.

Table 1: Impact estimations for NirMo in children <1 year old

<table>
<thead>
<tr>
<th>RSV-bronchiolitis</th>
<th>2023/2024 (29.333, 30.018) *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Program/Episode</td>
<td>95% CI</td>
</tr>
<tr>
<td>Catch-up &amp; Seasonal</td>
<td>10254/10528,10640/1079*</td>
</tr>
<tr>
<td>RSV-bronchiolitis hospitalizations</td>
<td>4534/4574, 4572</td>
</tr>
<tr>
<td>Catch-up &amp; Seasonal</td>
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</table>

B) NirMo impact estimations annually from Oct-Sep **

<table>
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Conflict of Interest: None declared

POTENTIAL IMPACT OF NIRSEVIMAB AND BIVALENT MATERNAL VACCINE AGAINST RSV BRONCHIOLITIS IN INFANTS: A POPULATION-BASED MODELLING STUDY

Mónica López-Lacort1,3, Ana Corberán-Vallet2, Francisco J. Santonja2, Cintia Muñoz-Quiles1,3,*, Javier Díez-Domingo1,3,4, Alejandro Orrico-Sánchez1,3,4.

1 Vaccine Research Unit, Fisabio-Public Health, Spain
2 Statistics and Operational Research Department, University of Valencia, Spain.
3 CIBER ESP, Madrid, Spain.
4 Universidad Católica de Valencia, Spain.

Presenting author: Alejandro Orrico-Sánchez

A new monoclonal antibody (nirsevimab; Beyfortus®) and a bivalent prefusion RSV vaccine (Abrysvo®) for maternal immunization have been approved recently. This is a modelling study to estimate the potential impact of different immunization programs with these products on RSV-bronchiolitis. Population-based real-world data from primary care and hospitalizations were considered. RSV bronchiolitis dynamics in absence of these immunization scenarios were explained by a multivariate age-structured Bayesian model. Then, the potential impact was simulated under different assumptions including the most recent clinical trial data. Differences in endpoints, populations, and timeframes between trials make the two products’ efficacy difficult to compare. Our results suggest that each strategy would effectively reduce RSV-bronchiolitis. A seasonal with catch-up program with nirsevimab would prevent up to 9,210 RSV bronchiolitis and up to 1,755 RSV hospitalizations per 100,000 infants-year. A year-round maternal immunization program would prevent up to 5,837 RSV bronchiolitis and up to 1,282 RSV-hospitalizations per 100,000 infants-year.

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</tr>
<tr>
<td>Catch-up &amp; Seasonal</td>
<td>10254/10528,10640/1079</td>
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HOSPITAL-ACQUIRED RESPIRATORY SYNCYTIAL VIRUS (HA-RSV) IN CHILDREN’S HOSPITALS IN THE UNITED STATES (US)

Lisa Saiman MD MPH1, Susan E. Coffin MD MPH2, D MPH2, Larry K. Kociolek MD MSCI3, Danielle M. Zerr MD MPH4, Aaron M. Milstone MD MHS5, Margaret L. Aldrich MD6, Celibell Y. Vargas MD1, Giovanny Zapata MPH7, Morgan A. Zalot MPH2, Megan E. Reyna BA3, Amanda A. Adler BA4, Annie Voskertchian MPH5, Emily R. Egbert MPH5, Luis Alba BS1, Sonia Gollerkeri MPH1, Tanaz Petigara PhD8, Madelyn Ruggieri MS8, Lyn Finelli DrPH MS9, Yoonyoung Choi PhD MS RPh8

1NewYork-Presbyterian Morgan Stanley Children’s Hospital, Columbia University Irving Medical Center, New York, NY; 2Children’s Hospital of Philadelphia, Philadelphia, PA, Perelman School of Medicine at UPenn, Philadelphia, PA; 3Ann & Robert H. Lurie Children’s Hospital of Chicago, Chicago, IL; 4Seattle Children’s Hospital, Seattle, WA; 5Johns Hopkins University School of Medicine, Baltimore, MD; 6Children’s Hospital at Montefiore, Bronx, NY; 7Mailman School of Public Health, Columbia University Irving Medical Center, New York, NY; 8Center for Observational and Real-World Evidence, Merck & Co., Inc., Rahway, NJ, USA

Presenting author: Tanaz Petigara

Background and Objectives: RSV is an important cause of morbidity in childhood. Estimates suggest up to 20% of children hospitalized for RSV acquired the infection during hospitalization for another condition. HA-RSV may complicate the clinical course for these patients and lead to worse outcomes. In this study, we assessed the independent contribution of HA-RSV to clinical outcomes among hospitalized children.

Methods: We prospectively identified children with HA-RSV infection who tested positive on PCR more than 72 hours after admission at six US children’s hospitals from October 2020-April 2022. For each HA-RSV patient, three patients without HA-RSV were matched by site, age, and length of stay. Conditional logistic regression analyses determined if HA-RSV was independently associated with clinical outcomes: escalation of respiratory support (new need for supplemental oxygen, increase in FiO2 on a non-invasive or invasive respiratory modality, intubation), ICU transfer, and death.

Results: Twenty-six children had HA-RSV infections and 78 matched patients were selected of whom 57.7% and 55.2%, respectively, had >2 comorbid conditions. HA-RSV patients were more likely to have cardiovascular (p=0.004) and less likely to have respiratory (p=0.02) comorbid conditions. Escalation of respiratory support was more likely in HA-RSV patients (38.5% vs. 18.0%, aOR 3.5, CI95 1.1, 10.7). There were no significant differences in ICU transfer or death between the two groups.

Conclusions: HA-RSV was independently associated with escalated respiratory support, suggesting increased healthcare resource utilization. This burden may be underestimated in countries where testing practices are not standardized, or HA-RSV identification is a lower priority.

Abstract category: Vaccines, Therapies & Treatments

Keywords: Hospital-acquired RSV, respiratory support, children

Conflict of Interest: Yoonyoung Choi, Madelyn Ruggieri, and Tanaz Petigara are employees of Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.
ARE MATERNAL VACCINES EFFECTIVE AND SAFE IN MOTHERS AND INFANTS?

A SYSTEMATIC REVIEW & META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

Drs. E. Phijffer (1), Drs. O. de Bruin (2,3), Dr. F. Ahmadizar (3), Prof. L. Bont (1), Dr. N. van der Maas (4), Prof. M. Sturkenboom (3), Dr. J. Wildenbeest (1), Prof. K. Bloemenkamp (2)

1) Department of Pediatrics, Wilhelmina Children’s Hospital, University Medical Center Utrecht, Utrecht, the Netherlands
2) Department of Obstetrics, Wilhelmina Children’s Hospital, Division Woman and Baby, University Medical Center Utrecht, Utrecht, the Netherlands,
3) Department of Biostatistics and Research support, Julius Center for Health sciences and Primary care, University Medical Center Utrecht, the Netherlands
4)Center for Infectious Disease Control, National Institute for Public Health and the Environment, Bilthoven, the Netherlands.

Presenting author: Emily Phijffer

BACKGROUND: RSV is a major cause of LRTIs in infants. Maternal RSV vaccination is a preventive strategy of great interest, as it could have a substantial impact on infant RSV disease burden. In the past 10 years the clinical development of maternal RSV vaccines advanced rapidly.

OBJECTIVE: To assess the efficacy and safety of maternal RSV vaccination for preventing RSV disease in infants.

METHODS: On 21 October 2022 a systematic search was conducted in Cochrane Pregnancy and Childbirth’s Trials Register, ClinicalTrials.gov and WHO ICTRP. The updated search was performed on 27 July 2023 in MEDLINE, Embase, CENTRAL, CINAHL, ClinicalTrials.gov and WHO ICTRP.

1) Primary outcomes: hospitalisation with clinically- or laboratory-confirmed RSV in infants.
2) Secondary outcomes: intra-uterine growth restriction (IUGR), stillbirth, maternal death, preterm birth, congenital abnormalities, infant death.

GRADE was used to assess certainty of evidence and meta-analyses to determine the RR and 95% CIs.

MAIN RESULTS: Twenty-five study reports describing 6 studies were included in the review. All studies were RCTs and involved 17991 pregnant women. Table 1 shows the summary of findings.

CONCLUSIONS: Maternal RSV vaccination reduces laboratory-confirmed RSV hospitalisations in infants. Due to the (very) low certainty of evidence, we must be careful with drawing conclusions about most safety outcomes. However, there is no convincing evidence for safety concerns, including preterm birth, although one vaccine (Dieussaert 2023) was associated with increased risk of severe prematurity. A subgroup analysis including a breakdown of gestational age at birth will be conducted to further investigate this potential safety signal.

This abstract is based on a draft and post-peer review version of a Cochrane Review. Upon completion and approval, the final version is expected to be published in the Cochrane Database of Systematic Reviews (www.cochranelibrary.com).

Abstract category: Vaccines, Therapies & Treatments

Keywords: vaccination, pregnancy, maternal, efficacy, safety, infant, systematic, review, meta-analysis.

Conflict of Interest: None declared.

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VACCINE PREPARATION TIME, RESOURCE USE AND ERROR RATES FOR RSV VACCINES REQUIRING RECONSTITUTION: SELF-REPORTED ASSESSMENT BY PHARMACIST IN THE UNITED STATES

Darshan Mehta (1), Parinaz Ghaswalla (1), Kristin Romak (2), Maria Del Pilar Martin Matos (1), Nicolas Van De Velde (1)

1. Moderna, Inc., Cambridge, MA, USA
2. Romak Solution, LLC

Presenting author: Maria Del Pilar Martin Matos

Background: In the United States (US), adults aged ≥60 years may receive a single dose of a respiratory syncytial virus (RSV) vaccine, using shared clinical decision-making. Currently approved vaccines, RSVPreF3 and RSVPreF, require reconstitution before being administered. The objective of this study was to evaluate pharmacist perception of vaccine preparation time, resource use, and error rates with RSVPreF3 and RSVPreF.

Methods: A 2-day double-blind online discussion board was conducted in December 2023 with 19 practicing pharmacists in the US. The discussion was independently moderated using a discussion guide. The panelists were engaged for approximately 30 minutes each day.

Results: Currently available RSV vaccines that require reconstitution are generally considered to be acceptable by practicing pharmacists. However, certain aspects of its implementation, including preparation time, impacts the level of satisfaction. Panelists reported on average 6.1 and 7 minutes (range: 2–16, 2–20 minutes)
to reconstitute RSVPreF3 and RSVPreF, respectively. They further reported 2-3 errors/100 RSV vaccines administered. Pharmacists asked for a pre-filled syringe (PFS) to help them decrease error rates and time spent on reconstitution. Panel members reported on average 2.4 min (range: 1–10 min) to work with a PFS vaccine. Panelists anticipate that a PFS would save them 5.2 minutes and 6.6 minutes compared to RSVPreF3 and RSVPreF, respectively, freeing up pharmacists, technicians, and interns to work on other tasks.

Conclusions: Pharmacists are generally reporting satisfaction with the current RSV vaccines, however, prefer alternative presentations, like PFS, to decrease error rates and time spent on reconstitution.

Abstract category: Vaccines, Therapies & Treatments

Conflict of Interest: DM, PG, MPMM, and NV are all employees of Moderna, Inc., and may hold stock/stock options in the company. KR is a shareholder in Romak Solution, LLC, which was contracted by Moderna, Inc., to conduct this study.

THE COST-EFFECTIVENESS OF PALIVIZUMAB FOR THE PREVENTION OF SEVERE RESPIRATORY SYNCYTIAL VIRUS (RSV) INFECTION IN 29–35wGA INFANTS BORN IN SINGAPORE

Anne Goh (1), Xavier Carbonell-Estrany (2), Bosco Paes (3), Jean-Eric Tarride (3,4), Barry Rodgers-Gray (5), Ian Keary (5), John Fullarton (5)

1. KK Women’s and Children’s Hospital, Singapore
2. Hospital Clinic, Barcelona, Spain
3. McMaster University, Hamilton, Ontario, Canada
4. St Joseph’s Healthcare, Hamilton, Canada
5. Violicom Medical Limited, Aldermaston, United Kingdom

Presenting author: Barry Rodgers-Gray

OBJECTIVE: To provide an up-to-date assessment of the cost-utility of palivizumab (vs no prophylaxis) in preventing severe respiratory syncytial virus (RSV) infection during the first year of life in otherwise healthy premature Singaporean infants born at 29–35 weeks’ gestational age (wGA).

METHODS: A cost-utility model considering the potential for medically-attended RSV infection (MARI) without RSV hospitalisation (RSVH), RSVH intensive care unit admission (ICU), mortality (applied only to infants in ICU) and long-term respiratory morbidity (LTRM) was adapted for Singapore. The population comprised all 29–31 and 32–35wGA infants identified as being high- or moderate-risk for RSVH by the International Risk Scoring Tool (IRST). Gestational age-specific palivizumab efficacy was derived from the IMpact-RSV study (RSVH relative risk for RSVH by the International Risk Scoring Tool (IRST). Gestational age-specific palivizumab efficacy was derived from the IMpact-RSV study (RSVH relative risk: 63.3% [29-31wGA]; 82.2% [32-35wGA]) and LTRM rates from available international datasets. The base case considered a lifetime horizon with costs and outcomes discounted at 3.0%.

RESULTS: For 29–35wGA infants, the incremental cost/quality-adjusted life year (QALY) gained with palivizumab was SGD37,579 (Table). The probability of palivizumab being cost-effective was 84.2% at a willingness-to-pay threshold of SGD75,000/QALY. Palivizumab was cost-effective in both individual subgroups (29–31wGA: SGD39,968; 32–35wGA: SGD36,926). The model was most sensitive to LTRM rates, health utility scores, palivizumab cost and efficacy.

CONCLUSION: Our model, the first for RSV prophylaxis in Singapore, found palivizumab to be cost-effective (vs no prophylaxis) in otherwise healthy 29–35wGA infants. Adoption of the IRST in Singapore should be considered to guide prophylaxis to the most vulnerable moderate to high risk 32–35wGA infants.

Abstract category: Vaccines, Therapies & Treatments

Keywords: Cost-effectiveness; preterm infants; prophylaxis; Asia

PARENTAL KNOWLEDGE AND UNDERSTANDING OF RESPIRATORY SYNCYTIAL VIRUS (RSV) AND HOW TO DECREASE THE RISK OF INFECTION: THE CANADIAN PREMATURE BABIES FOUNDATION NATIONAL SURVEY 2023

Bacchini F (1), Paes B (2), Edwards JO (3), Rodgers-Gray B (3), Bracht M (1)

1. Canadian Premature Babies Foundation, Etobicoke, Ontario, Canada
2. McMaster University, Hamilton, Ontario, Canada
3. Violicom Medical Limited, Aldermaston, United Kingdom

Presenting author: Barry Rodgers-Gray

Objective: To survey parent knowledge and understanding of respiratory syncytial virus (RSV) and its prevention.

Methods: The Canadian Premature Babies Foundation (CPBF) survey comprised 58 questions in English and was available online (SurveyMonkey) between July-August 2023, with invitations sent via email and social media.

Results: Of 331 respondents (95% female), 99% understood the seriousness of RSV, but 20% were not confident in their knowledge. RSV education was provided to 76% in the neonatal intensive care unit (NICU; nurse: 78%; printed materials: 72%; doctor: 50%). 99% of those who were not informed, wished they had. Post-discharge, 59% were unconfident of protecting their baby against RSV and 71% searched for information (84% internet; 46% doctor; 24% CPBF website). Parents recommended that the CPBF provide information via: website (66%); printed materials (60%); Facebook (57%); and, Instagram (48%). Despite 99% understanding the importance of childhood immunizations and 93% feeling confident about them, 24% remained anxious about immunizing their baby. 65% received information about palivizumab in the NICU/clinic and 97% were confident about prophylaxing their baby. Although 79% had never heard of nirsevimab, 75% would accept it for their baby if offered before discharge. 73% would accept maternal RSV vaccination. The main survey limitation was that respondents might be more knowledgeable about RSV than the general parent population due to their association with CPBF and/or prior RSV experience.
Conclusions: Parents require accurate, reliable and consistent information on RSV and its prevention, which should be provided in the NICU, following discharge and via well-founded online resources.

