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Severity of respiratory syncytial virus compared with SARS-CoV-2 and influenza among hospitalised adults ≥65 years

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SUMMARY

Introduction: Our aim was to estimate the risk of pneumonia, admission to intensive care unit (ICU) or death in individuals ≥65 years old admitted to hospital with RSV, compared to influenza or COVID-19.
Methods: We included hospitalised patients from Severe Acute Respiratory Infection Surveillance in Spain between 2021–2024, aged ≥65 years, laboratory confirmed for RSV, influenza or SARS-CoV-2. Using a binomial regression with logarithmic link, we estimated the relative risk (RR) of pneumonia, ICU admission

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Pneumonia
Mortality
Vaccination

and in-hospital mortality, in patients with RSV compared to influenza or SARS-CoV-2, adjusting for age, sex, season and comorbidities. We stratified the estimates by vaccination status for influenza or SARS-CoV2.
Results: Among patients unvaccinated for influenza or SARS-CoV-2, those with RSV had similar or lower risk of pneumonia [vs. influenza: RR= 0.91 (95% Confidence Interval: 0.72–1.16); vs. SARS-CoV-2: 0.81 (0.67–0.98)], ICU admission [vs. influenza: 0.93 (0.41–2.08); vs. SARS-CoV-2: 1.10 (0.61–1.99)] and mortality [vs. influenza: 0.64 (0.32–1.28); vs. SARS-CoV-2: 0.56 (0.30–1.04)]. Among the vaccinated, results were largely similar except for a higher risk of ICU admission with RSV [vs. influenza: 2.13(1.16–3.89); vs. SARS-CoV-2: 1.83 (1.02–3.28)]
Conclusions: RSV presented similar or lower intrinsic severity than influenza or SARS-CoV2. Among vaccinated patients, RSV was associated to higher ICU-admission, suggesting the potential for preventive RSV vaccination.

Introduction

Respiratory syncytial virus (RSV) is frequently regarded as a paediatric infection, as hospitalisation rates are highest in children under 5 years of age. However, the burden of disease attributable to RSV is also considerably high among the elderly. Despite some heterogeneity across countries,[1] it is estimated that around 158,000 adults ≥18 years of age are hospitalised annually due to RSV in the European Union (EU); of these, 92% are ≥65-years-olds.[2] In Spain, individuals aged ≧65 years are an estimated 36% of all hospitalisations due to RSV and 78% of RSV hospitalisations among ≥15 year-olds.[3]

Prior to the start of the SARS-CoV-2 pandemic in 2020, the clinical severity of patients admitted due to RSV infection was compared to that of seasonal influenza, with mixed results. Some studies found a higher incidence of pneumonia, intensive care unit (ICU) admission rates and longer hospital stays among RSV patients[4,5] as well as an increased all-cause mortality, in-hospital or up to one year after discharge.[6,7] On the contrary, other studies found a greater risk of hospitalisation, need for invasive mechanical ventilation (IMV) and death in those with influenza A (H1N1) infection.[8,9]

The circulation and the disease burden of both RSV and influenza were deeply affected by the onset of the SARS-CoV2 pandemic. In the 2020–21 season, circulation of influenza and RSV decreased drastically, coinciding with widespread and high intensity circulation of SARS-CoV-2.[10] In the spring of 2021 RSV reappeared with an unprecedented late epidemic,[11] in parallel with a decrease in the pandemic stringent measures and an increase in SARS-CoV-2population immunity.[12–15] In the 2022–23 season, RSV and influenza have completely restored their usual pre-pandemic seasonal presentation and circulation intensity.[16]

In the summer of 2023, the European Medicines Agency (EMA) authorised two vaccines against RSV: Arexvy® (GSK) indicated for adults ≥60 years old; and Abrysvo® (Pfizer), indicated for ≥60 years old and during pregnancy.[17,18] The Center for Disease Control and Prevention (CDC) recommends RSV vaccination in population 60 years of age or older through joint physician-patient decision-making and prioritising highest risk persons.[19] In Spain, recommendations and/or vaccination measures for RSV in older people have not yet been implemented.

