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Estimated impact of nirsevimab prophylaxis on the economic burden of respiratory syncytial virus disease in Northern Italy

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Abstract

Background Respiratory syncytial virus (RSV) is a frequent cause of acute lower respiratory tract infection (LRTI) in infants; however, the health and economic burden of infant RSV-associated LRTI in Northern Italy has not been sufficiently assessed. We evaluated the clinical and economic burden of RSV-associated LRTI requiring emergency department (ED) access and/or hospitalization in infants less than 6 months old in two provinces in Northern Italy and estimated the potential impact of universal immunization with a recently approved monoclonal antibody.

Methods Epidemiological data during the 2021–2022 and 2022–2023 RSV seasons were obtained from administrative records and anonymized to comply with confidentiality requirements. Resource utilization was estimated using the costs associated with each event, obtained from the available literature and an analysis of national hospital discharge records. A static decision analytic model was used to estimate RSV-related health and associated cost outcomes.

Results Overall, 882 ED accesses and 430 hospital admissions associated with RSV were recorded during two consecutive epidemic seasons. Intensive care admission was needed in 85 cases. Universal immunization would avoid 406 ED accesses and 199 hospital admissions. The total economic burden was estimated at over €1.5 million, of which 51% was for hospitalization, 20% for intensive care, and 9% for ED access. An additional 10% was estimated for the management of long-term consequences of RSV-associated LRTI. Universal immunization would avoid expenses of €124,092 for ED accesses and €999,629 for hospital admissions.

Conclusions These findings underscore the substantial health and economic burden of RSV disease, highlighting the potential benefits of universal prevention strategies, while informing policymaker decisions regarding implementation of immunoprophylaxis.

Keywords Respiratory syncytial virus, Burden of disease, Modelling, Passive immunization, Nirsevimab

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Background

Respiratory syncytial virus (RSV) is a single-stranded RNA virus in the *Pneumoviridae* family that circulates in the fall and winter in temperate zones and causes respiratory tract infection (RTI) in humans. In Italy, the period of greatest RSV circulation occurs between October and March, with a peak in January–February [1–3].

Almost all children have been infected with RSV at least once by the age of 2 years [4], and approximately 1 in 5 will have had lower respiratory tract infections (LRTI) requiring medical attention [2, 5, 6]. In 2019, acute RSV-associated LRTIs caused an estimated 1.4 million hospitalizations and 45,700 deaths worldwide in children less than 6 months of age [7]. Most infants and children hospitalized for RSV disease are born at term and otherwise healthy [8, 9]. RSV-associated LRTI in infancy is associated with long-term health effects that can include recurrent wheezing or asthma later in childhood [10–12].

RSV data from Italian centers has also been reported [13–22]. The Respiratory Syncytial Virus Consortium in Europe (RESCEU) estimates that each year in Italy 40% of respiratory hospitalizations in children less than 5 years of age are associated with RSV, corresponding to approximately 250,000 admissions [23]. Real-world evidence in Italy identified an annual incidence rate of 175–195/100,000 in this age group, and confirmed that a large majority of RSV-related hospitalizations occur in otherwise healthy children born at full term [24].

RSV infection can place a substantial economic burden on healthcare systems, especially during the peak RSV season in temperate regions [25, 26], when RSV-associated respiratory disease can impact pediatric acute and critical care hospital capacity and quality of care [27, 28]. The estimated total global cost to healthcare systems in 2017 for children less than 5 years old was nearly 5 billion USD [29]. In Italy, the mean costs associated with RSV-bronchiolitis hospitalization in otherwise healthy infants and children are significantly higher compared with RSV-negative cases and age-matched general population [24, 30].

The lack of effective treatment for RSV-associated LRTI highlights the need for preventive strategies that can reduce the burden of RSV during the first months of life. Passive immunization of infants through maternal vaccination or monoclonal antibodies provides protection during this critical period.

Nirsevimab is an anti-RSV monoclonal antibody with an extended in vivo half-life that targets the prefusion form of the F protein [31]. A single intramuscular dose protects infants from RSV-associated LRTI requiring hospital admission or any kind of medical attention for at least 5 months [32–34]. Meta-analysis of data on 2,943 infants revealed significant reductions in the risk of medically-attended RSV-associated LRTI and hospitalization

for RSV-associated LRTI, with no significant difference in adverse events between the nirsevimab and placebo arms [35].