Abstract category: Vaccines, Therapies & Treatments

Keywords: Parents, knowledge, preterm infants

Conflict of Interest: BP has received research funding and/or compensation as advisor/lecturer from AstraZeneca and Sanofi outside the scope of this study. BRG and JOE employer has received payment from AstraZeneca for work on various projects outside the scope of this study. FB and MB have nothing to declare. The CPBF has received educational grants from AstraZeneca and Sanofi. Financial support for this study was provided in part by an unrestricted grant by Sanofi. Sanofi was not involved in the design, undertaking or interpretation of the survey results. All authors contributed to the development of the abstract and approved it for submission.

META-ANALYSIS OF THE EFFICACY OF PALIVIZUMAB AT PREVENTING MEDICALLY-ATTENDED RESPIRATORY SYNCYTIAL VIRUS INFECTIONS IN PRETERM INFANTS NOT REQUIRING HOSPITALISATION

Rodgers B (1), Carbonell-Estrany X (2), Fullarton J (1), Waghorne N (1), Keary I (1), Paes B (3)

1. Violicom Medical Limited, Aldermaston, United Kingdom
2. Hospital Clinic, Barcelona, Spain
3. McMaster University, Hamilton, Ontario, Canada

Presenting author: Barry Rodgers-Gray

Objective: To generate efficacy data for palivizumab at preventing medically-attended respiratory syncytial virus infections not requiring hospitalisation (MARI) in premature infants ≤35 weeks’ gestational age (wGA).

Methods: A systematic literature review (SLR) was undertaken in the PubMed, EMBASE and Cochrane Library databases (from database inception to 27 June 2023) to identify studies assessing passive immunoprophylaxis with monoclonals versus placebo/untreated preterm infants born ≤35wGA, in the prevention of RSV-related hospitalisations and/or MARI. Identified studies were included in a logical block diagram to generate a Bayesian inferential output (10,000 Markov-Chain-Monte-Carlo iterations) of MARI rate for palivizumab versus placebo/untreated infants and nirsevimab.

Results: The SLR assessed 654 citations and 3 relevant randomised placebo-controlled trials were included in the meta-analysis. All 3 studies had a low risk of bias (Cochrane Risk of Bias Tool). Palivizumab significantly reduced the MARI rate from 9.5% (placebo) to 2.8% (70.5% relative reduction; median ratio 1:3.425, respectively, 95% credible interval [CrI] 1:1.75 to 1:6.17; Figure). The difference in MARI efficacy between palivizumab and nirsevimab was nonsignificant (median difference between palivizumab vs placebo compared with nirsevimab vs placebo: 0.27, 95% CrI -2.20 to 2.37). A minor limitation was that one study included only 33-35wGA infants while the other two spanned 29-35wGA. Additionally, none of the studies evaluated MARI in infants <29wGA.

Conclusions: This meta-analysis provides confirmatory data that palivizumab is highly effective at preventing MARI in 29-35wGA infants with an efficacy similar to nirsevimab.

Abstract category: Vaccines, Therapies & Treatments

Keywords: Preterm; medically-attended lower respiratory tract infections; palivizumab; meta-analysis

Conflict of Interest: XCE and BP have received research funding and/or compensation as advisor/lecturer from AstraZeneca and Sanofi. BRG, IK, NW and JF have received payment from AstraZeneca for work on various projects. Financial support for this study was provided by AstraZeneca. All authors contributed to the development of the publication and maintained control over the final content.

COST-UTILITY ANALYSIS OF PALIVIZUMAB FOR THE PREVENTION OF RESPIRATORY SYNCYTIAL VIRUS (RSV) INFECTION IN OTHERWISE HEALTHY MALAYSIAN INFANTS BORN AT 29-31 WEEKS’ GESTATIONAL AGE (WGA)

Asiah Kassim (1), Barry Rodgers-Gray (2), Bosco Paes (3), John Fullarton (2), Jean-Eric Tarride (3,4), Xavier Carbonell-Estrany (5), Ian Keary(2)

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2. Violicom Medical Limited, Aldermaston, United Kingdom
3. McMaster University, Hamilton, Ontario, Canada
4. St Joseph’s Healthcare, Hamilton, Ontario, Canada
5. Hospital Clinic, Barcelona, Spain

Presenting author: Barry Rodgers-Gray

Objective: To adapt an up-to-date cost-utility model to provide the first formal assessment of the cost-effectiveness of palivizumab versus no prophylaxis in Malaysian infants born at 29-31 weeks’ gestational age (wGA).

Methods: All 29-31wGA infants were considered in a decision tree in which they received palivizumab or no prophylaxis. Subsequently, infants experienced either a respiratory syncytial virus (RSV)-associated hospitalisation (RSVH), medically-attended, non-hospitalised RSV-infection (MARI), or were uninfected/non-medically attended. Palivizumab reduced the RSVH rate by 63.3% (baseline rate: 11.6%). Mortality (0.43%) was applied only to infants admitted to the intensive care unit.
All survivors could experience respiratory morbidity for ≤18 years. Vial sharing (5% wastage) was permitted (note: palivizumab vials are single use only), with outcomes modelled over a lifetime horizon with 3.0% discounting. Commensurate with local RSV epidemiology and clinical practice, infants were assumed to receive an average of 4 doses of palivizumab (MYR3551.02/100mg vial).

Results: Palivizumab generated a cost-quality-adjusted life year (QALY) of MYR40,255 versus no prophylaxis. Including indirect costs, the cost/QALY was MYR39,729 (Table). The model was most sensitive to palivizumab cost, long-term sensitivities rates, non-prophylaxed hospitalisation rate and palivizumab efficacy in deterministic sensitivity analyses (±20% on main variables). Probabilistic analyses (10,000 iterations) resulted in incremental costs of MYR43,523/QALY, with a 50.4% probability of cost-effectiveness at a MYR44,143 willingness-to-pay threshold.

Conclusions: This new analysis, the first cost-utility analysis of palivizumab in Malaysia, found palivizumab to be cost-effective in 29-31wGA infants (vs no prophylaxis). The model could be further improved by increased availability of local RSV epidemiological data.

Abstract category: Vaccines, Therapies & Treatments

Keywords: Cost-effectiveness; preterm infants; prophylaxis; Asia

Conflict of Interest: XCE and BP have received research funding and/or compensation as advisor/lecturer from AstraZeneca. BRG, IK and JF employers have received payment from AstraZeneca for work on various projects. AK and JET have nothing to disclose. Financial support for this study was provided by AstraZeneca.

All authors contributed to the development of the publication and maintained control over the final content.

### OPTIMAL USE OF RISK FACTORS TO GUIDE PROPHYLAXIS AGAINST SEVERE RESPIRATORY SYNCTIAL VIRUS INFECTION IN MODERATE-TO-LATE PRETERM INFANTS

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2. Paediatric Emergency Unit, IRCCS Ospedale Policlinico of Bologna, Bologna, Italy
3. Violicom Medical Limited, Aldermaston, Berkshire, United Kingdom
4. Neonatology Service, Hospital Clinic, Barcelona, Catalonia, Spain

Presenting author: Barry Rodgers-Gray

Objective: To summarise the key attributes of an ideal Risk Scoring Tool (RST) for identifying moderate-to-late preterm infants at greatest risk of respiratory syncytial virus hospitalisation (RSVH).

Methods: Eight published RSTs/predictive models were reviewed for the following attributes: robustness and applicability of source data; simplicity and accuracy; validation and applicability; and, cost-effectiveness.

Results: Most RSTs/models (7/8) were developed from large, prospective, observational studies specifically designed to identify risk factors for RSVH in moderate-to-late preterm infants (Table). The International RST (IRST) encompassed the largest dataset, using pooled data from 6 studies across 28 countries (n=13,475). Fifteen distinct risk factors were identified, the most common being age relative to the RSV season (8/8 RSTs/models), followed by siblings and daycare attendance (both 7/8) and maternal or family history (all 8/8). RSTs/models comprised 3–8 risk factors, with the IRST having the fewest factors (3) and the second highest predictive accuracy. Where reported, the infant proportion ascribed as high risk for RSVH ranged from 11–42% (IRST: 24%). Validations were reported for 6/8 RSTs/models, with the IRST proven accurate using data from Ireland, Colombia and Brazil. Cost-utility analyses of palivizumab were below threshold for 4/8 RSTs/models; only the Dutch RST proved not cost-effective in reducing the burden of RSV disease. The IRST proved to guide prophylaxis cost-effectively in 4 continents (North America, Europe, Asia and Latin America).

Conclusions: Adoption of the IRST can support reimbursement following local validation and ensure that the most vulnerable moderate-to-late preterm infants receive prophylaxis.

Abstract category: Vaccines, Therapies & Treatments

Keywords: Risk factors, risk scoring tools, prophylaxis, moderate-to-late preterm infants

Conflict of Interest: BRG, IK and JF employers have received payment from AstraZeneca for work on various projects outside the scope of this review. XCE, BP and ML have received research funding and/or compensation as advisor/lecturer from AstraZeneca and/or Sanofi and/or Pfizer outside the scope of this review. This study was not funded.

### Table: Cost-effectiveness of palivizumab versus no prophylaxis in Malaysian 29–31wGA infants

<table>
<thead>
<tr>
<th>Difference in costs</th>
<th>Cost per QALY</th>
</tr>
</thead>
<tbody>
<tr>
<td>MYR6,589 (USD1,498)</td>
<td>0.164</td>
</tr>
<tr>
<td>MYR6,503 (USD1,478)</td>
<td>0.164</td>
</tr>
<tr>
<td>MYR8,729 (USD2,032)</td>
<td></td>
</tr>
</tbody>
</table>

QALY: quality-adjusted life-year; wkGA: weeks’ gestational age

### Table: Comparison of risk factor-guided approaches to identify moderate-to-late preterm infants at increased risk of RSVH

<table>
<thead>
<tr>
<th>Country</th>
<th>IRST</th>
<th>FLIP-2</th>
<th>RISK</th>
<th>RISK-II</th>
<th>POMI</th>
<th>FLIP</th>
<th>CRST</th>
<th>SM/Local Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study design</td>
<td>Pooled data from 6 studies across 28 countries (n=13,475).</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risk Factor</td>
<td>1. Birth between 35 and 36 weeks gestation or in the 1st trimester or 5% wastage</td>
<td>1. Birth between 35 and 36 weeks gestation or in the 1st trimester</td>
<td>1. Birth between 35 and 36 weeks gestation or in the 1st trimester</td>
<td>1. Birth between 35 and 36 weeks gestation or in the 1st trimester</td>
<td>1. Birth between 35 and 36 weeks gestation or in the 1st trimester</td>
<td>1. Birth between 35 and 36 weeks gestation or in the 1st trimester</td>
<td>1. Birth between 35 and 36 weeks gestation or in the 1st trimester</td>
<td>1. Birth between 35 and 36 weeks gestation or in the 1st trimester</td>
</tr>
<tr>
<td>Sensitivity/Specificity</td>
<td>0.69/0.75</td>
<td>0.62/0.79</td>
<td>0.64/0.79</td>
<td>0.69/0.79</td>
<td>0.69/0.79</td>
<td>0.69/0.79</td>
<td>0.69/0.79</td>
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</tr>
<tr>
<td>ROC AUC</td>
<td>0.72</td>
<td>0.72</td>
<td>0.72</td>
<td>0.72</td>
<td>0.72</td>
<td>0.72</td>
<td>0.72</td>
<td>0.72</td>
</tr>
<tr>
<td>Validations</td>
<td>Internal ROC AUC 0.79 External with US, Colombia &amp; Brazil data</td>
<td>Internal ROC AUC 0.79 validation with external data</td>
<td>Internal ROC AUC 0.79 validation with external data</td>
<td>Internal ROC AUC 0.79 validation with external data</td>
<td>Internal ROC AUC 0.79 validation with external data</td>
<td>Internal ROC AUC 0.79 validation with external data</td>
<td>Internal ROC AUC 0.79 validation with external data</td>
<td>Internal ROC AUC 0.79 validation with external data</td>
</tr>
<tr>
<td>Risk score</td>
<td>Low risk: ≤ 19; Moderate risk: 20-44; High risk: ≥ 45</td>
<td>Low risk: ≤ 19; Moderate risk: 20-44; High risk: ≥ 45</td>
<td>Low risk: ≤ 19; Moderate risk: 20-44; High risk: ≥ 45</td>
<td>Low risk: ≤ 19; Moderate risk: 20-44; High risk: ≥ 45</td>
<td>Low risk: ≤ 19; Moderate risk: 20-44; High risk: ≥ 45</td>
<td>Low risk: ≤ 19; Moderate risk: 20-44; High risk: ≥ 45</td>
<td>Low risk: ≤ 19; Moderate risk: 20-44; High risk: ≥ 45</td>
<td>Low risk: ≤ 19; Moderate risk: 20-44; High risk: ≥ 45</td>
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<tr>
<td>Cost-effectiveness (Yes/No)</td>
<td>Yes (Canada), No (Korea)</td>
<td>Yes (Korea)</td>
<td>Yes (has success)</td>
<td>Yes (Korea)</td>
<td>Yes (Korea)</td>
<td>Yes (Korea)</td>
<td>Yes (Korea)</td>
<td>Yes (Korea)</td>
</tr>
<tr>
<td>Outcome measures</td>
<td>Not assessed</td>
<td>Not assessed</td>
<td>Not assessed</td>
<td>Not assessed</td>
<td>Not assessed</td>
<td>Not assessed</td>
<td>Not assessed</td>
<td>Not assessed</td>
</tr>
</tbody>
</table>

MODELING AVERTABLE ILLNESS THROUGH RSV VACCINATION IN U.S. ADULTS AGED ≥60 YEARS

Lauren E. Roper (1), Michael Melgar (1), Amadea Britton (1), Fiona P. Havers (1), Michael Whitaker (1), Megan Wallace (1), Danielle L. Mouia (1), Katherine E. Fleming-Dutra (1)

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Presenting author: Lauren Roper

In June 2023, the U.S. Centers for Disease Control and Prevention (CDC) recommended the first two vaccines to prevent respiratory syncytial virus (RSV) disease in U.S. adults aged ≥60 years using shared clinical decision-making. In clinical trials, both RSV vaccines (GSK’s RSVPreF3 and Pfizer’s RSVpreF) were shown to be efficacious at preventing RSV lower respiratory tract disease through at least two RSV seasons. As part of the evidence base for this new policy, we estimated the number of RSV-attributable outpatient visits, hospitalizations, intensive care unit admissions, and in-hospital deaths potentially avertable over two hypothetical RSV seasons per 1 million persons vaccinated with a single dose of each vaccine product. Model assumptions were informed by published incidence rates of RSV illness, unpublished hospitalization rates from CDC’s RSV Hospitalization Surveillance Network, and vaccine efficacy data from phase 3 clinical trials in older adults.

We estimated that RSV vaccination of 1 million adults, aged ≥60 years, could potentially avert 2,130 (range: 1,506–3,309) RSV-attributable hospitalizations and 108 (76–172) deaths with GSK’s RSVPreF3 vaccine or 2,421 (1,712–3,854) hospitalizations and 123 (87–196) deaths with Pfizer’s RSVpreF vaccine. Potentially avertable outcomes increased with increasing age of vaccinees and were similar between products (Figure 1 and Figure 2).

These results suggest that RSV vaccines could prevent a significant number of hospitalizations and deaths in older adults, depending on uptake. These results also may inform shared clinical decision-making discussions between patients and providers about the benefits of RSV vaccination.