The recent authorisation of RSV vaccines for the elderly, with potential implementation as population-wide vaccinations, makes it relevant to characterise the severity of RSV in relation to other co-circulating vaccine-preventable respiratory infections, such as influenza and SARS-CoV-2. Our main objective was to estimate the risk of pneumonia, admission to ICU or in-hospital death, in people ≥65 years of age admitted to hospital due to RSV infection, compared to those admitted due to influenza or SARS-CoV-2.

Methods

Study design and setting

A retrospective cohort study was conducted using data from the Spanish Acute Respiratory Infection Surveillance System (SiVIRA). In 2020, the Spanish Sentinel Influenza Surveillance System was adapted into an integrated system for the surveillance of acute respiratory infections (ARI) in Primary Care settings and severe acute respiratory infections (SARI) in hospital settings. Among the main objectives of SiVIRA are to monitor the impact and severity of RSV, influenza and SARS-CoV2 viruses and the assessment of the effectiveness and impact of prevention and control measures.[20]

Within SiVIRA, SARI surveillance consists on weekly identification of patients admitted to any of up to 38 sentinel hospitals in 17 Spain regions (autonomous communities), with variations across seasons), with symptoms of ARI (cough, shortness of breath, coryza or sore throat and clinical judgement of an infection) with acute onset in the last 10 days and who required hospitalisation for ≥24 h.[20] In contrast to the European Centre for Disease Prevention and Control (ECDC) case definition,[21] fever is not a requirement. SARI case identification is frequently achieved by extraction of ICD-10 diagnostic codes or by identification of key words in hospital clinical records, followed by manual revision. Those admitted on pre-defined week-days are systematically selected for the collection of a respiratory sample (preferably within 7 days after symptoms onset) for RSV, influenza and SARS-CoV-2 laboratory testing, as well as for collection of in-depth clinical, epidemiological and vaccine information. Outcomes of infection, including pneumonia, ICU admission and death from any cause, are assessed up to in-hospital decease or discharge.

For the purpose of this study, between October 2021 (week 40/2021) and May 2024 (week 20/2024), adults aged ≥65 years admitted to sentinel hospitals and systematically selected for laboratory testing and in-depth data collection were eligible. We included all patients who received a positive RSV, influenza or SARS-CoV-2 laboratory test result. Patients with co-infections by any of these three viruses were excluded, while laboratory results for other pathogens, including bacteria, were not systematically collected and were not used as exclusion criteria.

Data analysis

We estimated the risk of pneumonia, ICU admission and/or death during the hospital stay, as the proportion with each outcome, separately for patients admitted due to RSV, influenza or SARS-CoV-2 infection. Patients from regions with ≥10% missing values in a given outcome were excluded for the respective outcome-specific analysis. The relative risk (RR; and 95% confidence interval, 95%CI) of each

outcome was estimated by comparing the risk among those admitted due to RSV, compared to the risk among: i) those admitted due to influenza, or; ii) those admitted due to SARS-CoV-2. Binomial regression with a logarithmic link was used to model the RR.

We adjusted the RR estimates by age (continuous), gender, respiratory season (weeks 40/2021 to 39/2022; 40/2022 to 39/2023; and 40/2023 to 20/2024) and risk factors. A composite variable was created for risk factors with three categories: low risk (no comorbidities, hypertension, metabolic disease including diabetes, obesity and/or smoking habit), intermediate risk (chronic respiratory disease, cardiovascular disease, kidney disease, liver disease and/or other non-specified chronic diseases), and high risk (immunosuppression). Obesity was defined as Body Mass Index ≥30.