Preliminary real-world evidence suggests that the effectiveness rate is similar to immunization efficacy results from randomised trials [36–40], including for severe cases of RSV-associated bronchiolitis admitted to the pediatric intensive care unit (ICU) [41]. In Italy, a prospective observational cohort study enrolled all nirsevimab-eligible infants born in the Valle d'Aosta region of Italy between 1 May 2023 and 15 February 2024 ($n=537$, of which 369 received nirsevimab) to monitor hospitalization rates for RSV-associated bronchiolitis [39]. Coverage was 69% and 14 of the 168 infants who did not receive prophylaxis (8.3%) required hospitalization for RSV-associated bronchiolitis, while none of the immunized infants did ($p<0.001$).

The need to establish the potential impact of universal prophylaxis on the economic burden of RSV on healthcare systems is currently unmet. In the present report, we assess the disease burden of RSV in two Italian provinces and evaluate potential cost savings through the introduction of universal prophylaxis.

Methods

Study design and population

This retrospective observational study assessed the economic burden associated with hospitalization and emergency department (ED) access for laboratory-confirmed RSV infection among infants aged 0–6 months in the Italian provinces of Biella and Pavia during the 2021–2022 and 2022–2023 RSV seasons. Participating centers included the IRCCS Policlinic San Matteo in Pavia (OSC Neonatology and Neonatal Intensive Care, and the OSC Pediatrics hub for the province of Pavia), the ASST Pavia (including facilities in Voghera, Broni-Stradella, and Vigevano), and the Degli Infermi Hospital, which serves the province of Biella. The healthcare systems in these provinces have a similar organization and case mix.

We searched administrative databases in participating hospitals for RSV-associated ED accesses, and admissions to pediatric wards and/or ICUs. Results were anonymized to comply with confidentiality requirements. RSV detection was conducted using reverse transcriptase polymerase chain reactions (RT-PCR) on nasopharyngeal washings or bronchoalveolar lavages from infants with a clinical presentation consistent with RSV infection (i.e., cough, fever, tachypnea, labored breathing, wheezing, hypoxemia and/or signs of bronchiolitis). According to hospital protocols, infants less than two years of age presenting with these symptoms were eligible for testing.

Assessment of costs

Building on a previously published study by Bini et al. [42], we adapted the epidemiological and economic model to real-world data from the two centers included in this analysis. The original work by Bini et al. aimed to estimate the seasonal burden of RSV in Italy—both in terms of health events and associated costs—comparing the current prophylaxis strategy (targeting only palivizumab-eligible infants) with an alternative scenario involving universal immunization using nirsevimab. In the present study, the risk of RSV-related events per patient, as estimated by Bini et al., was applied to our real-world population in order to simulate the overall clinical and economic burden. The cost of each event was incorporated into the model to reflect the total impact within the context of actual healthcare resource utilization.

The analysis focused solely on the costs of ED accesses and admissions to a pediatric ward or intensive care unit. It did not consider age, gestational age at birth, or comorbidities, because the goal was to evaluate costs based on the hospital department. The economic assessment included direct costs associated with RSV-related health events leading to ED access or admission to a pediatric ward or pediatric intensive unit, and indirect costs related to the subsequent management after RSV-related episodes. Associated family financial burdens resulting from RSV infections were also considered in terms of productivity loss due to RSV related events, evaluated as income lost due to premature death and considering an average age of exit from the labor market equal to 62 years [42]. Using a conservative approach, it was postulated that the costs associated with each health incident remained uniform throughout the simulated cohort. Estimation of cost related to hospital and ICU admissions were derived from a retrospective study of national hospital discharge records [42], focusing on RSV admissions among infants younger than two years of age between 2016 and 2019. Costs associated with ER visits were extrapolated from data provided by the Italian Ministry of Health's Mattoni project [43] updated to the fiscal year 2021. Costs for primary care visits were estimated by using the national tariff for outpatient general consultations [44].