Figure 1. Estimated RSV-Associated Outcomes* Avertable per 1 Million People Vaccinated with GSK RSVPreF3 Vaccine Over Two RSV Seasons in the U.S., Stratified by Age

Figure 2. Estimated RSV-Associated Outcomes* Avertable per 1 Million People Vaccinated with Pfizer RSVpreF Vaccine Over Two RSV Seasons in the U.S., Stratified by Age

Abstract category: Vaccines, Therapies & Treatments

Conflict of Interest: None declared

COST-EFFECTIVENESS OF RSVpreF VACCINE AMONG OLDER ADULTS IN GERMANY

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Presenting author: Reiko Sato

Background. Respiratory syncytial virus (RSV) is a common cause of lower respiratory tract illness (LRTI), especially among older adults. We evaluated the cost-effectiveness of Pfizer’s novel RSVpreF vaccine for use among older adults in Germany.

Methods. Lifetime clinical outcomes and economic costs of RSV-LRTI with use of RSVpreF and, alternatively, no intervention were evaluated using a static cohort model. Population included adults aged 60-99 years. Inputs were based on local data, where possible. Assumed vaccine uptake was 30-51%, depending on age and absence/presence of chronic medical or immunocompromising conditions that increase RSV-LRTI risk. Vaccine effectiveness was derived from trial data and was assumed to wane over the two years following vaccination. Base case analyses considered the full model population; subgroup analyses considered only persons with elevated RSV-LRTI risk. Sensitivity analyses were conducted.

Results. Use of RSVpreF—in lieu of no intervention—among 23.4 million adults aged 60-99 years (74% of whom had risk conditions) prevented 71,547 cases of hospitalized RSV-LRTI, 76,283 cases of ambulatory RSV-LRTI, and 6,707 RSV-related deaths and yielded 38,020 quality-adjusted life-years (QALYs) (Table 1a). With total costs higher by 1.3 billion € (-255.6M€ medical care; 1.6B€ vaccine), cost-effectiveness was 35,462€/QALY (healthcare system perspective). Among the subgroup of adults with risk conditions, cost-effectiveness was 29,053€/QALY (Table 1b). In probabilistic sensitivity analyses 100% of replications were <50,000€/QALY (full population).

Conclusions. Use of RSVpreF among adults ≥60-years is anticipated to greatly reduce the clinical and economic burden of RSV-LRTI and would represent a cost-effective use of resources in Germany.
EPITOPE CHIMERIC VACCINE CANDIDATE AGAINST RESPIRATORY SYNCYTIAL VIRUS (RSV) DISEASE

Robert Adamu Shey (1,2), Tangan Yannick Aqua Stong (1), Stephen Mbigha Ghogomu 1, Ntang Emmaculate Yaah (1), Yengo Bernis Neneyoh (1), Cabirou Mounchili Shintouo (1,3,4), Luc Vanhamme 2, and Jacob Souopgui 2.

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Presenting author: Robert Adamu Shey

RSV is the leading global cause of respiratory infections in infants and the second most frequent cause of death during the first year of life - responsible for approximately 3 million hospitalizations and 120,000 deaths annually among children under the age of 5 years. Despite its high disease burden, there is currently no effective vaccine against RSV in children though one was recently approved for adults above 60 years. A multi-epitope vaccine against RSV would be an invaluable addition to current control efforts. In this study, several B-cell and CD8 epitopes key viral proteins were combined with a built-in adjuvant to create a multi-epitope vaccine candidate which was predicted to have high antigenicity and immunogenicity. Immune simulation analyses showed that the vaccine candidate can elicit both humoral and cellular immune responses against RSV. Conservation of the selected proteins and predicted epitopes suggests that the generated chimera could be helpful for cross-protection against different virus strains. The 3D structure was predicted, refined, and validated using bioinformatics tools. Protein–protein docking of the chimeric vaccine candidate with the TLR4 (reported to be involved in protection) predicted efficient binding. Further experimental validation of the vaccine construct is needed to confirm its efficacy and safety in vivo. Our study provides a promising approach for the design of multi-epitope vaccines against RSV and other infectious diseases. Overall, the constructed multi-epitope vaccine candidate demonstrated antigenicity superior to current treatment against Respiratory syncytial virus.

IN-SILICO DESIGN OF A MULTI-EPITOPE CHIMERIC VACCINE CANDIDATE AGAINST RESPIRATORY SYNCYTIAL VIRUS (RSV) DISEASE

Robert Adamu Shey (1,2), Tangan Yannick Aqua Stong (1), Stephen Mbigha Ghogomu 1, Ntang Emmaculate Yaah (1), Yengo Bernis Neneyoh (1), Cabirou Mounchili Shintouo (1,3,4), Luc Vanhamme 2, and Jacob Souopgui 2.

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MODELED IMPACT OF ADJUVANTED RSVPreF3 VACCINATION ON RSV-RELATED HEALTH OUTCOMES IN ADULTS AGED 50-59 YEARS WITH CARDIOPULMONARY DISEASES IN THE UNITED STATES

David Singer(1), Elizabeth La(1), Jonathan Graham(2), Mei Grace(2), Sara Poston(1), Daniel Molnar(3)
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2. RTI Health Solutions, Research Triangle Park, NC, USA
3. GSK, Wavre, Belgium

Presenting author: David Singer

BACKGROUND: Cardiopulmonary disease is associated with an increased risk of severe respiratory syncytial virus (RSV) disease in adults. This study estimated the potential public health impact of adjuvanted RSVPreF3 vaccination in adults 50-59 years of age (YOA) with select cardiopulmonary diseases in the United States (US).

METHODS: A Markov model with a 3-year time horizon projected outcomes associated with one-time adjuvanted RSVPreF3 vaccination in US adults 50-59 YOA with chronic obstructive pulmonary disease (COPD) (n=3,299,241), heart failure (HF) (n=712,959), coronary artery disease (CAD) (n=2,865,359), and asthma (n=3,439,066). Model inputs were informed by scientific literature and public data sources. Outcomes, including RSV acute respiratory illness (ARI) cases, healthcare resource use, and mortality, were compared between scenarios with and without vaccination, assuming the same vaccination coverage as for influenza vaccines in this age group (50.1%).

RESULTS: Without vaccination, 3-year cumulative RSV-ARI cases in adults 50-59 YOA were projected to range from 117,232 to 573,262 in the HF and asthma populations, respectively. One-time adjuvanted RSVPreF3 vaccination resulted in 22,730 to 110,668 fewer RSV-ARI cases for HF and asthma, respectively. An estimated 582, 237, 392, and 294 RSV-related deaths were avoided by vaccination in the COPD, HF, CAD, and asthma populations, respectively. Vaccination prevented the loss of 3,081 to 8,860 quality-adjusted life years across populations when accounting for reduced RSV-related morbidity and mortality (Table 1).

CONCLUSIONS: Findings suggest that the adjuvanted RSVPreF3 vaccine has the potential to substantially reduce RSV burden among US adults 50-59 YOA with cardiopulmonary diseases.

FUNDING: GlaxoSmithKline Biologicals SA (VEO-0000556)

A QUALITATIVE EXPLORATION OF PEER INFLUENCES ON DECISION-MAKING FOR A FUTURE MATERNAL RSV VACCINE AMONG PREGNANT AND LACTATING PEOPLE IN KENYA

Prachi Singh (presenting author) (1), Berhaun Fesshaye, MSPH (1), Clarice Lee, MSPH (1), Ruth A. Karron, MD (1), Molly Sauer, MPH (1), Rupali J. Limaye, PhD (1)
1. Department of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA

Presenting author: Prachi Singh

Introduction: Respiratory syncytial virus (RSV) is a leading cause of respiratory illness in infants and young children globally. New maternal RSV vaccines which provide protection to neonates are on the horizon. This study explored peer influences on vaccine decision-making for future maternal RSV vaccines in Kenya.

Methods: This qualitative study conducted in-depth interviews with pregnant people, lactating people, and community members (e.g., male partners, other family members) in one rural and one urban county in Kenya. Data were analyzed using a grounded theory approach.

Results: 34 participants were interviewed: 6 pregnant people, 18 lactating people, 10 community members. Participants identified the pregnant person themself, their male
partner, other family members, peers, and healthcare workers as key influencers for the maternal immunization decision-making process (see Fig. 1); however, the majority of participants believed that the pregnant person should ultimately decide whether to receive a vaccine due to their autonomy and their perceived roles as infant caregivers. Community members also identified mothers as the key decision-makers. Healthcare providers emerged as an important influence, and participants identified peers, family members, and male partners as additional influences.

Conclusions: Understanding vaccine-decision making influences in the context of current and future maternal vaccines will help inform maternal RSV vaccine demand generation strategies. Targeting key potential influences is paramount to improve vaccine acceptance and uptake. While maternal autonomy was the greatest factor in maternal vaccination decision-making in this study, peers still played a strong role in the decision-making process; however, this will vary by setting.

Abstract category: Vaccines, Therapies & Treatments

Keywords:

Conflict of Interest: None declared

THE POTENTIAL PUBLIC HEALTH BENEFIT OF AN MRNA-BASED RESPIRATORY SYNCYTIAL VIRUS (RSV) VACCINE AMONG ADULTS ≥60 YEARS IN THE UNITED STATES

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2. Principal; Quadrant Health Economics, Inc., Cambridge, ON, Canada
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5. Executive Director & Program Lead; Moderna, Inc. Cambridge, MA, USA
6. Executive Director, Health Economics & Outcomes Research; Moderna, Inc. Cambridge, MA, USA

Presenting author: Sonia Stoszek

Background: RSV causes acute respiratory disease (ARD), including severe lower respiratory tract disease (LRTD), which can result in hospitalization and death in older adults. The study objective was to estimate the potential clinical impact of a single dose of an investigational RSV vaccine, mRNA-1345, in older adults (≥60 years) over a two-year timeframe in the United States.

Methods: A decision-analytic model (Figure 1) was developed to compare no vaccination to a single dose of mRNA-1345 administered before the RSV season. Based on clinical trial data (Wilson et al. 2023) projected over a 2-year period, the vaccine is assumed to be effective against RSV-ARD, RSV-LRTD, and RSV-LRTD hospitalizations; Table 1 shows the key inputs. Outcomes included number of RSV-ARD and RSV-LRTD cases, RSV-LRTD hospitalizations, in-hospital deaths, and numbers needed to vaccinate (NNV) to prevent each of these outcomes.

Results: The model predicted 10.4 million cases of RSV-ARD, including 2.6 million RSV-LRTD cases without vaccination; mRNA-1345 reduced RSV-ARD and RSV-LRTD cases by 770,000 (30%) and 2.6 million (25%). The model predicted 309,000 RSV-LRTD hospitalizations and 23,400 deaths without vaccination and reductions of 133,100 hospitalizations (43%) and 10,100 deaths (43%) with vaccination. The NNV to prevent one RSV-ARD case was 30; NNVs to prevent one RSV-LRTD case, hospitalization, and death were 103, 593, and 7,827, respectively.

Conclusions: mRNA-1345 could substantially reduce the public health burden associated with RSV in adults ≥60 years of age, with model-predicted reductions of 43% for RSV-LRTD hospitalizations and deaths compared to no vaccination.

Abstract category: Vaccines, Therapies & Treatments

Conflict of Interest: MK is a shareholder in Quadrant Health Economics Inc., which was contracted by Moderna, Inc., to conduct this study. KF, MM, and MCW are consultants at Quadrant Health Economics Inc. DM, NV, and PG are employees of Moderna, Inc., and hold stock/stock options in the company.

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THE PUBLIC HEALTH IMPACT OF INTRODUCING AN MRNA-BASED RESPIRATORY SYNCTIAL VIRUS (RSV) VACCINE AMONG ADULTS ≥65 YEARS IN THE UNITED KINGDOM

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2. Quadrant Health Economics, Inc., Cambridge, ON, Canada
3. Moderna, Inc. Cambridge, MA, USA
4. Moderna, Inc. London, UK

Presenting author: Sonia Stoszek

Background: RSV is an important cause of lower respiratory tract disease (LRTD) in older adults and may cause substantial morbidity, mortality, and economic disruption. The Joint Committee on Vaccination and Immunisation (JCVI) advised introducing a one-off RSV vaccine into the national immunisation schedule for adults aged 75-80. Potential impact of mRNA-1345, an RSV vaccine, was explored for UK adults aged ≥65, aligned with current influenza vaccine recommendations.

Methods: A decision-analytic model (Figure 1) was developed to estimate the clinical impact of mRNA-1345 compared with no vaccine over two-years from a UK perspective. Trial data (Wilson et al 2023) was used to populate mRNA-1345 efficacy in preventing RSV-LRTD, RSV-acute respiratory disease (ARD), and RSV-hospitalizations, projected over two-years. Table 1 shows key inputs. Outcomes included RSV-case numbers, RSV-LRTD hospitalisations, numbers needed to vaccinate (NNV) to prevent these outcomes, incremental life years and quality-adjusted life-years (QALYs).

Results: When targeting UK adults aged ≥65, compared to no vaccination, administering mRNA-1345 could result in a 33.8%, 38.6%, and 52.0% reduction in cases of RSV-ARD, RSV-LRTD, and deaths respectively. A reduction of 29,412 RSV-LRTD hospitalisations (52.0%) were estimated. Vaccination was estimated to save 95,556 QALYs and 121,885 life-years over two-years for a total population of 12,537,031. The NNV to prevent one RSV-LRTD case, one RSV-hospitalisation and one death was 57, 426 and 755, respectively.

Conclusions: In UK adults aged ≥65, implementing mRNA-1345 could have a significant impact on reducing RSV-related morbidity and mortality, and subsequently reduce healthcare resource use and improve population quality of life.

Abstract category: Vaccines, Therapies & Treatments

Conflict of Interest: MK is a shareholder in Quadrant Health Economics Inc., which was contracted by Moderna, Inc., to conduct this study. KF is a consultant at Quadrant Health Economics Inc. KJ, SKS, PG, and OB are employees of Moderna, Inc., and hold stock/stock options in the company. SH, RD, and HD have no conflicts to report.

Table 1: Key Model Parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Data Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population, by age group (year 1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>70 to 74</td>
<td>3,429,416</td>
<td></td>
</tr>
<tr>
<td>75 to 79</td>
<td>2,490,287</td>
<td></td>
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<tr>
<td>80 to 84</td>
<td>2,998,442</td>
<td></td>
</tr>
<tr>
<td>85+</td>
<td>1,493,152</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>12,837,401</td>
<td></td>
</tr>
<tr>
<td>Vaccination coverage 265</td>
<td>79%</td>
<td>Gov.uk. Seasonal influenza vaccine uptake in GP patients monthly data, 2021 to 2022</td>
</tr>
<tr>
<td>Annual incidence of RSV-ARD</td>
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<tr>
<td>75+</td>
<td>5.41%</td>
<td></td>
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<tr>
<td>Percentage with RSV-LRTD</td>
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<tr>
<td>65 to 74</td>
<td>42.08%</td>
<td>Derived from Fleming et al. (2015), BMC Infect Dis. 2015 Oct 21;15(1).</td>
</tr>
<tr>
<td>75+</td>
<td>52.12%</td>
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<tr>
<td>RSV-LRTD-related infant mortality</td>
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</tr>
<tr>
<td>65 to 74</td>
<td>35.72%</td>
<td>Derived from Fleming et al. (2015), BMC Infect Dis. 2015 Oct 21;15(1).</td>
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<tr>
<td>75+</td>
<td>66.24%</td>
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<tr>
<td>RSV-LRTD infant treatment</td>
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<td></td>
</tr>
<tr>
<td>RSV-LRTD infant treatment</td>
<td>0.0193</td>
<td></td>
</tr>
<tr>
<td>RSV-LRTD outpatient treatment</td>
<td>0.0185</td>
<td>Derived from Hutton et al. (2022) based on unpublished data. ACP Presentation S10c; February 22-26, 2023 Meeting</td>
</tr>
<tr>
<td>RSV-LRTD no treatment</td>
<td>0.0185</td>
<td></td>
</tr>
<tr>
<td>RSV-LRTD no treatment</td>
<td>0.0185</td>
<td></td>
</tr>
</tbody>
</table>

believed that there is sufficient workforce to deliver a new maternal vaccine without compromising existing programs.