Because vaccination for influenza and SARS-CoV-2 is known to affect the disease severity of influenza infection and SARS-CoV-2, respectively,[22,23] we considered that the RR of severe outcomes for RSV compared to these viruses might be different among vaccinated or unvaccinated patients. Therefore, we considered vaccination as a potential effect modifier. We stratified the model to estimate RR of severe outcomes for RSV vs. influenza by influenza vaccination status, defined as vaccination in the current respiratory season. We stratified the model to estimate RR of severe outcomes for RSV vs. SARS-CoV-2 by SARS-CoV-2 vaccination status, defined as any COVID-19 vaccine dose received in the previous 6 months.

Results

The number of hospitals participating in the SiVIRA network increased from 15 in season 2021–22, to 23 in 2023–24 and 36 in 2023–24, with up to 38 hospitals participating at some point in time. The average number of patients included in the study per season was 67.2 (range 2 to 298). Of 20,185 patients aged ≥65 years included in surveillance, 6546 had a positive test result for influenza, SARS-CoV-2 or RSV, of which 132 were excluded due to co-infection.

Of the 6546 patients included in the study, 12.7% (N = 829) were diagnosed with RSV, 25.3% (N = 1659) had influenza, and 62.0% (N = 4058) had SARS-CoV-2. Cases appeared simultaneously in time, particularly during the last two seasons in the study, 2022–23 and 2023–24 (Fig. 1). The characteristics of patients admitted with RSV, influenza or SARS-CoV-2 differed by sex (proportion of females 61.9%. 52.1% and 44.1%, respectively), age (median 83, 81 and 83 years, respectively) and presence of comorbidities (low risk: 9.5%, 13.4% and 10.9%; intermediate risk: 80.7%, 78.3% and 75.6%; and high risk: 9.7%, 8.3% and 13.5%, for RSV, influenza and SARS-CoV-2, respectively) (Table 1). Of the study sample 59.6% (3901/6546) were vaccinated against influenza in the current season, 37.9% (2481/6546) were vaccinated against SARS-CoV-2 <6 months ago and 33.1% (2167/6546) had received both vaccinations.

The proportion of patients diagnosed with pneumonia was 28% for RSV, 31% for influenza and 46% for SARS-CoV-2. The adjusted overall risk of pneumonia was not different for RSV compared to influenza (RR= 0.92; 95% CI: 0.80–1.06; Table 2) but was 24% lower compared to SARS-CoV-2 (RR: 0.76; 95% CI: 0.67–0.87; Table 3). The lower risk for RSV compared to SARS-CoV-2 was observed similarly for unvaccinated and vaccinated patients: Adjusted risk of pneumonia for RSV vs. SARS-CoV-2 was 19% lower (RR= 0.81; 95% CI: 0.67–0.98) in unvaccinated patients and 27% lower (RR= 0.73; 95% CI: 0.62–0.86) among patients vaccinated for SARS-CoV-2 <6 months ago (Fig. 2).

The proportion of patients requiring ICU admission was 3.8% for RSV, 3.1% for influenza and 3.6% for SARS-CoV-2. The adjusted overall risk of ICU admission was 43% higher for RSV compared to influenza (RR= 1.43; 95% CI: 0.91–2.25; Table 2) and 37% higher compared to SARS-CoV-2 (RR: 1.37; 95% CI: 0.90–2.08; Table 3), though results had wide confidence intervals that included the null value. However, the apparent higher risk of ICU with RSV was at the expense of vaccinated patients while, among the unvaccinated, the risk of ICU admission was similar, though again with wide confidence intervals. Adjusted risk of ICU with RSV vs. influenza was similar (RR= 0.93; 95% CI: 0.41–2.08) in unvaccinated patients and 213% higher (RR= 2.13; 95% CI: 1.16–3.89) in patients vaccinated for influenza during the current season. For RSV vs. SARS-CoV-2, risk of ICU was similar (RR= 1.10; 95% CI: 0.61–1.99) in unvaccinated patients and 83% higher (RR= 1.83; 95% CI: 1.02–3.28) among patients vaccinated for SARS-CoV-2 <6 months ago (Fig. 2).