The economic implications of mid- to long-term complications following RSV hospitalization, specifically the management of recurrent wheezing, were estimated by considering the hospitalization costs for bronchitis and asthma, as aligned with the national tariff, while the risk was obtained from a previously published study [42]. Recurrent wheezing costs were calculated using hospitalization costs for bronchitis and asthma during the first year of life, and the cost of 5.5 primary care visits annually for the second and third years as estimated in the literature [42]. Asthma management costs were derived from the literature and projected over 18 years with a 3% annual discount [42]. A one-off cost for asthma management was determined as a weighted average of discounted annual asthma management costs over 18 years, adjusted for age-stratified probabilities of asthma-related hospitalization following RSV infection [42]. This cost was linked to the one-time probability of asthma hospitalization after RSV hospitalization [42]. The model compared the immunization strategy for infants at high risk of severe RSV using palivizumab at a coverage rate of 75%, versus a new immunization strategy using nirsevimab to protect all infants against RSV with coverage rates of 60% for term infants and 75% for palivizumab-eligible infants [42]. The overall immunization efficacy of nirsevimab was assumed to be 88.4%, based on the most recent systematic review and meta-analysis [45].

Costs associated with asthma management were obtained from a national observational study by Calabria et al. [46], which utilized an Italian administrative database to assess health resource utilization and costs for patients diagnosed with asthma, chronic obstructive pulmonary disease, and mixed disorders. In this case the overall cost was also assumed to be equal to previously published estimates [42]. The aggregate direct costs associated with RSV-related health events were estimated for the overall population, influenced by the coverage rates of the immunization strategy and efficacy in mitigating medically-attended RSV events [42]. Table 1 shows the cost parameters used in the study.

Table 1 Cost parameters used in the study

Health event	Cost (€) per event ^a	Source
Inpatient hospitalization	2,050.9	Bini et al. 2023 [42]
ICU	5,484.2	Bini et al. 2023 [42]
ED accesses	305.6	Progetto Mattoni [43] actualized at 2021
Primary care visit	20.7	National tariff for outpatient visits [44]
Asthma hospitalization	787.4	Bini et al. 2023 [42]
Recurrent wheezing (annual cost)	1,538.0	National tariff for acute hospital services [44], Bini et al. 2023 [42]

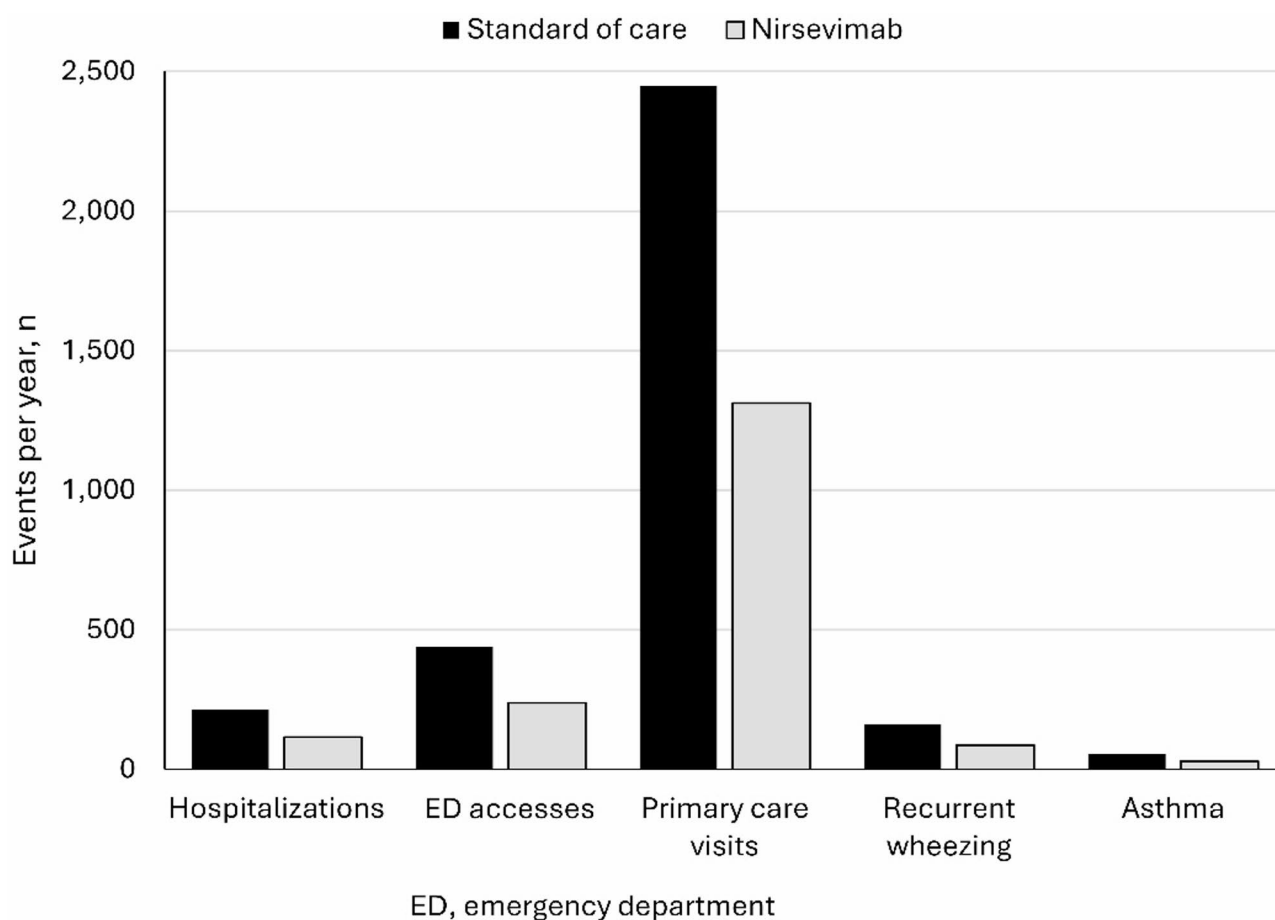
^a Cost per event unless indicated otherwise