Conclusions: Surveillance of maternal and neonatal mortality exists, but there is room for improvement for the surveillance of vaccine preventable diseases (VPDs). There is a need for creating better awareness on the burden of VPDs among OBs. There exist gaps in the current ANC for vaccination in pregnancy and there is need for clarifying the roles and responsibilities of the NIP and Antenatal Care/Maternal Neonatal Child Health personnel regarding implementation of vaccination in pregnancy.

Abstract category: Vaccines, Therapies & Treatments

Keywords: Maternal Immunization, Antenatal care, Tetanus toxoid, Tdap, MIACSA checklist, vaccination in pregnancy

Conflict of Interest: K. Thakrar, R. Sini de Almeida, M. A. Fletcher, B. Taysi are employees of Pfizer and may hold stock or stock options of Pfizer.

**COST-EFFECTIVENESS OF WASTEWATER SURVEILLANCE COMPARED TO CLINICAL SURVEILLANCE TO GUIDE RESPIRATORY SYNCYTIAL VIRUS PROPHYLAXIS IN CANADA**

Nisha Thampi (1), Elisabeth Mercier (1), Bosco Paes (2), John Fullarton (3), Ian Keary(3), Robert Delatolla (1), Barry Rodgers-Gray (3)

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2. McMaster University, Hamilton, Ontario, Canada
3. Violicom Medical Limited, Aldermaston, United Kingdom

**Presenting author:** Nisha Thampi

Objective: To compare the cost-effectiveness of wastewater-based surveillance (WBS) versus clinical surveillance (CS)-guided respiratory syncytial virus (RSV) prophylaxis programs in Canada.

Methods: A cost-utility model was developed comprising two identical decision trees for WBS and CS. Children could receive nirsevimab prophylaxis or not at the start of the RSV season and subsequently experience an RSV-associated hospitalisation (RSVH), medically attended, non-hospitalised RSV-infection, or be uninfected/non-medically attended. Infants admitted to intensive care could die and all survivors could experience subsequent respiratory morbidity (RM). All prophylaxis and RSV-related cost inputs were identical for WBS and CS. No costs were assumed for CS; however, a cost of CAD1,469,020 in year 1 and CAD 806,020 in subsequent years was assumed if a new RSV-WBS was initiated and CAD76,581/year if RSV was added to an existing WBS system. Dedicated on data from the 2022-23 RSV season in Ontario, WBS provided a 15.1% benefit for earlier initiation of the prophylaxis program versus CS. Outcomes were modelled over a 6-year time horizon with 1.5% discounting.

Results: WBS was found to dominate (lower costs and higher utilities) CS, with a cost/quality-adjusted life year of negative-CAD20,571 when RSV was added to an existing WBS and negative-CAD12,226 for a newly initiated RSV-WBS (Table). The model was most sensitive to RSVH and RM rates in deterministic sensitivity analyses (±20% on variables). WBS remained dominant over CS in scenario analyses modifying the benefit by ±10%.

Conclusions: WBS is a highly cost-effective strategy (vs CS) to guide earlier launch of RSV seasonal prophylaxis in Canada.

Abstract category: Vaccines, Therapies & Treatments

Keywords: wastewater-based surveillance, economics, pediatric hospitalization, community incidence, season start date, passive immunoprophylaxis, hospital level preparedness

**A PHARMACOKINETIC AND SAFETY STUDY OF SISUNATOVIR, A POTENT RSV FUSION INHIBITOR WITH DEMONSTRATED ANTIVIRAL ACTIVITY, IN HOSPITALIZED INFANTS WITH RSV LOWER RESPIRATORY TRACT INFECTION**

Cristina Calvo (1), Sima S. Toussi (2), Brett Haumann (3), Elaine Thomas (2), Ryan M. Franke (2), Maria Kudela (2), Anindita Banerjee (2), Sally Rees (4), Heather Welch (3), Iolanda Jordan Garcia (5), Klaita Srisingh (6), Mariana Daud (7), Agnes Nemeth (8), Teck Hock Toh (9) and Negar Niki Alami (2)

1. Hospital La Paz, Madrid, Spain
2. McMaster University, Hamilton, Ontario, Canada
3. University of Ottawa, Ottawa, Ontario, Canada
4. Moonlake Immunotherapeutics AG, UK
5. Hospital Sant Joan de Déu, Barcelona, Spain
6. Hospital Raja Perempuan Zainab II, Kelantan, Malaysia
7. Hospital Sibu, Sibu, Malaysia
9. Naresuan University Hospital, Phitsanulok, Thailand

**Presenting author:** Sima Toussi

Background: RSV infection in pediatric patients can range from mild upper respiratory tract symptoms to life-threatening lower respiratory tract infection (LRTI). Sisunatovir (PF-07923568), a potent inhibitor of RSV F protein with antiviral activity against RSV A and B, was shown to be effective in an adult challenge study. We performed a single- and multiple-ascending dose pharmacokinetic and safety study of sisunatovir in hospitalized infants with RSV LRTI.

Methods: Forty-one children (1-36 months) with RSV LRTI were dosed with sisunatovir; 19 received single ascending oral doses of 1mg/kg, 2mg/kg or 2.5mg/kg (Part A) and 22 received multiple ascending q12
oral doses of 2.5 mg/kg, 3.5 mg/kg or 5 mg/kg for 5 days (Part B). Nine participants received matched placebo in Part B. Nasopharyngeal swabs were collected at baseline and timepoints post-dose for RSV viral load and RSV F-protein sequence.

Results: Following multiple doses, sisunatovir mean free plasma steady-state trough concentrations were 22x EC90 at the highest dose assessed for each age group. The most frequently reported treatment emergent adverse events (TEAE) were gastrointestinal events (10/41, 24%). No treatment-related serious TEAEs were reported. All TEAEs were mild or moderate. Upon analysis of RSV F-protein gene sequence no emergent F protein substitution was observed in this study.

Conclusion: Sisunatovir was safe and tolerated in young children at doses that covered multiples above the in vitro EC90 and exposures effective in an adult challenge study, suggesting a favorable therapeutic index. Further development is planned to evaluate efficacy and inform dose selection in pediatric RSV-infected patients.

Abstract category: Vaccines, Therapies & Treatments
Keywords: RSV, antiviral, respiratory tract infection
Conflict of Interest: Pfizer employees may hold stock options

RESPIRATORY SYNCYTIAL VIRUS PREFUSION F PROTEIN VACCINE (RSVPREF3 OA) IS IMMUNOGENIC AND WELL-TOLERATED IN ADULTS 50-59 YEARS, INCLUDING ADULTS AT INCREASED RISK FOR RSV DISEASE

Dr. Murdo Ferguson (1), Prof. Tino F Schwarz (2), Dr. Sebastián A. Núñez (3), Dr. Juan Rodríguez Garcia (4), Dr. Marek Mital (5), Dr. Carlos Zala (6), Bernhard Schmitt (7), Dr. Nicole Tousarskissian (8), Dr. Dolores Ochoa Mazarro (9), Dr. Josef Großkopf (10), MD Christine Voors-Pette (11), Dr. Hemalini Mehta (12), Dr. Hwot Amare Halemariam (13), Dr. Magali de Heusch (13), MSc Silvia Damaso (13), MSc Marie-Pierre David (13), Dr. Dominique Descamps (13), MD Judith Hill (13), Dr. Corinne Vandermeulen (13), Dr. Veronica Halstrøm (13), on behalf of the RSV OA=ADJ=018 study group

Presenting author: Corinne Vandermeulen

Background: Adults 50-59 years of age (YOA) with specific chronic medical conditions are at increased risk for severe RSV disease. We report immunogenicity and safety data of RSVPref3 OA in adults 50-59 YOA without/with chronic conditions that increase the risk for RSV disease.

Methods: This phase 3, observer-blind, placebo-controlled multi-country study (NCT05590403) enrolled adults 50-59 YOA, including those at increased risk (AIR) for RSV disease due to specific chronic conditions. Participants were randomized (2:1) to receive RSVPreF3 OA (AIR-RSV, non-AIR-RSV) or placebo (AIR-placebo, non-AIR-placebo). A control group of adults 50-65 YOA received RSVPref3 OA (OA-IR). We assessed non-inferiority of the humoral immune response in 50-59 YOA versus ≥60 YOA, cell-mediated immunity and safety.

Results: 1533 participants received RSVPref3 OA or placebo. Non-inferiority criteria were demonstrated for RSV-A and RSV-B neutralization titers (Figure 1). RSVPref3 OA-specific CD4+ T-cell median frequencies increased at 1 month post-versus pre-vaccination in all RSV groups. Some solicited adverse events (AEs) were reported with higher incidences (Figure 2), but similar severity and duration, in 50-59 YOA versus OA-IR. Across all groups, 10.5%-16.3% of participants reported unsolicited AEs within 30 days post-vaccination, and 0.5%-3.6% of participants reported serious AEs within 6 months post-vaccination. One potential immune-mediated disease (cold-type hemolytic anemia, OA-RSV group) was considered vaccine-related by the investigator. No deaths were reported.

Conclusions: RSVPref3 OA immune responses in adults 50-59 YOA were non-inferior to the immune responses in ≥60 YOA, in whom efficacy was demonstrated. The overall safety profile in 50-59 YOA was consistent with the favourable safety profile in ≥60 YOA.

Funding: GlaxoSmithKline Biologicals SA

![Figure 1. Non-inferiority of immunogenic responses to RSVPref3 OA in adults 50-59 YOA compared with adults ≥60 YOA at 1 month post vaccination (per-protocol set for humoral immunogenicity).](image-url)
Abstract category: Vaccines, Therapies & Treatments

Keywords: RSV-A, RSV-B, prefusion F protein, neutralizing antibody, RSV vaccine, immunogenicity, safety, adults, at increased risk, risk reduction

Conflict of Interest: SD, M-PD, DD, HAH, MDH, D. VA, CV are/were GSK employees at the time when the study was conducted/developed. SD, M-PD, DD, HAH, MDH, VA, CV hold shares/stocks from GSK as part of their employee remuneration. M-PD is co-applicant for a pending patent for GSK. MF received study-related payments for training and the conduct of the study from GSK. TFS received honoraria from AstraZeneca, Bavarian Nordic, Biogen, CSL-Seqirus, GSK, Janssen-Cilag, Merck-Serono, Moderna, Novavax, MSD, Pfizer, Roche, Sanofi-Aventis, Takeda; he participated on advisory boards for Bavarian Nordic, CSL-Seqirus, BioNTech, GSK, Moderna, Novavax, Takeda. SAN received support from GSK to his institution, and to attend investigator meetings. JR-G received honoraria for continuing medical education from GSK, Pfizer, and Sanofi; support for attending meetings and/or travel from Pfizer and Sanofi; participation on data safety monitoring boards or advisory boards from GSK and Pfizer; and declares being unpaid member of the Vaccination group, Spanish Society of Preventive Medicine, Public Health and Sanitary Management (SEMPSPGS), and Associated Professor of the Balearic Islands University. CZ received grants from GSK for the conduct of this study, and support for attending meetings. JG declares study-related payments from GSK; grants from Novartis, Pharmalog, New Amsterdam Pharma, Syneos, W eleven Pharma, and Lilly; consulting fees, honoraria, payment for expert testimony, and support for attending meetings and/or travel from GSK. CV-P is employee of QPS Netherlands B.V. MM, BS, NT, DOM, and HM have nothing to disclose. All authors declare no other financial or non-financial interests, relationships and activities.

THE RESPIRATORY SYNCTIVIAL VIRUS PREFUSION F PROTEIN-BASED VACCINE FOR OLDER ADULTS (RSVPREF3 OA) EXHIBITS BROAD EFFICACY AGAINST CONTEMPORARY AND ANTIGENICALLY DIVERSE RSV STRAINS

Jonathan De Smedt (1*), Olivier Gruselle (2*), Lionel Sacconnay (1*), Delphine Baup (2), Aurélie Olivier (2), Marie-Pierre David (2), Christophe Lambert (1), Marie Van der Wielen (2), Nancy Dezutter (2), Lucile Warter (1)

1. GSK, Rixensart, Belgium
2. GSK, Wavre, Belgium

*These authors contributed equally to the work.

Presenting author: Lucile Warter

Background: RSVPref3 OA has demonstrated high efficacy against RSV-associated lower respiratory tract disease (RSV-LRTD) in an ongoing trial (ARESVi-006/NCT04886596). In a previous global polymorphism analysis (GPA), we characterized amino acid (aa) variations at pref-specific antigenic sites (Ø/V) relative to the RSVPref antigen in RSVPref3 OA, among all RSV-F sequences reported in NCBI/GISAID databases during Jan/1990-Feb/2022 and evaluated their potential impact on pref-neutralizing antibody interactions. We identified one RSV-A combination of five aa variations (M5) and two RSV-B combinations of 14/16 aa variations (M14A/M16), found in globally dominant RSV strains. RSVPref3 OA elicited broad neutralization against all tested RSV strains.

Methods: The GPA was updated to include RSV sequences reported until Jun/2023 and all F protein antigenic sites (Ø/V) relative to the RSVPref antigen in RSVPref3 OA. Among RSV-F sequences reported in NCBI/GISAID databases during Jan/1990-Feb/2022 and evaluated their potential impact on pref-neutralizing antibody interactions. We identified five RSV-A combinations of five aa variations (M5) and two RSV-B combinations of 14/16 aa variations (M14A/M16), found in globally dominant RSV strains. RSVPref3 OA elicited broad neutralization against all tested RSV strains.

Results: The updated GPA showed that most aa variations occurred at pref-specific sites Ø/V, while other sites, particularly II-IV, were highly conserved. During Feb/2022-May/2023, RSV-A M5 remained dominant, while RSV-B M14A and M16 largely disappeared and a new combination (M17) emerged. Across ARESVi-006 seasons, 34 combinations were identified (14 RSV-A/20 RSV-B), with ≥6 to ≤25 aa variations. Predominant combinations in isolates from trial participants mirrored the updated GPA.

Conclusions: Our results show rapid emergence of new RSV sequences. The observed high vaccine efficacy and the fact that RSV isolates in ARESVi-006 were representative of worldwide circulating strains indicate broad efficacy of RSVPref3 OA against antigenically diverse strains.

Funding: GlaxoSmithKline Biologics SA

Abstract category: Vaccines, Therapies & Treatments

Keywords: RSV-A; RSV-B; prefusion F protein; RSV vaccine; older adults; antigenic sites; amino acid variants

Conflict of Interest: All authors are GSK employees and O. Gruselle, L. Sacconnay, A. Olivier, M.-P. David, C. Lambert, M. Van der Wielen, N. Dezutter, and L. Warter hold shares/stocks from GSK as part of their employee remuneration. N. Dezutter and L. Warter have stock options from Halexon. J. De Smedt, L. Sacconnay, N. Dezutter, and L. Warter are inventors on patent applications entitled "Vaccination Against RSV", which was filed in the U.K. Intellectual Property Office under application numbers 2218080.6 and 2303002.6. M.-P. David, A. Olivier, and M. Van der Wielen are co-applicants on a pending patent filed by GSK. C. Lambert is co-leader of AVDTIG subgroup DE, acting without payment. The authors declare no other financial or non-financial interest.

The Respiratory Syncytial Virus Prefusion F Protein-Based Vaccine for Older Adults (RSVPref3 OA) Exhibits Broad Efficacy Against Contemporary and Antigenically Diverse RSV Strains

Jonathan De Smedt (1*), Olivier Gruselle (2*), Lionel Sacconnay (1*), Delphine Baup (2), Aurélie Olivier (2), Marie-Pierre David (2), Christophe Lambert (1), Marie Van der Wielen (2), Nancy Dezutter (2), Lucile Warter (1)

1. GSK, Rixensart, Belgium
2. GSK, Wavre, Belgium

*These authors contributed equally to the work.