The proportion of patients who died in-hospital was 6.3% for RSV, 8.3% for influenza and 12.8% for SARS-CoV-2. The adjusted overall risk of death was 29% lower for RSV compared to influenza (RR= 0.71; 95% CI: 0.47–1.08; Table 2) and 37% lower compared to SARS-CoV-2 (RR: 0.63; 95% CI: 0.42–0.94; Table 3). Similar results were observed for unvaccinated and vaccinated patients, though confidence intervals were wide and included the null value. Adjusted risk of death for RSV vs. influenza was 36% lower (RR= 0.64; 95% CI: 0.32–1.28) in unvaccinated patients and 24% lower (RR= 0.76; 95% CI: 0.45–1.30) in patients vaccinated for influenza during the current season. For RSV vs. SARS-CoV-2, risk of death was 44% lower (RR= 0.56; 95% CI: 0.30–1.04) in unvaccinated patients and 35% lower (RR= 0.65; 95% CI: 0.39–1.09) among patients vaccinated for SARS-CoV-2 <6 months ago (Fig. 2).

Discussion

In this longitudinal study of patients ≥65 years of age admitted to hospital with acute respiratory infection caused by RSV, influenza or SARS-CoV-2, we found that those admitted with RSV had similar or lower risk of pneumonia, ICU admission or in-hospital death compared to those admitted with influenza or SARS-CoV-2. This somewhat intrinsic severity was assessed in the group of patients unvaccinated for the respective pathogen, and indicates that, although a considerable proportion of patients with RSV experienced adverse outcomes in hospital (28% had pneumonia, 4% were admitted to ICU and 6% died), its severity was not higher compared to the other two viruses. In contrast, when restricting to patients vaccinated for influenza or SARS-CoV-2, the risk of ICU admission was much higher in those admitted with RSV, showing the protective effect of those vaccines in the most severe end of the clinical spectrum and the preventive potential for a future RSV vaccine used in the elderly.

Our results offer significant perspectives into the severity of illness and consequences among hospitalised individuals aged ≥65 years with respiratory infections triggered by RSV, influenza, and SARS-CoV-2. Previous studies among hospitalised adults ≥60 years of age in the United States of America,[4,24] have found a more severe disease for RSV compared to COVID-19 or influenza. Also, studies including adults ≥18 years of age in China, Finland, Germany and Israel, found that in-hospital complications were comparable or higher in those admitted due to RSV compared to influenza.[5–7,12] Variations in age distribution, clinical practice and lack of accounting for previous vaccination could explain the heterogeneity in the results. For example, the proportion of admissions to ICU among patients with RSV was 19% in the German study[12] and 24% in the USA[24] compared to 4% in Finland and Israel,[6] or 3.8% in our study.

Only a recent study among US hospitalised adults ≥18 years[25] has also accounted for previous vaccination for influenza or SARS-CoV-2, allowing disentangling the effects of intrinsic virus severity or of the fact of RSV being the one virus with no vaccine available to the elderly. In agreement with our results, the US study[25] found similar disease severity of RSV compared to COVID-19 and influenza among unvaccinated hospitalised patients, but higher severity among vaccinated ones. However, they found a higher risk among those with RSV for ICU admission as well as for a composite outcome of mechanical ventilation or death, while we did not find any difference in