ICU, Intensive Care Unit; ED, Emergency Department

Table 2 Modeling of burden associated with RSV-related events and the estimated impact of universal prophylaxis with nirsevimab in the Italian provinces of Biella and Pavia during the 2021–2022 and 2022–2023 seasons

Event	2021–2022 Season			2022–2023 Season		
	Standard of care	Nirsevimab	Difference	Standard of care	Nirsevimab	Difference
Total events	2,585	1,387	-1,198	4,056	2,175	-1,880
Hospitalizations	153	82	-71	277	149	-128
ED accesses	536	289	-247	346	187	-159
Primary care visits	1743	933	-810	3155	1689	-1466
Recurrent wheezing	115	62	-53	208	112	-96
Asthma	38	21	-18	70	38	-32
RSV-related death	0.28	0.00	-0.28	0.18	0.00	-0.18

ED, Emergency Department; RSV, Respiratory syncytial virus

**Fig. 1** Modeling of the annual burden of RSV-related events based on data from the Italian provinces of Biella and Pavia during the 2021–2022 and 2022–2023 seasons

Results

During the study period, there were 6,640 RSV-related events leading to in-hospital management (2,585 in 2021–2022, and 4,056 in 2022–2023) in the Italian provinces of Biella and Pavia. Among these, we identified a total of 882 RSV-related ED accesses, 430 hospital admissions, and 85 intensive care accesses. The modeling of the event burden and potential impact of universal

immunization, and the annual burden over the same period are displayed in Table 2; Fig. 1.