Presenting author: Lucile Warter

Background: RSVPref3 OA has demonstrated high efficacy against RSV-associated lower respiratory tract disease (RSV-LRTD) in an ongoing trial (ARESVi-006/NCT04886596). In a previous global polymorphism analysis (GPA), we characterized amino acid (aa) variations at pref-specific antigenic sites (Ø/V) relative to the RSVPref antigen in RSVPref3 OA, among all RSV-F sequences reported in NCBI/GISAID databases during Jan/1990-Feb/2022 and evaluated their potential impact on pref-neutralizing antibody interactions. We identified one RSV-A combination of five aa variations (M5) and two RSV-B combinations of 14/16 aa variations (M14A/M16), found in globally dominant RSV strains. RSVPref3 OA elicited broad neutralization against all tested RSV strains.

Methods: The GPA was updated to include RSV sequences reported until Jun/2023 and all F protein antigenic sites (Ø/V) relative to the RSVPref antigen in RSVPref3 OA. Among RSV-F sequences reported in NCBI/GISAID databases during Jan/1990-Feb/2022 and evaluated their potential impact on pref-neutralizing antibody interactions. We identified one RSV-A combination of five aa variations (M5) and two RSV-B combinations of 14/16 aa variations (M14A/M16), found in globally dominant RSV strains. RSVPref3 OA elicited broad neutralization against all tested RSV strains.

Results: The updated GPA showed that most aa variations occurred at pref-specific sites Ø/V, while other sites, particularly II-IV, were highly conserved. During Feb/2022-May/2023, RSV-A M5 remained dominant, while RSV-B M14A and M16 largely disappeared and a new combination (M17) emerged. Across ARESVi-006 seasons, 34 combinations were identified (14 RSV-A/20 RSV-B), with ≥6 to ≤25 aa variations. Predominant combinations in isolates from trial participants mirrored the updated GPA.

Conclusions: Our results show rapid emergence of new RSV sequences. The observed high vaccine efficacy and the fact that RSV isolates in ARESVi-006 were representative of worldwide circulating strains indicate broad efficacy of RSVPref3 OA against antigenically diverse strains.

Funding: GlaxoSmithKline Biologics SA

Abstract category: Vaccines, Therapies & Treatments

Keywords: RSV-A; RSV-B; prefusion F protein; RSV vaccine; older adults; antigenic sites; amino acid variants

Conflict of Interest: All authors are GSK employees and O. Gruselle, L. Sacconnay, A. Olivier, M.-P. David, C. Lambert, M. Van der Wielen, N. Dezutter, and L. Warter hold shares/stocks from GSK as part of their employee remuneration. N. Dezutter and L. Warter have stock options from Halexon. J. De Smedt, L. Sacconnay, N. Dezutter, and L. Warter are inventors on patent applications entitled "Vaccination Against RSV", which was filed in the U.K. Intellectual Property Office under application numbers 2218080.6 and 2303002.6. M.-P. David, A. Olivier, and M. Van der Wielen are co-applicants on a pending patent filed by GSK. C. Lambert is co-leader of AVDTIG subgroup DE, acting without payment. The authors declare no other financial or non-financial interest.
ANTI-INFLAMMATORY EFFECTS OF CURCUMIN-LOADED NIOSOMES ON RESPIRATORY SYNCYTIAL VIRUS (RSV) INFECTION IN MICE MODEL

Saeed Samadzadeh (1), Romina Yavari (1,2), Aliresa Tahamant (1,2)
1: Department of Microbiology, School of Medicine, Golestan University of Medical Sciences, Gorgan, Iran.
2: Infectious Diseases Research Centre, Golestan University of Medical Sciences, Gorgan, Iran.

Presenting author: Romina Yavari

Background: Respiratory syncytial virus (RSV) is the most common cause of lower respiratory tract infection in pediatrics. While antivirals are apparent candidates to treat RSV-induced diseases, they have not yet met the expectations and remained in infancy. There is growing evidence to suggest that modulating the exacerbated inflammation during RSV infection can improve the disease outcome. In this study, we evaluated the effects of curcumin-loaded niosomes on RSV-induced immunopathology in a mouse model.

Methods and Results: Curcumin-loaded niosomes were prepared using the thin-film hydration method and characterized in vitro. Female Balb/c mice were infected by RSV-A2 and treated daily with curcumin-loaded niosomes. The potential anti-inflammatory effects of curcumin-loaded niosomes were evaluated on day 5 after infection. The results showed that curcumin-loaded niosomes decrease immune cell influx to the lung and the inflammatory mediators (MIP-1α, TNF-α, and IFN-γ) production, resulting in alleviated lung pathology following RSV infection.

Conclusion: These findings indicate that curcumin-loaded niosomes have anti-inflammatory potential and could be a promising candidate to alleviate RSV-associated immunopathology.

Abstract category: Vaccines, Therapies & Treatments

Keywords: RSV; curcumin; niosome; curcumin-loaded niosomes; immunomodulator

Conflict of Interest: There is no conflict of interest.

PUBLIC HEALTH IMPACT ASSESSMENT OF RSVPREF3 OA ADJUVANTED VACCINE ON RESPIRATORY SYNCYTIAL VIRUS IN SELECTED EUROPEAN COUNTRIES

Eleftherios Zarkadoulas (1); Alexandra Kostakis (2); Gerrit Uhl (3); Bernard Selke (1); Nikoliane Vestergaard Dich (4); Andrea Garcia (5); Laura A. Vallejo-Aparicio (5); Janne Jakola (6); Andreas Akratos (7); Desmond Lucy (8); John O’Kane (8); Sofie Berghuis (9); Gabriëlle Jongeneel (9); Lea Gjonnes (10); Gudrun Boge (10); Paulo Bota (11); Kristina Mardberg (12); Linda Danielsson (12); Alen Marijam (1)
1. GSK, Wavre, Belgium
2. GSK, Brentford, United Kingdom
3. GSK, Vienna, Austria
4. GSK, Copenhagen, Denmark
5. GSK, Tres Cantos, Madrid, Spain
6. GSK, Helsinki, Finland
7. GSK, Athens, Greece
8. GSK, Dublin, Ireland
9. GSK, Amsterdam, Netherlands
10. GSK, Oslo, Norway
11. GSK, Lisbon, Portugal
12. GSK, Stockholm, Sweden

Presenting author: Eleftherios Zarkadoulas

BACKGROUND: Respiratory syncytial virus (RSV) infections pose a significant health burden among adults aged≥60 in Europe. This study aims to assess the potential public health impact of the GSK RSVPREF3 OA adjuvanted vaccine, the first approved preventive intervention for RSV for the older adult aged≥60 population in Austria, Belgium, Denmark, Finland, Greece, Ireland, the Netherlands, Norway, Portugal, Spain, and Sweden.

METHODS: A monthly-cycle static Markov model was developed to assess RSVPREF3 OA adjuvanted vaccine impact on adults aged≥60 across selected countries. Comparing no-vaccination to a single RSV vaccine dose over a three-year time-horizon, the model captured lower respiratory tract disease (LRTD) RSV cases, deaths, and healthcare resource utilization. Data inputs were based on systematic literature reviews, supplemented by the best available data when local information was lacking.

RESULTS: Preliminary model outputs estimate that RSV vaccination can prevent 1,360,223 to 1,408,594 LRTD cases, 173,019 to 179,254 hospitalizations and 16,930 to 17,550 deaths. The number of adults needed to vaccinate (NNV) to prevent one LRTD case is between 19 and 25; for hospitalizations, it spans from 164 to 210 and for deaths varies from 1,249 to 2,401.

CONCLUSIONS: Results reveal a significant preventive effect of the RSVPREF3 OA adjuvanted vaccination on the health and healthcare utilization of older adults aged≥60, resulting in substantial public health benefits. While data from ongoing studies may enhance precision, extensive sensitivity analysis highlights the importance of averting RSV to preserve health and well-being of the older adult population in Europe.

Funding: GlaxoSmithKline Biologics SA

Abstract category: Vaccines, Therapies & Treatments

Keywords: Respiratory Syncytial Virus, Vaccination, Public Health Impact, Older Adults

Conflict of Interest: All authors are employed by GSK. EZ, AK, LAV-A, LG and AM hold shares in GSK. The authors declare no other financial and non-financial relationships and activities.
EVALUATION OF IMMUNOASSAY BIOMARKER AS CORRELATE OF PROTECTION AGAINST RSV IN THE MODERNA MRNA-1345 VACCINE EFFICACY STUDY

Chong Ma (1), Jiejun Du (1), Lan Lan (1), Archana Kapoor (1), Sanjay Garg (1), Sonia K. Stoszek (1), Christine A. Shaw (1), Jaya Goswami (1), Eleanor Wilson (1), Rituparna Das (1), Honghong Zhou (1), Lingyi Zheng (1)

1. Moderna, Inc., Cambridge, MA, USA

Presenting author: Lingyi Zheng

Background: Moderna’s mRNA-1345 is an investigational RSV vaccine that consists of a mRNA sequence encoding for a stabilized prefusion F (PreF) glycoprotein.

Methods: The ConquerRSV Phase 3 pivotal efficacy trial is a randomized, double-blind, placebo-controlled study of approximately 37,000 adults ≥60 years (NCT05127434). The primary vaccine efficacy (VE) endpoints were RSV-lower respiratory tract disease (LRTD) with two or more symptoms, and RSV-LRTD with three or more symptoms. RSV-acute respiratory disease (RSV-ARD) was a secondary endpoint. A case-cohort sampling design was implemented for assessing RSV neutralizing antibody (nAb) titers and F binding antibody (bAb) concentrations in a subset of ~2130 participants. All nAb and bAb biomarker at Day 1 (pre-vaccination) and Day 29 post-vaccination were used to evaluate the Correlate of Risk (CoR) of RSV-LRTD/RSV-ARD and Correlate of Protection (CoP) of the mRNA-1345 vaccine against RSV-LRTD/RSV-ARD.

Results: The biomarker data showed that mRNA-1345 elicited strong immune responses observed by both nAb and bAb testing. Statistical analysis results support that RSV-A nAb and PreF bAb responses are excellent biomarkers that correlate to the protection of RSV-LRTD and RSV-ARD. The data analysis using Cox Proportional Hazards model demonstrated that Day 29 biomarkers contained the information of vaccine elicited response as well as the correlates to the risk of RSV-LRTD and RSV-ARD.

Conclusion: The results show that the Day 29 biomarkers can be surrogate endpoints for the prediction of RSV VE. The nAb titers and bAb concentrations for CoP at various VE targets are estimated based on the regression model.

Abstract category: Vaccines, Therapies & Treatments

Keywords: Vaccine efficacy, correlate of protection, correlate of risk, neutralizing antibodies, binding antibodies, biomarker

Conflict of Interest: All authors are employees of Moderna, Inc. and hold stock/stock options in the company.
Virology & Immunology
MOLECULAR CHARACTERIZATION OF RESPIRATORY SYNCYTIAL VIRUS, HRSVA AND HRSVB, GLYCOPROTEIN G GENE IN ISMAILIA PROVINCE, EGYPT, 2020-2023.

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Presenting author: Nourhan Ahmed

Limited data are available 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, 2020-2023. A total of 596 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 596 samples, 337 (56.54%) and 259 (43.46%) were male and female, respectively. Additionally, 174 (29.19%) were positive by real-time RT-PCR, but only 147 (24.66%) produced amplicons by conventional RT-PCR. Group A RSV predominates over group B RSV, with 67 strongly positive bands (61 hRSVA and 6 hRSVB) and 80 weakly positive (59 hRSVA and 21 hRSVB). On a phylogenetic tree, the majority of the characterized hRSVA strains (3/4,75%) were grouped with the ON1 genotype, 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. The phylogenetic analysis of hRSVB were closed to Argentina isolates. Further studies may be necessary to understand the regional and worldwide molecular epidemiology and evolution of RSV and their inducers for greater host adaptation.

Abstract category: Virology & Immunology

Keywords: Egypt, Molecular characterizations, RSV Genotypes, hRSVA, hRSVB

Conflict of Interest: There is no conflict of interest to declare

EPITHELIAL CELL REMODELING OF PEDIATRIC AND ADULT HUMAN NASAL ORGANOID DURING INFECTION WITH RESPIRATORY SYNCYTIAL VIRUS (RSV)

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Presenting author: Gina Aloisio

The respiratory epithelium is a dynamic, first-line defense against viral respiratory pathogens. Traditional models of RSV upper respiratory tract infection (URTIs) include in vitro cell culture systems and animal models that do not accurately represent the human population. We have pioneered the pediatric and adult human nasal organoid-air liquid interface (HNO-ALi) platform to study viral pathogenesis. HNO-ALIs are comprised of cell types seen in the human respiratory epithelium, can be infected with RSV, and mimic cytokine responses similar to those detected in RSV URTIs (Rajan et. Al 2022). Here we studied how two contemporary RSV isolates, RSV/A/Ontario and RSV/B/Buenos Aires, replicate and modulate cell proliferation, cytokine response, and major cell type composition (ciliated apical cells, goblet cells, club cells, & basal cells,) in 4 different pediatric and 4 adult HNO-ALIs. RSV/A/ON and RSV/B/BA replication peaked at 5 days post-inoculation (dpi) with active replication extending through at least 8 dpi in adult HNO-ALIs. Similar viral kinetics were observed in pediatric HNO-ALIs, however peak replication occurred earlier at 2 dpi. Enhanced mucous production during RSV infection was observed in both pediatric and adult HNO-ALIs, but more pronounced (~2-3x) in pediatric lines and more extensive ciliary damage (~5x) compared to adults during infection. Furthermore, pediatric derived HNO-ALIs elicited approximately 1.3-fold greater overall inflammatory cytokine response compared to their adult counterparts. Taken together, these data from HNO-ALIs suggest a potential mechanism for worse respiratory outcome of RSV infection in children when compared to adults.

Abstract category: Virology & Immunology

Keywords: RSV, organoids, goblet cells, cilia

Conflict of Interest: None declared

VIRUS-SPECIFIC IMMUNITY AND INFLAMMATORY MARKERS ASSOCIATED WITH EXPERIMENTAL RSV INFECTION OF OLDER ADULTS

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Presenting author: Stephanie Ascough

RSV is recognised as a major global disease burden in adults over 65 years. Recent market approval of protein subunit-based vaccines, targeting consequences of RSV infection in older adults, has shown it’s possible to design successful interventions for this age group. Factors influencing severity and heterogeneity of immune responses remain poorly understood. Therefore, it remains important to understand mechanisms of age-related susceptibility to infection. In an experimental challenge, 27 healthy volunteers aged 60-75 years were inoculated with RSV Memphis-37 by intranasal administration. Viral load was determined by qPCR and symptom scores calculated by self-completed diaries. Immune-related cytokines were quantified in blood and respiratory tracts throughout infection by MSD. Antigen-specific T cell responses to viral proteins were shown using flow cytometry, ELISpot and ICS in peripheral blood and airway cells.

Conflict of Interest: None declared
Increased age was associated with greater susceptibility to PCR+ infection following challenge with RSV: 67% of these older participants were infected, with an age-related increase in viral shedding. We observed higher pro-inflammatory mediators in the airways and blood following infection. These were associated with activated and proliferating antigen-specific populations of T cells during infection. The magnitude of self-reported symptoms, which decreased with increasing age, correlated with inflammatory markers, rather than viral load.

Even in the absence of co-morbidities, age-related changes in susceptibility occur, with higher viral loads in older individuals, and inflammatory responses driving severity of symptoms. Thus, controlled challenges of older volunteers provides unique insight into biomarkers associated with disease enabling direct testing of potential interventions in this age group.