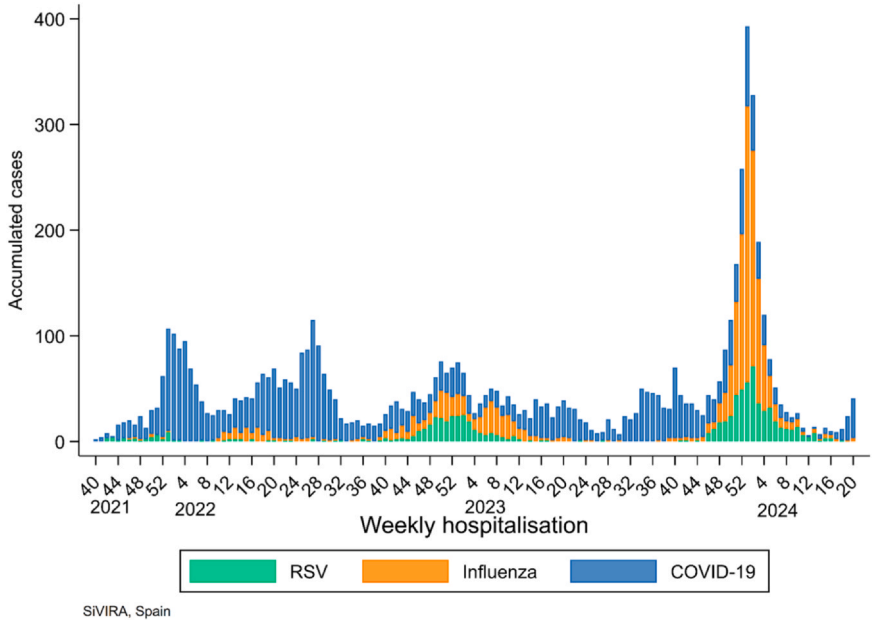

Fig. 1. Weekly number of hospital admissions due to RSV, SARS-CoV-2 or influenza virus infection in ≥65-year-olds included in the study. Spain, October 2021– May 2024.

Table 1
Characteristics of adults aged ≥65 years hospitalised with respiratory syncytial virus (RSV), SARS-CoV-2, or influenza virus infection included in the study. Spain, October 2021–May 2024.

Characteristic		Virus type						p-value
		RSV (N = 829)		Influenza (N = 1659)		SARS-CoV-2 (N = 4058)		
	Category	N	%	N	%	N	%	
Age (years)[a]	-	83.0	[75–89]	81.0	[74–88]	83.0	[76–89]	< 0.001
Sex	Female	513	61.9	865.0	52.1	1790.0	44.1	< 0.001
	Male	316	38.1	794	47.9	2266	55.9	
Cardiovascular disease	Yes	469	56.6	792	47.7	2096	51.7	< 0.001
	No	334	40.3	805	48.5	1873	46.2	
Hypertension	Yes	563	67.9	1013	61.1	2734	67.4	0.001
	No	230	27.7	567	34.2	1243	30.6	
Chronic respiratory disease (includes asthma)	Yes	386	46.6	718	43.3	1470	36.2	< 0.001
	No	387	46.7	811	48.9	2328	57.4	
Immunosuppression	Yes	81	9.8	137	8.3	548	13.5	< 0.001
	No	634	76.5	1262	76.1	3146	77.5	
Metabolic disease (includes diabetes)	Yes	357	43.1	747	45.0	1880	46.3	0.446
	No	390	47.0	728	43.9	1899	46.8	
Liver disease	Yes	32	3.9	63	3.8	189	4.7	0.546
	No	683	82.4	1351	81.4	3512	86.6	
Kidney disease	Yes	175	21.1	337	20.3	883	21.8	0.991
	No	553	66.7	1080	65.1	2816	69.4	
Other chronic diseases	Yes	451	54.4	813	49.0	2393	59.0	< 0.001
	No	307	37.0	684	41.2	1408	34.70	
Obesity (BMI≥30)	Yes	129	15.6	253	15.3	591	14.6	0.014
	No	355	42.8	757	45.6	2129	52.5	
Smoking habit	Yes	199	24.0	471	28.4	1001	24.7	< 0.001
	No	187	22.6	338	20.4	1218	30.0	
Comorbidities	No-low risk	79	9.5	222	13.4	442	10.9	< 0.001
	Intermediate risk	669	80.7	1300	78.3	3068	75.6	
	High risk	81	9.7	137	8.3	548	13.5	
Respiratory seasons	40/2021 to 39/2022	66	8.0	120	7.2	2055	50.7	< 0.001
	40/2022 to 39/2023	267	32.2	437	26.4	1170	28.8	
	40/2023 to 20/2024	496	59.8	1102	66.4	833	20.5	
Influenza vaccination status (vaccinated in the season)	Unvaccinated	225	27.1	686	41.4	1550	38.2	< 0.001
	Vaccinated	590	71.2	939	56.6	2372	58.5	
	Vaccination unknown	14	1.7	34	2.1	136	3.3	
COVID-19 vaccination (vaccinated < 6 months ago)	Unvaccinated	319	38.5	798	48.1	2851	70.2	< 0.001
	Vaccinated	499	60.2	835	50.3	1147	28.3	
	Vaccination unknown	11	1.3	26	1.6	60	1.5	