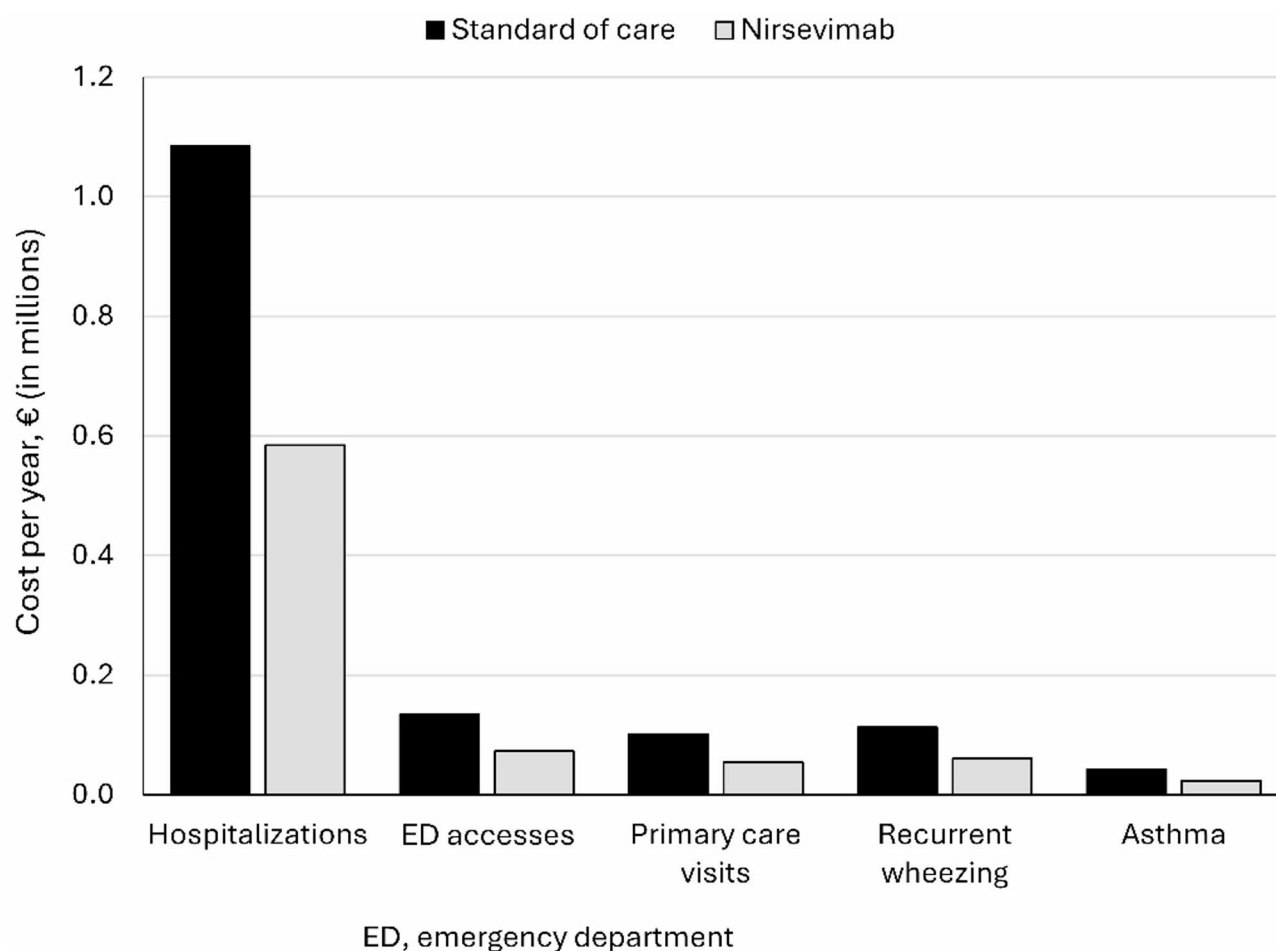
Universal immunization would have avoided over 3,000 RSV-related events in the two considered seasons (Table 2). Of these, 74% would be primary care visits avoided, 13% ED accesses and 6% inpatients hospitalizations.

Pharmacoeconomic assessment included modeling of costs and the potential impact of universal prophylaxis

Table 3 Modeling of costs associated with RSV-related events and the estimated impact of universal prophylaxis with nirsevimab in the Italian provinces of Biella and Pavia during the 2021–2022 and 2022–2023 seasons

Costs by event (€)	2021–2022 Season			2022–2023 Season		
	Standard of care	Nirsevimab	Difference	Standard of care	Nirsevimab	Difference
Total costs	1,173,434	602,607	-570,827	1,869,181	988,055	-881,126
Hospitalizations	771,675	415,993	-355,682	1,397,085	753,138	-643,947
ED accesses	163,776	88,364	-75,412	105,721	57,041	-48,680
Primary care visits	72,010	38,558	-33,452	130,371	69,807	-60,564
Recurrent wheezing	80,269	43,246	-37,022	145,323	78,296	-67,028
Asthma	30,351	16,445	-13,906	54,949	29,773	-25,176
RSV-related death	55,353	0	-55,353	35,731	0	-35,731

ED, Emergency Department; RSV, respiratory syncytial virus

**Fig. 2** Modeling of the annual costs of RSV-related events based on data from the Italian provinces of Biella and Pavia during the 2021–2022 and 2022–2023 seasons

with nirsevimab on healthcare budgets in the two Italian provinces (Table 3), and the annual burden over two seasons (Fig. 2).

The total economic burden was estimated at over €1.5 million on average in the two considered seasons (Table 3). Of this economic impact, 51% was related to hospitalization, 20% to intensive care, 9% to ED access and 10% to managing the long-term consequences of

RSV-associated LRTI. Universal immunization would have avoided €124,092 for emergency visits and €999,629 for hospital admissions in the two seasons (Table 3).

Discussion

RSV is the most frequent cause of hospitalization for LRTI in children less than 1 year of age. The introduction of universal immunization with nirsevimab is likely

to significantly lower the clinical burden of RSV and, depending on the cost per dose, reduce the economic burden on the healthcare system.