**Abstract category:** Virology & Immunology

**Keywords:** Controlled Human Infection Models, Inflamm-ageing, Immunosenescence, Immunology, Challenge studies, B cell, T cell, cytokines

**Conflict of Interest:** None declared.

### STABILITY OF RESPIRATORY SYNCYTIAL VIRUS (RSV) NEUTRALIZING AND FUSION SITE-SPECIFIC ANTIBODY LEVELS IN ADULTS DURING THE CORONAVIRUS DISEASE 2019 PANDEMIC WHEN RSV WAS NOT CIRCULATING

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**Presenting author:** Vasanthi Avadhanula

**INTRODUCTION.** We evaluated if lack of RSV circulation during the COVID-19 pandemic affected RSV antibody levels in adults during a 14-month period of the COVID-19 pandemic in the Houston metropolitan.

**METHODS.** Our study included 100 adults, whose sera were collected at Visit 1 (01April2020-31July2020), Visit 2 (01Aug2020-31Dec2020), and Visit 3 (01Jan2021-30Apr2021). Neutralizing antibodies were measured against RSV/A and RSV/B strains, and F site-specific competitive antibody concentration (CAC) were measured against sites Ø, II, and IV for all samples. Repeated measures analysis of variance was performed to evaluate differences in the antibody levels between visits, and a linear mixed effects model examined the time effect. A best fit line provided an estimated slope or antibody decay rate.

**RESULTS.** Mean age was 49 years; 63% females; 72% white, and 19% Hispanic. The geometric mean neutralizing antibody titers (GMNATs) were comparable between the three visits against RSV/A/Tracy, RSV/A/Ontario, RSV/B/18537, and RSV/B/Buenos Aires. Similarly, F site-specific CAC against sites Ø and IV were stable, however, site II CAC experienced a significant but minor drop of 3.5 µg/ml. The 30-day decay rates for RSV GMNATs and F site-specific CACs to sites Ø and IV were not significant, however it was statistically significant for site II (log 2 -0.0143 µg/ml; 95%CI: -0.0223, -0.0062).

**CONCLUSION.** Overall, neutralizing antibody levels against RSV and F site-specific CAC against sites Ø and IV were stable in adults during a median duration of 313 days when RSV was not circulating in the community.

**Abstract category:** Virology & Immunology

**Keywords:** RSV antibodies, covid19, antibody levels

**Conflict of Interest:** None declared.

### MUCOSAL ANTIBODY RESPONSES TO SEVERE RESPIRATORY SYNCYTIAL VIRUS (RSV) INFECTION IN INFANTS

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**Presenting author:** Emma Coindy

**Respiratory syncyntial virus** (RSV) is the commonest cause of infantile bronchiolitis. All adults have circulating antibodies to RSV which can transfer to the infant transplacentally in late pregnancy. Maternal antibodies help protect infants postnatally and maternal vaccination may enhance this protection. Maternal vaccine efficacy could be evaluated in infants by measuring immunologic indicators of RSV infection such as antibody titres. Mucosal anti-RSV IgA antibody was measured in 148 nasosorption samples of infants aged <24 months with various infection statuses (healthy control, RSV infected) to evaluate mucosal IgA as a biomarker of previous response to RSV infection.

**Specific IgA** was detected in RSV infant nasosorption samples although median titres (0.378 AU/ml [IQR=0.098-1.207]) were lower than in healthy infants (0.415 AU/ml [IQR=0.122-7.090]). Anti-RSV IgA titres increased during RSV infection and broadly correlated with infant age, indicating positive RSV infections. Anti-RSV IgA titres increased with days after symptom onset and indicated positive RSV infections at 4-5 and 3-4 days in infants <6 months and 18 to <24 months, respectively. Infant age, previous infection and timing of sample collection therefore influenced IgA titres in the nose. Uncertainty over infection history of control infants likely resulted in an overestimate of the threshold indicating positive RSV infection.

In future studies, we aim to collect samples from healthy controls from all age groups, confirm RSV infection history and collect sequential samples through convalescence to evaluate the accuracy of mucosal IgA as a marker of previous RSV infection.

**Abstract category:** Virology & Immunology

**Keywords:** Respiratory syncytial virus; RSV; Nasosorption samples; Mucosal antibodies; Anti-RSV IgA; Maternal antibody transfer; Maternal RSV vaccine; Biomarker of previous RSV infection

**Conflict of Interest:** None declared.
ASSEMBLY MECHANISM OF THE TRIPARTITE AND RNA CONDENSATES OF THE RESPIRATORY SYNCYTIAL VIRUS FACTORY PROTEINS: ROLE OF THE TRANSCRIPTION ANTITERMINATOR M2-1
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Presenting author: Gonzalo de Prat Gay

A wide variety of viruses replicate in liquid-like condensed structures often referred to as viral factories. Non-segmented negative stranded RNA viruses share a nucleoprotein (N) and a phosphoprotein (P) that emerge as main drivers of the condensation process. The syncytial respiratory virus includes a transcription antiterminator, M2-1 which binds RNA and maximize processivity through a not fully understood mechanism. In this work, we recapitulate the mechanism of assembly of condensates of the main protein drivers and the role played by RNA. M2-1 displays a strong propensity for condensation through the formation of protein-RNA coacervates, finely tuned by stoichiometric ratios. M2-1 readily incorporates to tripartite condensates with N and P, strongly modulating their size. RNA is incorporated to the tripartite condensates with an heterogeneous distribution, reminiscent of the M2-1 RNA iBAG granules described within RSV viral factories. Ionic strength dependence reveals that whereas M2-1 and M2-1-RNA condensates are highly electrostatic, P-M2-1 and P-N and tripartite condensates are salt independent, indicating a different nature of interactions. This suggests that M2-1 displays a different behavior when in the protein phase than the protein-RNA phase, subcompartmentalized within the condensates. This work recapitulates and dissects biochemical backgrounds for the formation and fate of the RSV condensates in vitro. A recent report of compounds with antiviral activity that harden the viral factories and hamper replication points at M2-1 as the target. The viral condensates constitute a novel platform for drug discovery and highlight the impact of this processivity factor on the modulation of the viral factories.

Abstract category: Virology & Immunology
Keywords: Viral factories; biomolecular condensation; antiviral platform; transcription antiterminator
Conflict of Interest: None to declare

DIFFERENCES IN INTERFERON RESPONSE IN LUNG TISSUE OF INFANTS INFECTED EX-VIVO WITH RSV AND SARS-CoV-2
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Presenting author: Ana Paula Duarte de Souza

Background: The RSV and SARS-CoV-2 present different morbidity and mortality impacts in children under 5 years old. The immune response mechanisms in this critical period of life, which lead to such different impact between RSV and SARS-CoV-2, is still not well defined. Composition of immune system cells is different across tissues, with variations in gene expression, metabolic pathways, and functional regulation. Studying the immune response direct in the lung can bring important responses for protection against different pathogens. Methods: We are currently recruiting pediatric patients under 2 years of age that will undergo lung recession by bronchoscopy or thoracic surgery for other medical reasons. Written informed consent is obtained from all relatives or authorized legal guardians. Fresh lung samples from uninfected children were sectioned infected ex-vivo with RSV and SARS-CoV-2 virus. After 24h the lung tissues were collected from culture and RNA extraction was performed for gene expression analysis using Real-time PCR. Findings: We analyzed samples from 5 different patients. Viral genes amplified confirming the tissue infection. Lactate dehydrogenase levels in the supernatant were similar between the groups confirming the tissue infection. RNA condensates are highly electrostatic, P M2-1 and N-P and tripartite condensates are salt independent, indicating a different nature of interactions. This suggests that M2-1 displays a different behavior when in the protein phase than the protein-RNA phase, subcompartmentalized within the condensates. This work recapitulates and dissects biochemical backgrounds for the formation and fate of the RSV condensates in vitro. A recent report of compounds with antiviral activity that harden the viral factories and hamper replication points at M2-1 as the target. The viral condensates constitute a novel platform for drug discovery and highlight the impact of this processivity factor on the modulation of the viral factories.

Abstract category: Virology & Immunology
Keywords: RSV, SARS-CoV-2, lung, infants, interferon, interferon lambda
Conflict of Interest: None declared

BURDEN OF RESPIRATORY SYNCYTIAL VIRUS (RSV) ASSOCIATED ACUTE LOWER RESPIRATORY TRACT DISEASE AMONG UK ADULTS PRESENTING TO PRIMARY CARE, 2022/23
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Presenting author: Polly Duncan

Background: In UK primary care, RSV testing is not routinely conducted. There are limited data amongst adults on RSV-related acute lower respiratory tract disease burden (aLRTD; comprising acute lower respiratory tract infection and exacerbation of chronic lung disease and heart failure). We assessed RSV-associated aLRTD frequency amongst adults presenting to primary care. Methods: This ongoing prospective cohort study (AvonCAP-GP2) recruits adults (aged ≥18 years) registered at six participating GP practices in Bristol (total ~83,000 registered adults), presenting with aLRTD. We report results for participants recruited between 01Apr2022–31Mar2023 with naso-/oropharyngeal or saliva samples. Specimens were tested for RSV using CerTest VIASURE RT-PCR Detection Kits.

Conflict of Interest: None declared

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Results: Among 1000 aLRTD patients, 24 (2.4%, 95% CI: 1.6–3.5%) were RSV-positive. RSV A and B comprised 8 (33%) and 16 (67%), respectively. Median time between symptom onset and GP consultation was 6 days (IQR: 3–11) and between consultation and sampling was 3 days (IQR: 1–4). Among persons with both saliva and naso/oropharyngeal swabs collected, adding saliva led to increased RSV detection compared to using swabs only (n=9 RSV-positive using both; n=9 RSV-positive on saliva only; n=6 RSV-positive on naso/oropharyngeal only). Eighteen (75%) RSV-positive tests were observed in-season (October 2022–February 2023), yielding 3.0% (95% CI: 1.9–4.7%) prevalence for that period.

Conclusion: These preliminary results give an indication of community RSV-associated aLRTD burden. However, the delay between symptom onset and specimen collection (median 9 days) may have led to false negative results, and underascertainment of the true burden of RSV-associated aLRTD.

**Abstract category:** Virology & Immunology

**Keywords:** Respiratory syncytial virus; primary care; lower respiratory tract infection; vaccines; adults; general practice.

**Conflict of Interest:** AF is a member of the Joint Committee on Vaccination and Immunization (JCVI) and was, until December 2022, chair of the World Health Organization European Technical Advisory Group of Experts on Immunization (ETAGE) committee. AF and LD in addition to receiving funding from Pfizer for the AvonCAP GP2 study, were also funded by another project investigating transmission of respiratory bacteria in families jointly funded by Pfizer and the Gates Foundation. Persons with Pfizer affiliations are employees of Pfizer and may own Pfizer stock.

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**DISSECTION OF ANTIGENIC AND IMMUNOMODULATORY PROPERTIES OF RSV GLYCOPROTEIN**

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**Presenting author:** Juan Gutman

Respiratory Syncytial Virus (RSV) presents three envelope proteins, one of them being the attachment glycoprotein (G) with multiple striking features: its evolutionary origin is still unknown; efforts to obtain its molecular structure have been sterile (since it is highly disordered and glycosylated) and it encompasses an alternative initiation codon that results in a truncated secreted version, a property that has not been observed in related viruses. In addition, G is physiologically relevant both due to its immunogenicity and immunomodulatory roles. G epitopes (localized in the central conserved region) account for a significant part of the neutralizing antibodies after exposition to RSV. This central conserved region also exerts immunomodulatory effects, mainly via interaction with the fractalkine receptor CX3CR1. We have set out to study this interaction using a combination of bioinformatics, molecular modeling, molecular dynamics, and cellular and molecular biology focusing on the fifty non glycosylated residues of the central conserved region of G. We are currently evaluating the immunomodulatory properties of this domain, obtaining novel results in dendritic cells, neutrophils, and lymphocytes. This information has led us to the design of point mutations that aim to conserve the neutralizing epitopes, while disrupting its immunomodulatory properties. These mutations may be leveraged by generating a recombinant virus encompassing these point mutations, to elicit a robust immune response, providing a promising vaccine prototype.

**Abstract category:** Virology & Immunology

**Keywords:** Attachment glycoprotein, immune modulation, molecular dissection

**Conflict of Interest:** None declared

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**ASSOCIATION BETWEEN CYCLE THRESHOLD VALUES AND DISEASE SEVERITY IN CHILDREN WITH RESPIRATORY SYNCYTIAL VIRUS INFECTION AT VANDERBILT UNIVERSITY MEDICAL CENTER (2016–2020)**

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Introduction: Real-time polymerase chain reaction (rtPCR) cycle threshold (Ct) values are used as a surrogate measurement of viral load in diagnostic specimens, with lower Ct values corresponding to higher viral loads. This study investigates the association between Ct values and disease severity in children with respiratory syncytial virus (RSV) at Vanderbilt University Medical Center (VUMC).

Methods: We conducted active, population-based surveillance of children <5 years old with RSV determined by rtPCR from 12/01/2016 to 03/31/2020 at VUMC within the CDC New Vaccine Surveillance Network. Children with RSV co-detected with another virus were excluded. Disease severity was assessed by the level of care (emergency department (ED) vs. inpatient (IP)), intensive care unit (ICU) admission, oxygen use during hospitalization, and intubation. We compared characteristics of children in the ED to IP and Ct values between clinical outcomes.

Results: Of 4,411 children tested, 15.7% had RSV detection. Among these cases, 54.9% were hospitalized. Table shows the demographics and clinical characteristics of RSV-positive children by setting, highlighting that hospitalized children were younger. Of those hospitalized, 57.0% were on oxygen, 20.1% were admitted to the ICU, and 1.6% were intubated. Comparison of Ct values indicated that there was no difference in average Ct values between those who did and did not experience severe outcomes during hospitalization (Figure – next page).

Conclusion: There was no observed significant association between Ct values and disease severity in RSV-positive children. Further research is needed to determine the role of Ct values in the clinical evaluation of children with RSV.
Background: Severe acute lower respiratory infection (ALRI) due to viral pathogens is the most common cause of hospitalization in young children. Data from Indonesian children is scarce. Therefore, we conducted a study to determine the prevalence of respiratory syncytial virus (RSV) and influenza virus among children aged < 5 years hospitalized with severe ALRI in West-Nusa-Tenggara Province Hospital, Indonesia.

Methods: This study was a prospective observational study in a tertiary hospital from October 2018 to August 2019. We screened children hospitalized with severe-ALRI and collected demographic data, clinical symptoms, and nasopharyngeal swab for RSV and influenza virus detection using polymerase-chain-reaction.

Results: Of 120 children enrolled to the study, about 46 (38.3%) were positive for any virus. Respiratory syncytial virus was the most common virus detected (n=28, 23.3%), followed by influenza (n=14, 11.7%). Among 28 subjects with RSV+, 3 were RSV-A and 25 were RSV-B. Fourteen subjects were influenza+ (9 influenza A; 5 influenza B), and 13 (92.9%) of them were breastfed (p=0.024). All RSV+ were aged ≥ 24 months (p=0.07), and influenza+ had similar tendencies (p=0.176). Fourteen (50%) RSV+ and 4 (28.6%) influenza+ were found in children < 6 months. Comorbid were less likely occurred in RSV+ (n=3; 10.7%), p= 0.032. Dyspnea, cough and fever were the most common symptoms in both RSV and influenza virus infections.

Conclusions: Our study found RSV was the most common respiratory virus in children aged < 5 years hospitalized with severe-ALRI. These findings may help healthcare provider to implement appropriate strategies for treatment and prevention.

Abstract category: Virology & Immunology

Keywords: severe, ALRI, children, virus

Conflict of Interest: Cissy B Kartasasmita and Eric A.F. Simoes report grants from World Health Organization and USAID during the conduct of the study. The funders had no role in the design of the study; in the collection, analyses, or interpretation of the data; in the writing
REMOVAL OF THE N-GLYCANS IN P27 OF THE RESPIRATORY SYNCYTIAL VIRUS FUSION PROTEIN

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Presenting author: Lotte Jacobs

The RSV fusion protein (F) is the major focus in RSV vaccine development. This F protein has a unique type of maturation, since for activation it needs to be cleaved twice by furin with the concomitant removal of a 27 amino acid peptide p27, containing 2 to 3 N-glycans. Whether these two cleavages occur during virus production, or during entry of the virus, is still a matter of debate. Previously, we showed that removal of the N-glycan sequon at position 116 (N116Q), located in p27, results in higher neutralizing antibody responses and better protection upon RSV challenge. In this work, we elaborate on our previous findings, which only included conserved N-glycosylation sites, by investigating all glycomutants within the p27 peptide of F.