[a] Median [25th percentile – 75th percentile]; This table omits the missing data, but they are included in the percentage estimates, which is why they will not sum up to 100%.

Table 2
Relative Risk (RR) and 95% Confidence Intervals (95%CI) of pneumonia, ICU admission and in-hospital death among hospitalised adults aged ≥65 years admitted due to RSV compared to influenza virus infection. Spain, October 2021– May 2024.

	Cumulative Outcome Incidence n/ N (%)		RSV[a] vs. Influenza RR [95% CI][b]
Outcome/population group	RSV	Influenza	
Pneumonia			
Overall	214/772 (27.7%)	481/1565(30.7%)	0.92 [0.80–1.06][c]
Unvaccinated	60/214 (28.0%)	209/671 (31.2%)	0.91 [0.72–1.16]
Vaccinated	151/549 (27.5%)	262/871 (30.1%)	0.93 [0.79–1.10]
Vaccination unknown	3/9 (33.3%)	10/23 (43.5%)	0.84 [0.30–2.36]
ICU admission			
Overall	29/767 (3.8%)	48 /1551 (3.1%)	1.43 [0.91–2.25][c]
Unvaccinated	7/210 (3.3%)	27/666 (4.1%)	0.93 [0.41–2.08]
Vaccinated	22/548 (4.0%)	18/863 (2.1%)	2.13 [1.16–3.89]
Vaccination unknown	0/9 (0.0%)	3/22 (13.6%)	NA[d]
Death			
Overall	28/444 (6.3%)	81/973 (8.3%)	0.71 [0.47–1.08][c]
Unvaccinated	9/130 (6.9%)	39/416 (9.4%)	0.64 [0.32–1.28]
Vaccinated	18/305 (5.9%)	40/540 (7.4%)	0.76 [0.45–1.30]
Vaccination unknown	1/9 (11.1%)	2/17 (11.8%)	0.83 [0.09–7.67]

[a] Patients admitted due to RSV were the exposed group, using as reference group patients admitted due to influenza virus;
[b] adjusted by age, sex and comorbidities;
[c] additionally adjusted by vaccination status.
[d] Not available: due to the absence of cases with ICU admission in the "vaccination unknown" category, its coefficient could not be estimated.

mortality among patients with RSV, influenza, or SARS-CoV-2, regardless of vaccination status. The differences in the definition of the outcome, its frequency (12% composite outcome vs. 6% lethality in our study) and the age distribution in the study population (median of 67 years vs. 83 in our study) could account for the apparently discrepant results. It could be possible that the clinical presentation of the different viruses do entail different relative risk of death in the elderly than in the younger population. However, since estimates in our study were based in a low number of deaths when stratifying by vaccination status and had low precision, it is difficult to draw strong conclusions on the differences in mortality by virus based solely on our results.

