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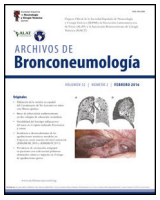

Editorial

Why RSV Infection Matter in Older Adults? The Urgent Need for Vaccination

Respiratory syncytial virus (RSV) is a major cause of lower respiratory tract infections in older adults.[1] Data from a systematic review and meta-analysis in the US reported annual RSV incidence per 100,000 adults aged 65 years and older: 178 hospitalizations, 133 emergency room admissions and 1.519 outpatient visits. These figures reflect the huge impact of RSV on older adults.[2] Results from a prospective study that analyzed 2.865 cases of severe pneumonia admitted to the intensive care unit (ICU)—and compared 92 cases of severe pneumonia caused by RSV with 163 influenza virus pneumonia[3]—showed that the incidence of pneumonia caused by RSV was lower than that caused by influenza virus (3.4% vs 8.1%). However, in hospital-acquired pneumonia (HAP), the incidence was slightly higher (3.8% vs 3.5%). A higher proportion of immunocompromised patients presented pneumonia caused by RSV (58% vs. 34%); there was also a higher proportion of HAP (48% vs. 41%). The 90-day mortality was similar between RSV and influenza groups (39% vs. 41%). A population-based cohort study from Spain identified 544 RSV hospitalizations in 642,622 person-years, representing an average annual rate of 84.7/100.000. The groups with a higher risk were those residing in nursing homes or those living with functional dependence, hematologic cancer, COPD, asthma, cardiovascular disease, severe obesity, diabetes, or chronic kidney disease.[4] All these results showed the impact of RSV in older adults.

Furthermore, an experimental study on human lung cells showed the formation of hybrid viral particles (HVPs) during co-infection of RSV and influenza virus. These HVPs incorporate components from both viruses (glycoproteins from RSV and ribonucleoproteins from influenza), allowing them to evade influenza-targeted antibodies and infect cells lacking influenza receptors. This observation suggests a novel mechanism for enhanced viral pathogenesis, immune evasion, and expanded tropism.[5] Additionally, another study showed that asymptomatic RSV infections increase susceptibility to *Streptococcus pneumoniae* colonization. In the study, RSV-infected individuals had a higher pneumococcal colonization rate and density compared to those with either other respiratory viruses or no viral infection, highlighting the potential of RSV in facilitating bacterial colonization and transmission.[6] These findings confirm that up to 29% of adults hospitalized with RSV pneumonia are at increased risk of bacterial co-infection, including common pathogens like *S. pneumoniae*, *Haemophilus influenzae*, and *Staphylococcus aureus*.[1] These results underscore the importance of preventing viral infections, especially RSV.

It is also important to remember serious complications related to severe viral RSV infections. Results from a multicenter study from China that included 915 adult patients with viral pneumonia reported viral sepsis in 40% of the cohort. This is similar to the percentage of sepsis cases caused by influenza virus and non-influenza virus.[7] In the study, RSV was identified in 9% of the population. Another study from Spain analyzing data from 4.028 patients with CAP (mean age 66 years)[8] reported viral sepsis in 3% of those admitted with CAP diagnosis; 19% of those in ICU; and 61% of those with a viral sepsis diagnosis. RSV was reported in 10% of patients with viral sepsis belonging to the study. Severe RSV infections can also cause cardiovascular complications, such as acute coronary syndrome, worsening heart failure, and arrhythmias; it has been reported between 10 and 22% of the cases.[1] A study of 6.248 hospitalized patients aged ≥50 years (mean age 72.7 years)[9] reported that 22% presented acute cardiac events, including acute heart failure (16%) and acute ischemic heart disease (8%). Patients with underlying cardiovascular disease had a significantly higher risk of acute cardiac events. Acute cardiac events increased the risk of ICU admission (26% vs. 17%) and in-hospital mortality (8% vs. 4%). These results showed that 1 in 4 adults hospitalized with RSV had an acute cardiac event, with heart failure being the most frequent.

Three vaccines have been approved by the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) against RSV: RSVpreF (Abrysvo™ by Pfizer), RSVPreF3 OA (Arexvy™ by GSK), and mRNA-1345 (mRESVIA™ by Moderna). RSVPreF3 OA has demonstrated an efficacy of 82.6% for RSV-associated lower respiratory tract infection (LRTI) and 94.1% for severe RSV-associated LRTI in a phase 3 clinical trial of 24,966 adults aged ≥60 years (similar efficacy for RSV A and B).[10] In adults ≥60 years, RSVPreF3 OA showed a 67.2% efficacy rate in preventing RSV-related LRTI with a single dose and 78.8% for severe LRTI, with similar results after revaccination.[11]

The RSVpreF vaccine showed high efficacy in the phase 3 RENOIR trial, which had 17.215 adults aged ≥ 60 enrolled. It was 66.7% effective against RSV-related LRTI with ≥2 symptoms, and 85.7% effective against severe disease (≥3 symptoms). The vaccine provided 88.9% protection after one dose in the first RSV season and 78.6% in the second.[12,13]

Neutralizing antibody levels increased by ~12-fold one month post-vaccination for both RSV-A and RSV-B; the elevated levels were maintained by the second season. Strong immune responses were noted among all age groups (60–≥80) and in the presence

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Table 1
The Burden of RSV Infection in Adult Populations.