Our study estimated the clinical and economic burden of RSV disease among infants aged 0–6 months in two provinces in Northern Italy, and the potential for reducing this burden through universal immunization with nirsevimab. Our findings show that implementing universal immunization would provide substantial reductions in pediatric emergency access and hospital admission rates for RSV disease during the epidemic season, as well as post-hospitalization follow-up outpatient visits.

This translates into a substantial reduction in public spending, in line with what has been already shown in other settings [47]. The extent of the above-mentioned decrease in the RSV-associated financial burden will depend on the actual cost per dose of nirsevimab in Italy, and on the actual coverage of this practice over the years. Immunization coverage is one of the most uncertain factors influencing outcomes; therefore, we have used conservative models with an immunization coverage of 60%, which may underestimate the impact of such interventions. For example, actual coverage was 69% (86% during the RSV season) in the prospective observational cohort study conducted in the Valle d'Aosta region of Italy between 1 May 2023 and 15 February 2024 [39], and ranged from 78.7 to 98.6% in real-world effectiveness studies conducted in Spain [36, 40, 48–51].

In our study, hospital admission was the main driver of healthcare costs, comprising 51% of the burden. This finding is in agreement with a study on electronic medical records data conducted in two Spanish regions during the 2017–2018 RSV season, which estimated that 45.8% of the healthcare cost of RSV-associated acute lower respiratory tract infections was attributable to hospital admissions and identified a mean cost for RSV-associated hospitalization of €2,335 [52]. Inpatient hospitalization was also the greatest cost in a retrospective study of Danish national health and administrative registers, which identified a cost of €2,821 per hospitalization [53]. A retrospective cost analysis conducted in the Spanish National Healthcare System revealed mean RSV-associated hospitalization costs for patients without known risk factors for severe complications of €2,827 for patients aged 0–5 months and €2,687 for those aged 6–12 months [54]. Cutrera et al. conducted a retrospective study of Italian hospital discharge records (HDR) for patients aged 0–12 months, identifying a cost for RSV-associated hospital admissions that ranged from €2,483 to € 2,617 over four RSV seasons ending in 2019 [55]. These costs are somewhat higher than the conservative inpatient hospitalization cost of €2,051 that we used in our model.

Limitations of our study include the risk of missing data due to the retrospective design. Also, the duration

of this study covered only two consecutive seasons; however, data from this period will be important for comparison after the anticipated implementation of universal RSV prophylaxis in the near future. The economic impact of RSV hospitalizations can significantly differ based on the age of the affected infants, with younger infants typically incurring higher costs. Future studies in this setting should include an assessment of costs stratified by patient age to optimize healthcare strategies.

Study strengths include its multicentric design covering two provinces in Northern Italy, use of a model based on conditions in the Italian healthcare system, and assessment of only pediatric admissions with laboratory-confirmed RSV disease, rather than estimated rates of clinical cases, which can be affected by seasonal differences in RSV circulation.

Conclusions

These findings underscore the substantial health and economic burden of RSV-associated disease and highlight the need to develop effective prevention strategies. The findings should also inform policymaker decisions regarding implementation of immunoprophylaxis programs in Northern Italy as well as providing a baseline for assessing the potential benefits of such intervention strategies.

Abbreviations

Ab	Antibody
ER	Emergency Room
ICU	Intensive Care Unit
LTRI	Lower respiratory tract infection
mAb	Monoclonal antibody
RSV	Respiratory syncytial virus
QoL	Quality of life
RESCEU	Respiratory Syncytial Virus Consortium in Europe
RNA	Ribonucleic acid
RSV	Respiratory syncytial virus
RTI	Respiratory tract infection
RT-PCR	Reverse transcriptase polymerase chain reactions
USD	United States dollars

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Author contributions

Study conception and design: CT; data collection: LD, SG, AL, GM, ET; analysis and interpretation of results: AM; manuscript drafting and revising: CT, AM, PM. All authors have reviewed and approved the final version of the manuscript.

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Data availability

Not applicable.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

LD, AL, AM, ET and GM declare that they have no conflicts of interest. CT declares the following COI: AstraZeneca and Sanofi (Speaker) and Sanofi (Advisory Board). SG declares the following COI: Azienda Socio-Sanitaria ASST Pavia (Speaker) and Entegron (Consultant). PM declares the following COI: Pfizer, Sanofi, MSD, Moderna, Enanta (Speaker, Advisory Board).

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