Finally, the lower frequency of pneumonia among patients with RSV, particularly when compared to SARS-CoV-2, observed both among vaccinated and unvaccinated individuals, is consistent with the typical presentation of RSV in older adults.[26,27]

Our study findings are subject to at least some limitations. First, the suspicion of RSV in elderly individuals with respiratory symptoms is often secondary or infrequent, resulting in underdiagnosis of this disease, possibly depending on specific symptoms and severity. However, our study was based on patients recruited during routine surveillance, in which samples are systematically collected (one or two days per week) from patients hospitalised with acute respiratory infection. This should have minimised underdiagnosis of RSV and increased the representativeness of our study sample. Second, different hospitals incorporated (or left) the SiVIRA network over the three seasons. Also, RSV testing was incorporated into the surveillance protocol in the 2023–24 season (before that, it was voluntary for hospitals), which resulted in an increase from 58.9% of all samples tested for RSV in 2021–2022 to 78.4% in 2022–2023 and 91.5% in 2023–2024. This could produce calendar-time differences in the composition of the stud sample. However, the participating hospitals were always instructed to select patients for swabbing systematically, so even when testing rates were lower, the likelihood that RSV was tested or not depending on the clinical condition of the patient is less plausible than if testing had been indicated by the treating physician. Third, differences in clinical practice may imply low generalisability of our results to other contexts. Analysing additional outcomes, such as requirement for oxygen supplementation or mechanical ventilation, could have added useful information, but

Table 3
Relative Risk (RR) and 95% Confidence Intervals (95%CI) of pneumonia, ICU admission and in-hospital death among hospitalised adults aged ≥65 years admitted due to RSV compared to SARS-CoV-2. Spain, October 2021– May 2024.

	Cumulative Outcome Incidence n/ N (%)		RSV[a] vs. SARS-CoV-2 RR [95% CI][b]
Outcome/population group	RSV	SARS-CoV-2	
Pneumonia			
Overall	214/772 (27.7%)	1679/3684 (45.6%)	0.76 [0.67–0.87][c]
Unvaccinated	86/304 (28.3%)	1145/2587 (44.3%)	0.81 [0.67–0.98]
Vaccinated	126/464 (27.2%)	518/1066 (48.6%)	0.73 [0.62–0.86]
Vaccination unknown	2/4 (50.0%)	16/31 (51.6%)	1.34 [0.48–3.79]
ICU admission			
Overall	29/767 (3.8%)	150/3636 (3.6%)	1.37 [0.90–2.08][c]
Unvaccinated	12/299 (4.0%)	112/2556 (4.4%)	1.10 [0.61–1.99]
Vaccinated	17/464 (3.7%)	33/1049 (3.1%)	1.83 [1.02–3.28]
Vaccination unknown	0/4 (0%)	5/31 (16.1%)	NA[d]
Death			
Overall	28/444 (6.3%)	311/2422 (12.8%)	0.63 [0.42–0.94][c]
Unvaccinated	10/182 (5.5%)	216/1693 (12.8%)	0.56 [0.30–1.04]
Vaccinated	17/258 (6.6%)	91/703 (12.9%)	0.65 [0.39–1.09]
Vaccination unknown	1/4 (25.0%)	4/26 (15.4%)	2.48 [0.36–17.05]

[a] Patients admitted due to RSV were the exposed group, using as reference group patients admitted due to SARS-CoV-2;
[b] adjusted by age, sex, respiratory season and comorbidities;
[c] additionally adjusted by vaccination status.
[d] Not available: due to the absence of cases with ICU admission in the "vaccination unknown" category, its coefficient could not be estimated.