Author/Year/Country	Study/Population	Results
McLaughlin et al., 2022, US	Systemic review and meta-analysis/14 studies, all based on NP or nasal swab RT-PCR testing alone.	**RSV Incidence per 100,000 adults (≥65 years):** • Hospitalizations: 178 cases • Emergency room admissions: 133 cases • Outpatient visits: 1519 cases
Kim et al., 2023, Korea	Prospective, 2865 severe pneumonia, compared 92 severe RSV pneumonia with 163 severe influenza pneumonia cases	**Incidence:** • RSV pneumonia: 3.4% (lower than influenza: 8.1%). • RSV hospital-acquired pneumonia (HAP): 3.8% (slightly higher than influenza: 3.5%) **Immunocompromised patients:** • RSV pneumonia: 58% vs. Influenza: 34%. • RSV-related HAP: 48% vs. Influenza: 41%. **90-Day mortality:** • RSV: 39% vs. Influenza: 41% (similar rates)
Vera-Punzano et al., 2025, Spain	Population cohort base-study; 642,622 adults ≥60 years old (2016–2020)	544 RSV hospitalizations over 642,622 person-years Annual hospitalization rate: 84.7 per 100,000 **High-risk groups:** • Nursing home residents. • Individuals with functional dependence. • Patients with hematologic cancer, COPD, asthma, cardiovascular disease, severe obesity, diabetes, or chronic kidney disease.
Mitsi et al., 2024, UK	Experimental human intranasal pneumococcal challenge	Volunteers with asymptomatic RSV infection exposed to intranasal pneumococcus serotype 6B had a higher colonization rate (88%) compared to Parainfluenza virus (71%) and Rhinovirus (66%)
Cilloniz et al., 2019, Spain	Retrospective study, 4024 hospitalized adults with CAP	**Viral sepsis:** • 3% of patients with diagnosis of CAP • 19% of ICU-admitted patients. • 61% of those with defined microbiological diagnosis. RSV was found in 10% of patients with viral sepsis.
Woodruff et al., 2024, US	Cross-sectional study, 6248 hospitalized adults	**Cardiac events:** 22% of patients experienced acute cardiac events: • 16% had acute heart failure • 8% had acute ischemic heart disease. Higher risk in patients with underlying cardiovascular disease Acute cardiac events increased the risk of: ICU admission: 26% vs. 17%. In-hospital mortality: 8% vs. 4%.

of chronic conditions, with GMFRs of 11.4–14.4. The vaccine had an acceptable safety profile and the overall frequency of adverse events was comparable between the groups (10.8% vs. 10.5% in the vaccine and placebo groups, respectively).[14]

Finally, a real-world study in the UK and Europe reported a 62.1% (95% CI 35 0–79 8) reduction in RSV-related hospitalizations among vaccinated adults (74–79 years). This is consistent with the RENOIR trial efficacy rate (85.7%) and US effectiveness data (80%), confirming strong population-level protection.[15]

The mRNA-1345 vaccine was approved based on the ConquerRSV randomized control trial (RCT) that included 35.064 adults aged ≥60 years. Vaccine efficacy was 68.4% against RSV-associated acute respiratory infection, though efficacy was higher against RSV A compared with RSV B (78.5% vs. 51.7%).[12]

Experts have identified critical priorities that include burden assessment, diagnostics, surveillance, planning, and coverage.[16] Spain has set an example in infant immunization[16] and recommends adult vaccination beginning at the age of 60, prioritizing high-risk groups. Healthcare personnel should also be vaccinated given their higher risk of RSV infection and transmission, with timing of vaccination based on local RSV seasonality.[1] To simplify the vaccination process, co-administrations of vaccines are done. This improves vaccine uptake by reducing the number of healthcare visits, which, in turn, ensures timely protection against multiple pathogens and an optimization of resources.[1] A recent review article found that co-administrations of vaccines are safe for all combinations assessed by the authors (influenza plus COVID, influenza plus RSV, influenza plus other vaccines), with most adverse events being mild to moderate and short-lived.[17]

Despite the significant impact of RSV on the older adult population (Table 1), the true burden of RSV infection remains uncertain due to underreporting and the lack of systematic testing. It is crucial to establish extensive RSV vaccination programs for older high-risk adults and increase awareness among healthcare professionals.

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Conflicts of Interest

The authors declare no conflicts of interest.

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