Glycomutants were constructed and surface expression and fusion capacity were evaluated. Total and neutralizing antibody responses in mice were observed after immunization with p27-mutants and correlated with viral loads after RSV challenge. Post-challenge serum was tested against different RSV isolates to evaluate the breadth of protection.

Removal of glycans had no major effect on both surface expression and fusogenicity of the F-protein. Upon immunization of mice, subtle differences are observed in neutralizing antibodies, which are better defined upon challenge, with significantly higher antibody titers for N116Q and N120-126Q compared to WT and significantly lower lung viral loads for N116Q, N120Q, N126Q and N116-120Q. These results indicate that N-glycans located in the p27 peptide can influence the F-specific immune response, yet the mechanism involved is not clear.

Abstract category: Virology & Immunology
Keywords: Fusion protein, p27 peptide, N-glycans, immunization

Conflict of Interest: None declared

UNDERSTANDING THE RELATIVE ROLE OF VIRAL INTERFERENCE AND NON-PHARMACOLOGICAL INTERVENTIONS IN SHAPING RSV EPIDEMICS: A MODELING STUDY

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Presenting author: Ke Li

Respiratory syncytial virus (RSV) is a major respiratory pathogen that primarily affects infants, young children and older adults. RSV epidemics typically follow a seasonal pattern in the United States (US), beginning in fall and peaking in December or January. During the COVID-19 pandemic, RSV disappeared for more than a year in the Northern Hemisphere and then reemerged out of the normal season. This was likely due to the implementation of non-pharmaceutical interventions (NPIs) to reduce the spread of SARS-CoV-2. Despite the limited implementation of NPIs, disrupted RSV activity was also observed following the 2009 influenza pandemic, suggesting viral interference from influenza. While the presence of viral interference has been shown at an individual level, it remains unclear whether the disruption of RSV following the influenza pandemic can be attributed to viral interference. In this work, we first apply the dynamic time warping computational method to analyse laboratory reports of weekly positive tests of RSV and A/H1N1 pandemic (pdmH1N1) influenza virus in different regions of the US. We observe a reduction in RSV activity following the pandemic, which is associated with intense influenza activity. We then develop an age-stratified, two-pathogen model to test various hypotheses regarding viral interference mechanisms. Based on our model estimates, we demonstrate that individuals infected with pdmH1N1 virus can interfere subsequent RSV infections by three mechanisms: 1) reducing susceptibility to RSV infection; 2) shortening RSV infectious period, and 3) reducing RSV infectivity. Our study offers statistical support for the occurrence of atypical RSV seasons following the 2009 influenza pandemic. Our work also offers new insights into the mechanisms of viral interference that contribute to RSV epidemics following the pandemic and establishes a model-fitting framework that enables the analysis of new surveillance data for studying viral interference at the population level.

Abstract category: Virology & Immunology
Conflict of Interest: None declared

THE LANDSCAPE OF INFECTIOUS DISEASE EXPOSURE OVER TWO DECADES IN SUB-SAHARAN AFRICAN CHILDREN

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Presenting author: Maureen Mburu

Children under 5 years are particularly vulnerable to infections due to the ongoing development of their immune system. Currently, there are about 73 deaths per 1000 live births in Sub-Saharan Africa attributed to infectious diseases, which remain prevalent despite several advances made to reduce transmission. Here, we carried out a longitudinal and single timepoint serosological analysis in young children to define the infectious disease landscape in a typical rural setting in Kilifi, Kenya over the last two decades with an aim of providing data-driven approach for prioritizing candidates for vaccine development or rollout. A customized protein microarray chip was designed to measure serum IgG to a range of 38 common and emerging pediatric infections and statistical analysis was carried out using R.

We analyzed 1134 serum samples from two cohorts over a span of 15 years, January 2002 to June 2017. In the first cohort, the seroprevalence was estimated using serial samples collected at birth from 124 children and sampled prospectively at 3 months intervals for about 2 years. The second cohort was a pediatric inpatient cohort and only a single sample was collected from the admission of 176 children ranging between 1 day and 57 months. In the first 12 months of age, Respiratory Syncytial Virus (RSV) had the highest disease burden, with a seroprevalence of 60%. In conclusion, the results of this study offer compelling evidence supporting the introduction of RSV vaccination in low resource settings.

Abstract category: Virology & Immunology
Keywords: Vaccine, RSV, Low resource setting
Conflict of Interest: None declared
**AGE-DEPENDENT CONSTITUTIVE EXPRESSION AND ANTIVIRAL ACTIVITY OF INTERFERON EPSILON AGAINST RESPIRATORY SYNCYTIAL VIRUS IN AIRWAY EPITHELIUM**

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**Presenting author:** Mary McCabe

Respiratory syncytial virus (RSV) remains the most common cause of acute lower respiratory tract infection in infants <2 years old, with the disease burden greatest between 6 weeks and 6 months. Why infants <6 months are more frequently susceptible to severe disease is unknown.

RNA-seq analysis of RSV-infected well-differentiated primary nasal epithelial cell cultures (WD-PNECs) derived from infants sampled at birth and 1-year-old revealed that interferon epsilon (IFNE), a type I interferon, was significantly increased following RSV infection versus uninfected controls. Furthermore, IFNE expression was higher in 1-year versus newborn-derived WD-PNECs, both at baseline and following infection, suggesting a less robust antiviral activity at birth compared to 1-year.

To explore the role of IFNE/IFNε we characterised its expression in immortalised airway epithelial cell lines. Constitutive IFNE expression was detected in all cell types, irrespective of infection. To assess the relative antiviral activity of IFNε compared to other epithelium-derived IFNs, cell lines were pre-treated with recombinant human IFNε, IFNβ1 or IFNλ1 (100 ng/mL) and infected with RSV-A2/mKate2 and a RSV clinical isolate. IFNε induced a dose-dependent reduction in RSV infection that was similar to IFNλ1, but less than IFNβ1. Similar IFNε-induced antiviral activity was also evident against Sendai virus, influenza virus, SARS-CoV-2 and encephalomyocarditis virus (EMCV).

Our data suggest that constitutive expression of IFNε mitigates RSV infection of airway epithelium. Furthermore, lower IFNε expression at birth compared to 1-year may help explain, in part, the increased susceptibility to severe respiratory viral disease in early-life, and highlight opportunities for therapeutic interventions.

**Abstract category:** Virology & Immunology

**Keywords:** RSV, Innate Immunity, Interferons, Interferon Epsilon

**Conflict of Interest:** None declared

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**RSV NEUTRALIZATION ASSAY USING DRIED BLOOD: PROOF-OF-PRINCIPLE OF A TECHNOLOGY TRANSFER TO A GAVI ELIGIBLE COUNTRY**

Jude Yayra Mensah (1), Jonne Terstappen (2), Evangeline Obodai (1), Anouk Veronel (2), Nana Kobina Acquah (1), Comfort Nuamah Antwi (1), Emmanuel Gberbi (1), John Kofi Odoom (1), Daniela Cianti (2), Eveline Delemarre (2), Marco Viveen (2), Louis Bont (2), Natalie Mazur (2, 3)

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**Presenting author:** Jude Mensah

The Respiratory Syncytial Virus (RSV) vaccine and monoclonal antibody (mAb) landscape is highly active. Using trial data, a correlate of protection against RSV will likely be defined using neutralizing antibody (nAb) titers. Recently, we showed that dried blood is an alternative patient-centered sampling method to measure RSV neutralization. This approach to measure nAbs is lacking or limited in low-middle-income countries (LMICs), resulting in inequitable distribution of RSV burden and research. Vaccine efficacy may be dependent on geographical location underscoring the need for representative trials in low-resource settings. We aimed to show proof-of-concept of a technology transfer of this low-cost low-tech tool to measure clinical trial endpoints in LMICs.

A researcher from University of Ghana was trained on dried blood-based RSV neutralization at the Utrecht Medical Center Utrecht, The Netherlands, followed by an onsite support visit to setup assay in Ghana. Fifty whole blood samples from the healthy donor service, were left blank or spiked with 10 or 100 μg/mL palivizumab or RSM01, mAbs against two RSV epitopes. Duplicate volumetric absorptive micro sampling were tested in parallel by both laboratories.

Presently, the assay has been implemented and working effectively in the Ghana laboratory. Four researchers in Ghana have been trained on the assay. Preliminary analysis of blank and spiked VAMS samples showed good correlation between the two labs (R2 = 0.87; n = 39).

**Proof-of-concept of technology transfer of RSV neutralization in dried blood has been demonstrated. More importantly, the study has established a platform for clinical trials and accessible correlate of protection surveillance in children in LMICs.**

**Abstract category:** Virology & Immunology

**Conflict of Interest:** None declared
DISTINCT HOST TRANSCRIPTIONAL PROFILES OF ADULT AND PEDIATRIC HUMAN NOSE ORGANOIDS INFECTED WITH RESPIRATORY SYNCYTIAL VIRUS (RSV)

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Presenting author: Divya Nagaraj

RSV causes substantial illness and deaths, and the severity of infection is age-dependent. The innate immune mechanisms related to age-dependent susceptibility to RSV infection is unclear. We utilized human nose organoids (HNOs) as physiologically relevant models to study RSV induced pathogenesis and innate immune epithelial responses. Adult and pediatric HNOs were inoculated with contemporary RSV A and B strains. At early (day 1), peak (day 5), and late (day 8) infection stages apical wash samples were collected for virus kinetics and HNOs were harvested for RNA sequencing. RSV kinetics demonstrated age-related variations with RSV peaking earlier and at higher levels in pediatrics than in adult HNOs. Comparative gene expression analysis highlighted distinct responses. Adult HNOs exhibited robust early antiviral gene upregulation (e.g., IFIT1, IFIT1, IFIT3, Oas1, Oas2, Mx1, Mx2, Isg15, and Rsad2), while pediatric HNOs displayed a muted response. Furthermore, at peak infection, the adult HNO transcriptome was enriched in the production and response to type 1 interferon and regulation of viral genome replication. While pediatric HNOs consistently exhibited downregulated pathways (interferon-gamma, cytokine-cytokine receptor interaction, and chemokine signaling). Interestingly, the RIG-I signaling pathway, crucial for virus recognition was activated in pediatric HNOs only in the late stage of infection, which could explain the higher RSV replication seen in pediatric HNOs. This ongoing study provides crucial insights into the age-dependent host innate immune epithelial response to RSV infections. Understanding this relationship holds promise for mitigating RSV infections in high-risk pediatric populations and further our knowledge of RSV biology.

Abstract category: Virology & Immunology
Conflict of Interest: None declared

THE PREVALENCE OF RESPIRATORY SYNCYTIAL VIRUS AND METAPNEUMOVIRUS IN LOWER RESPIRATORY INFECTIONS IN INFANTS HOSPITALIZED IN BLIDA, ALGERIA.

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Presenting author: Mustapha Oumouna

Several viruses target the human respiratory tract, causing different clinical manifestations spanning from mild upper airway involvement to life-threatening acute respiratory distress syndrome. Among the viruses incriminated, the respiratory syncytial virus (RSV) and the metapneumovirus are the major cause of hospitalizations of young children throughout the world.

The objective of our study was to identify the viruses implicated in lower respiratory infections in infants in the central region of Algeria, and to assess the prevalence of RSV and the metapneumovirus compared to other respiratory viruses.

For this purpose 122 nasal, pharyngeal and nasopharyngeal samples were collected from children hospitalized for acute lower respiratory infections. The results allowed us to establish a diagram that shows the predominance of viruses responsible for lower tracts infections (LTI) (Fig. 1 and 2). Among the 122 patients sampled, 100 cases had (LTI) of viral origin, i.e. a rate of 81.97% and 22 subjects (18.03%) were negative for the viral diagnosis.

The results obtained confirm the viral origin with a rate of 82%, and reveal the predominance of the RSV (47.54%), followed by the rhinovirus (23.77%), and in third position comes the metapneumovirus (22.13%).

Among the subgroups of RSV we have found a prevalence of 81% RSVB and 19% RSVA, followed by rhinovirus (23.77%), and in third position comes the metapneumovirus (22.13%).

The figure No 03 represents the frequency of the various respiratory viruses highlighted during our study and shows the predominance of RSV found in 58/122 samples (47.54%).

Abstract category: Virology & Immunology
Keywords: Lower respiratory tract infections, Respiratory Syncytial Virus, Pneumovirus.
Conflict of Interest: None declared
SINGLE-CELL SEQUENCING ANALYSIS OF RESPIRATORY SYNCYTIAL VIRUS INFECTED PEDIATRIC AND ADULT HUMAN NOSE ORGANIDS REVEALS AGE DIFFERENCES, PROLIFERATIVE DIVERSITY, IDENTIFIES NOVEL TROPISM, AND ANTI-VIRAL RESPONSE

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Respiratory Syncytial Virus (RSV) is the leading cause for infant hospitalization across the globe. Age is a significant factor that contributes to the severity of infection in young children. RSV primarily infects the ciliated cells and induces mucus hypersecretion. Yet it is unclear how the ciliary cells become dysfunctional and result in deficient mucociliary clearance with excess mucous production. Better understanding of RSV infection at the cellular level is needed for development of effective therapeutic interventions. To investigate the age difference and comprehensively understand gene signatures associated with RSV infection, we performed single-cell transcriptomic analysis of adult and pediatric human nose organoids (HNOs) infected with RSV. Our analysis revealed a significant difference in transcriptomic signature associated with cellular differentiation and proliferative pathways between the adult and pediatric HNOs. Moreover, we found a distinct innate immune response to RSV infection, with pediatric HNO revealing a lower and dysregulated response. Through sub-clustering, we identified that primary ciliary cells but not the motile ciliary cells being more susceptible to RSV infection. Intriguingly and unexpectedly, we found that in the pediatric more than in the adult HNO RSV infects novel airway cells including basal cells, and ionocytes/tuft cells as demonstrated by increased RSV-gene counts and interferon-related pathways. Together, our study provides the first HNO cell atlas dissecting the heterogeneity of RSV infection in airway epithelium between adult vs. pediatric HNOs and identifying novel cell types that are susceptible to RSV infection, which altogether provides a key resource for research on RSV therapeutics and vaccines.

Abstract category: Virology & Immunology

Keywords: adult, pediatric, cilia, tropism, sc-RNA-seq, basal cells, ionocytes, differentiation, proliferation

Conflict of Interest: None declared

CHARACTERIZATION OF THE ANTIBODY BINDING AND NEUTRALIZATION RESPONSE IN INFANTS FOLLOWING INFECTION WITH RESPIRATORY SYNCYTIAL VIRUS (RSV)

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RSV infection is a leading cause of lower respiratory infections in children less than 2 years of age globally. We characterized the anti-RSV antibody responses in infants with PCR-confirmed RSV infections from a multi-country prospective influenza and RSV in infants study (IRIS). We enrolled 1129 infants <1 year of age from sites in Albania, Jordan, Nicaragua, and the Philippines during 2015-2017. Infant sera were collected at acute and convalescent time-points from which anti-RSV antibody titers to whole virus (WV) and prefusion-F and G proteins were evaluated by ELISA in 488 samples (244 pairs). A subset of 156 samples were tested for microneutralization (MN) titers against RSV-A2. In acute specimens, younger infants (<6 months) displayed higher IgG antibody titer to all the antigens as compared to older infants (6 months to 1 year) likely reflective of the presence of maternal antibodies. Conversely, convalescent sera antibody titers were not different by age group, but lower avidity was observed in older infants, demonstrating the response to a primary infection. Among the sera tested for MN titers, majority of the specimens (65/79) at the acute time-point had no detectable titers, most with neutralizing titers (11/13) were less than 6 months of age. MN titers increased in convalescent specimens with approximately half demonstrating neutralizing titers (42/79). Binding antibodies to RSV are detected in infants following confirmed RSV infection; however, not all infants develop neutralizing antibodies upon primary infection with RSV.