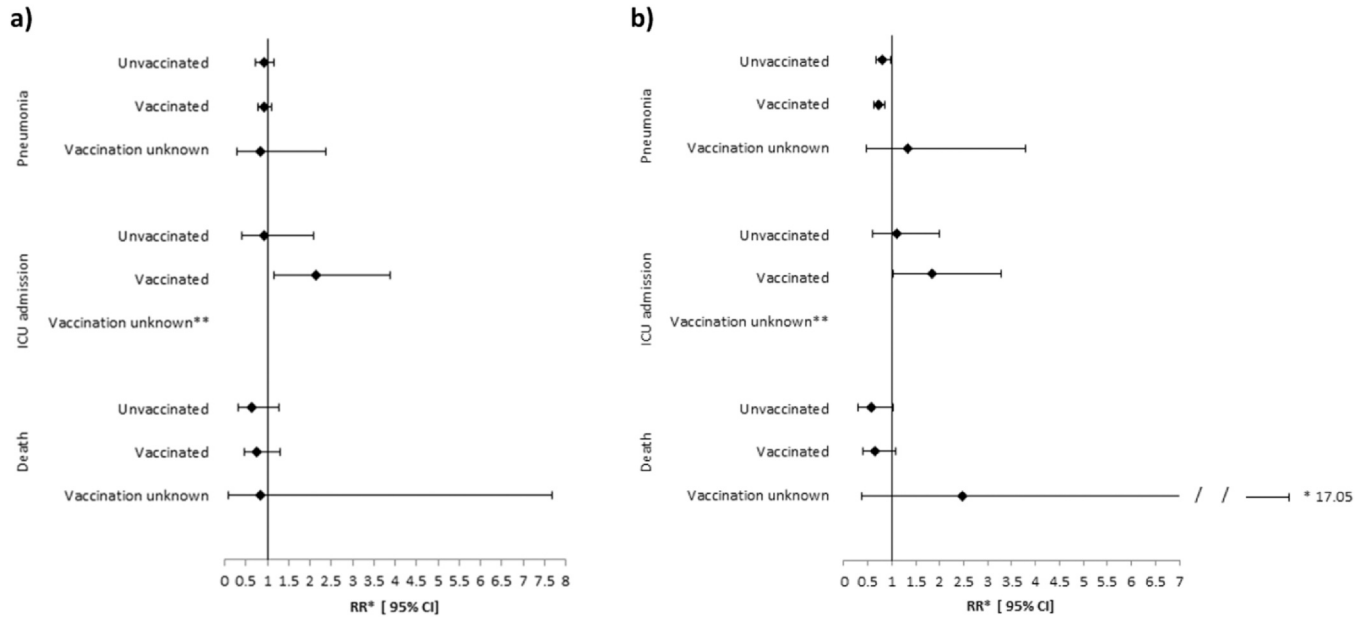

Fig. 2. Adjusted* Relative Risk (RR) and 95% Confidence Intervals (95%CI) of pneumonia, ICU admission and in-hospital death among hospitalised adults aged ≥65 years admitted: a) due to RSV compared to influenza (stratified according to influenza vaccination within the season) or; b) due to RSV compared to SARS-CoV-2 (stratified according to last SARS-CoV-2 vaccination in the previous 6 months). Spain, October 2021– May 2024. *a) Adjusted by age, sex, comorbidities *b) Adjusted by age, sex, comorbidities and respiratory season; ** Not available: due to the absence of cases with ICU admission in the "vaccination unknown" category, its coefficient could not be estimated.

they were not adequately collected, with a high proportion of missing data. Thirdly, it is possible that vaccination status was misclassified, although it is generally collected by data linkage with vaccination registries at the hospital or regional levels. Fourth, SARS-CoV-2 variants evolved throughout the study period, with different severity associated to each of them,[28,29] so the overall estimate for the comparison with SARS-CoV-2 may depend on the specific calendar time included in our study. Last, although the sample size appears sufficiently large for the presented results, some results were not sufficiently powered and confidence intervals were wide, particularly in the stratified analysis and for the mortality outcome.

Taken together, our findings highlight the importance of considering RSV as a relevant pathogen among older adults presenting with severe acute respiratory infection, and the associated burden in the most severe end of its clinical spectrum. Effective vaccination strategies, early diagnosis, and prompt clinical management will be essential for mitigating the burden of respiratory viral infections in this population.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jinf.2024.106292.

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