Abstract category: Virology & Immunology

Keywords: Respiratory Syncytial Virus, RSV, Immune response, Binding antibody, Neutralizing antibody, Multi-country, IRIS study

Conflict of Interest: None declared
CLINICAL PERFORMANCE EVALUATION OF TILING AMPICLON PANELS FOR WHOLE GENOME SEQUENCING OF RESPIRATORY SYNCYTIAL VIRUS (RSV-A AND RSV-B)

B. Ethan Nunley (1), Amelia Weixler (1), Seffir T. Wendm (1), Geon Kim (1), Hong Xie (1), Jaydee Sereewit (1), Pooneh Hajian (1), Margaret G. Mills (1), Carter McCormick (1), Jenolee Gov (1), Aliny Perez (1), Rebecca Dewar (3), Goncalo Fernandes (3), Kate E. Templeton (3), Daniel Maloney (3), Alexander L. Greninger (1,2), Pavitra Roychoudhury (1,2)

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Presenting author: Pavitra Roychoudhury

Introduction: Accurate genomic characterization of RSV is crucial for studies of epidemiology and viral evolution, and essential for monitoring of potential escape from newly authorized vaccines and antivirals. Whole genome tiling amplicon panels have offered a cost-effective and efficient approach for viral genomic surveillance, most notably SARS-CoV-2. We performed clinical validation of amplicon panels for whole genome sequencing (WGS) of RSV-A and RSV-B.

Methods: The ARTIC RSV primer scheme designed against global RSV-A/B sequences from 2019-2021 was adapted for use with the Illumina COVIDseq protocol, enabling high-throughput, automated library preparation. We determined assay sensitivity, specificity, breadth of genome recovery, accuracy, precision, and limit of detection of minor alleles using remnant clinical specimens and culture isolates. We developed a custom bioinformatic pipeline for genome assembly and variant calling, and established QC and genome acceptability criteria for consistent evaluation across runs.

Results: High quality genomes (>500X whole genome coverage, >1000X coverage of fusion gene, <5% ambiguous bases) were recovered from samples with Ct ≤ 30. No genomes were recovered from RSV-negative samples and no cross-reactivity seen with other respiratory viruses. We correctly identified minor variants in sample mixtures of 5:95 and higher to capture intra-host variation (Figure 1). The assay showed high accuracy when compared against Sanger, shotgun metagenomic, and hybridization capture-based sequencing with high repeatability and reproducibility (>99% pairwise identity between replicates).

Conclusion: Our data shows the utility of amplicon panels for surveillance and clinical testing. This assay is currently being used to generate FDA-reportable data for RSV clinical trials.

Abstract category: Virology & Immunology
Keywords: sequencing; RSV; clinical trials; validation; genomics; intra-host variation
Conflict of Interest: None declared

P2X7 RECEPTOR EXPRESSING FOLLICULAR T HELPER CELLS DURING PEDIATRIC RSV INFECTION


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Presenting author: Constanza Russo

Background: Respiratory syncytial virus (RSV) infection represents a major burden in infants. Follicular helper cells (Tfh) play a critical role in the generation of protective antibodies. The purinergic receptor P2X7R has been recognized as a signature gene of Tfh cells. The expression and function of P2X7R on Tfh cells from RSV-infected infants have not been analyzed previously.

Aims: 1) to characterize the circulating Tfh cells (cTfh) in non-severe and severe RSV children; 2) to quantify ATP levels in serum and nasopharyngeal aspirates (NPA); 3) to analyze the expression of P2X7R; 4) to explore the biologic response of cTfh cells upon incubation with ATP (P2X7R agonist) and KN-62 (P2X7R antagonist).

Results: We observed a decreased frequency of cTfh cells in non-severe (n=30) and severe RSV-infected infants (n=16) compared with controls (n=15, p<0.0001). Severe RSV-infected children also presented with higher levels of ATP in plasma and NPA in comparison with non-severe (p<0.05) and controls (p<0.01). Interestingly, severe children displayed an increased frequency of P2X7R+Tfh cells related to non-severe (p<0.05) and controls (p<0.01). Moreover, ATP exposure decreased the proliferative response (p<0.001, n=12) and induced apoptosis of cTfh (p<0.0001, n=16), which were significantly restored in the presence of P2X7R antagonist. Importantly, ATP also reduced IL-21 production by cTfh cells (p<0.001, n=12).

Conclusions: RSV infection induces up-regulation of P2X7 receptor in Tfh cells modifying their function. Levels of ATP in plasma and NPA could be useful biomarkers of disease severity. A better understanding of the Tfh cells in young infants is critical for vaccine development. Abstract category: Virology & Immunology
Keywords: RSV; Tfh; ATP; P2X7R
Conflict of Interest: None declared
RESPIRATORY SYNCYTIAL VIRUS OUTBREAK IN NEONATAL INTENSIVE CARE AT TWO NAIROBI HEALTH FACILITIES: CASE REPORT

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Presenting author: Vincent Ruttoh

Background: Respiratory Syncytial Virus (RSV) outbreaks in Neonatal Intensive Care Unit can lead to unfavourable outcomes, including respiratory distress and death in premature infants (1). An acute respiratory disease outbreak of unknown aetiology was reported at two primary healthcare facilities affecting the newborn units. The Acute Respiratory Infections Unit at the Kenya Medical Research Institute was requested for support in identifying the causative agent.

Objective: To describe the outbreak of acute respiratory infection among neonates at two Nairobi health facilities.

Design: Descriptive case series.

Setting: Pumwani Maternity Hospital and Mama Lucy Kibaki Hospital Kenya.

Results: In Pumwani Maternity Hospital, 8 out of 9 patients tested positive for RSV, indicating a high infection rate of 88.9%. Similarly, in Mama Lucy Kibaki Hospital, 11 out of 12 patients were positive for RSV, resulting in an infection rate of 91.7%. Out of the 11 RSV-positive samples analyzed from Mama Lucy Hospital, 4 cases (36.4%) were found to have coinfections with one or more ARI pathogens, namely; SARS-CoV-2, influenza A virus, human rhinovirus, and parainfluenza.

Discussion: The high prevalence of RSV infection observed underscores the vulnerability of neonates to RSV and emphasizes the urgent need for stringent infection control practices, including timely diagnosis, isolation, and adherence to preventive measures.

Conclusion: This highlights the importance of prompt and coordinated response to acute respiratory disease outbreaks in healthcare settings.

References:

Abstract category: Virology & Immunology
Keywords: RSV (Respiratory Syncytial Virus); Neonatal Intensive Care Unit; Acute respiratory infection; Coinfections

Conflict of Interest: None declared

COMPREHENSIVE ASSESSMENT OF PATHOGENESIS PATHWAYS IN RSV INFECTION: TRANSCRIPTIONAL VALIDATION IN RSV PATIENTS

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Presenting author: Vahid Salimi

Background: Respiratory syncytial virus (RSV) causes severe respiratory infections, leading to significant mortality, especially in infants under six months. RSV alters host gene transcription and translation, affecting protein function and gene expression patterns. Studying host transcription during infection helps understand host-pathogen interactions and disease prognosis. This study analyzed gene expression profiles of children infected with RSV using the GEO database.

Method: MetaMA was employed to identify significant differentially expressed genes (DEGs). Functional annotation of DEGs utilized GO and KEGG pathways. A PPI network was constructed in Cytoscape. Real-time PCR validated IFI27, IDO1, GZMB, OLR1, CXCL10, and FCGR1A expression in RSV inpatients and outpatients. Nasopharyngeal swabs from 36 children under two years old with RSV infection were collected for validation tests at Bahrami Children's Hospital.

Result: The expression of OLR1, IFI27, and IDO1 genes showed a significant increase in the inpatient group compared to the outpatient group. However, CXCL10 and FCGR1A were upregulated in inpatients compared to outpatients but did not reach statistical significance.

Discussion: This study examined the expression of OLR1, IFI27, and IDO1 genes in RSV-infected patients to identify potential biomarkers for disease severity prediction. Enrichment analysis revealed upregulated genes involved in immune response pathways, cytokine signaling, chemokine response, and virus life cycle regulation. Downregulated genes were associated with primary cilium development and cell motility. Protein-protein interaction analysis identified IFIT3, RSAD2, and MX1 as hub genes. These findings highlight the importance of immune response genes in RSV pathogenesis and suggest their potential role in modulating the immune system.

Abstract category: Virology & Immunology
Keywords: RSV, gene transcription, gene expression, GEO, immune response, Iran

Conflict of Interest: None declared
**FUNCTIONAL IMPLICATIONS OF F SEQUENCE VARIABILITY: A COMPARATIVE ANALYSIS USING CONTEMPORARY RSV ISOLATES**

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**Background:** The Respiratory Syncytial Virus (RSV) has a significant impact on health care systems worldwide. Therapeutic options against RSV are limited, but multiple new prophylactics have recently been licensed. The RSV fusion (F) glycoprotein is a crucial target in vaccine research. Currently, an adequate description of the translation of variability in the RSV F-sequence to phenotypical in vitro differences is lacking.

**Methods:** We analyzed full F-sequences of 105 contemporary RSV isolates, gathered from children presenting with a LRTI at a tertiary hospital. Based on the presence of SNPs in the different F antigenic sites, a panel of 20 isolates was chosen for extensive functional characterization.

**Results:** Although the overall diversity of RSV F is low, RSV-A strains show considerably more variation, mainly in SP, p27 and HRB, compared to RSV-B. Moreover, mAb binding sites seem highly conserved, resulting in limited differences in sensitivity to neutralization by these mAbs, which is highest for site 0 and site V mAbs. Despite discrete differences in growth kinetics and fusion capacity, no consistent correlation can be made between F-sequence and a certain in vitro phenotype.

**Conclusions:** Our analysis of 105 RSV strains shows that phenotypic and genonic variability among contemporary clinical RSV isolates is limited, but noticeable. A clear correlation between SNP's in the F-gene and a certain functional phenotype remains, however, elusive. The recent availability of new prophylactics targeting this RSV F protein corroborates the importance of RSV surveillance to promptly identify changes in the RSV F-sequence, including potential escape mutants.

**Abstract category:** Virology & Immunology

**Conflict of Interest:** None declared

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**EXPLORING THE LINK BETWEEN SERUM METABOLITES OF AMINO ACIDS AND LIPID METABOLISM IN RSV PATIENTS: IMPLICATIONS FOR DISEASE SEVERITY**

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**Presenting author:** Masoumeh Tavakoli-Yaraki

**Background:** Our understanding of how Respiratory syncytial virus (RSV) impact clinical outcomes through downstream molecules remains limited. Metabolomics aims to bridge this knowledge gap by extensively profiling functional metabolites and is perused in the current study

**Method:** The serum metabolome of 18 patients with RSV infection was analyzed using electrospray ionization tandem mass spectrometry (ESI-MS/MS). This technique allows for quantitative profiling of 16 main amino acids and 36 derivatives of carnitine, as well as clinical data, medical history, and biochemical data of the patients were collected.

**Result:** Severe cases exhibited distinct differences in serum metabolome profiles compared to non-severe controls. Specifically, in the lipid metabolome, significant decreases in free carnitine, acetyl-carnitine, and octadecenoylcarnitine were observed among patients, with a more pronounced attenuation observed in hospitalized patients. These reductions were associated with an increased risk of adverse outcomes. Additionally, elevated levels of alanine, leucine, phenylalanine, serine, and tryptophan, along with decreased levels of arginine, were identified in patients experiencing severe clinical symptoms and exhibiting high CRP levels.

**Discussion:** Our findings suggest that specific metabolites involved in lipid and amino acid metabolism play a role in the morbidity associated with RSV infection that may be influenced by inflammatory mediators and immune cells, which can affect protein breakdown and synthesis during inflammation. The serum metabolome signature of patients appears to be influenced by the interplay between the virus, the host’s systemic immune response, and the pathobiology of bronchiolitis and may provide valuable evidence for clinicians in the management and development of preventive strategies for RSV.

**Abstract category:** Virology & Immunology

**Keywords:** RSV, Metabolomics, tandem mass spectrometry, amino acids, carnitine, Iran

**Conflict of Interest:** None declared

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**EPIGENOMIC APPROACH TO STUDY POTENTIAL BIOMARKERS OF RSV DISEASE SEVERITY IN SALIVA OF YOUNG CHILDREN: A PILOT STUDY**

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**Presenting author:** Sandra Viz Lasheras

Respiratory Syncytial Virus (RSV) is the principal cause of acute lower respiratory infections in young children, associated with morbidity and mortality in childhood. The disease may progress to the lower airways, causing respiratory distress, leading to hospital admission and supportive therapy. The main objective is to investigate host molecular factors associated with severity of RSV infection using an epigenomics approach and non-invasive samples. Sixteen infants admitted to

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the hospital for an RSV infection were recruited for the study. Eight had a severe infection characterized by acute bronchiolitis, requiring pediatric intensive care unit admission and mechanical ventilation. Eight infants presented mild to moderate symptoms. DNA was extracted from saliva samples and analyzed with Illumina EPIC BeadChip.

A linear model was used to examine the association between DNA methylation and RSV disease severity. The analysis identified differentially methylated regions (DMRs) that could distinguish infants with severe infection from those with only mild to moderate symptoms. DMRs were identified in ZBTB38 and TRIM6 genes. Gene set analysis revealed significant enrichment for pathways involved in the expression and translocation of olfactory receptors, olfactory signaling and transduction, and biological processes involved in olfactory receptor activity. This study suggests that DNA methylation may play a role in the severity of RSV disease in the saliva of young children.

**Abstract category:** Virology & Immunology  
**Keywords:** RSV, Epigenetics, saliva  
**Conflict of Interest:** None declared

## BURDEN OF RESPIRATORY SYNCYTIAL VIRUS DISEASES AMONG UNDER 5 CHILDREN IN SUB-SAHARAN AFRICA: A SYSTEMATIC REVIEW AND META-ANALYSIS

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**Background:** A better knowledge of the true role of RSV in pediatric ALRIs is required in sub-Saharan Africa to help the preventive efforts. Therefore, we conducted a systematic review and meta-analysis of case–control studies to estimate the etiological role of RSV to ALRIs in under 5 years children in sub-Saharan Africa.

**Methods:** This study was done according to PRISMA guidelines. PubMed, EMBASE, SCOPUS, Web of Sciences databases, and Google Scholar were used to retrieve articles. The results of all the included studies were standardized to odds ratios (ORs) with accompanying 95% confidence intervals (95% CIs) and the pooled estimates of ORs, attributable fraction among the exposed (AFE), and population attributable fraction (PAF) were reported. The heterogeneity was assessed using Cochrane chi-square (I^2) statistics.

**Result:** A total of 6,200 cases and 4,986 controls from 14 articles that fulfilled the inclusion criteria were included. The pooled prevalence of RSV among cases and controls was 23.52% [95% CI (20.68-26.47)] and 4.33% [95% CI (3.11-5.73)], respectively. The pooled OR is 7.04 [95% CI (4.41-11.24)], which indicated a significant association between RSV and ALRI. Among ALRIs cases positive for RSV, the proportion of disease that was not attributable to the background rate (AFE) was 85.8% [95% CI (77.3-91.1)]. The fraction of ALRIs children that can be attributed to RSV (PAF) was 20.2% [95% CI (16-24.1)].

**Conclusion:** This study showed clear associations between RSV and ALRI hospitalization in young children in sub-Saharan Africa indicating the need for prophylactic measures against RSV in this age group.

**Abstract category:** Virology & Immunology  
**Keywords:** Respiratory syncytial virus, ALRIs, children, Naso/Oropharyngeal, sub-Saharan Africa  
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