Economic and Clinical Burden Associated with Respiratory Syncytial Virus (RSV) and Expected Impact of Universal Immunization with Nirsevimab Among All Infants in Their First RSV Season Against Standard of Care in Italy

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INTRODUCTION

- Respiratory syncytial virus (RSV) infection is the leading cause of severe lower respiratory tract illness in infants in US [1]. RSV has been estimated to be the primary cause of hospitalization and death among respiratory infections in children aged ≤1 year in lower income countries [2,3].
- Despite prematurity and the presence of comorbidities (congenital heart disease, chronic respiratory diseases, and immunodeficiency) are confirmed as risk factors for RSV disease [4], the vast majority of the burden of disease occurs in healthy full-term infants; in fact, as confirmed by recent national studies, at least 87% of infants hospitalized for RSV did not present underlying morbidities, were born at term or late preterm (>34 wGA) [5], while in infants with lower respiratory tract infection (LRTI) attended by a family pediatrician 92% of cases happened in children born at term, and 97% happened in children with no comorbidities or otherwise health [6].
- Until now, the only prophylaxis available at the national level has been palivizumab, recommended only for high-risk infants of ≤ 35 weeks of gestational age (wGa) aged <6 months at the beginning of the RSV season, infants aged <2 years treated for bronchopulmonary dysplasia in the last 6 months and infants aged <2 years with hemodynamically significant congenital cardiac disease [7].
- Nirsevimab is an extended half-life monoclonal antibody (mAb) for the prevention of RSV medically attended lower respiratory tract infections (RSV-MA-LRTIs) in all infants. Among term and preterm infants, nirsevimab demonstrated an overall efficacy of 79.5% (95% confidence interval [CI], 65.9%–87.7%) in the prevention of RSV-MA-LRTIs in a prespecified, pooled analysis of the pivotal phase 2b and phase 3 MELODY studies [8].

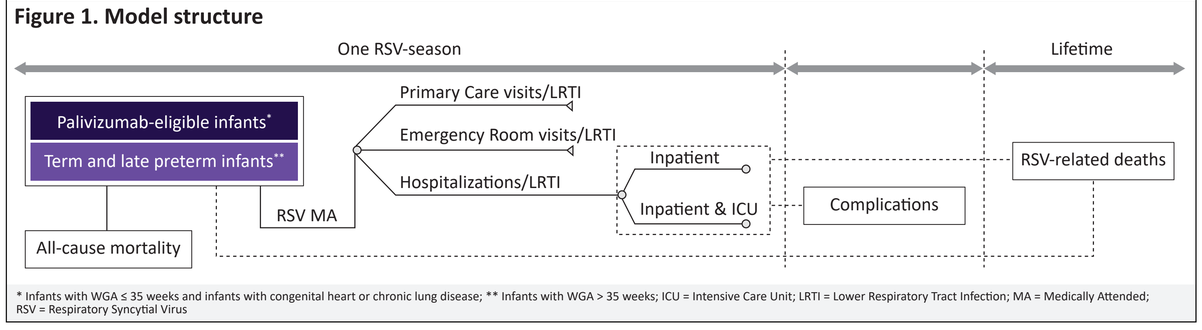
OBJECTIVE

- To describe the seasonal RSV burden in Italy in terms of health events and associated costs and to compare the epidemiological and economic burden associated with the current prophylaxis strategy (recommended only for high-risk infants) with an alternative scenario where a universal immunization strategy with nirsevimab is adopted.

METHODS

- A static decision analytic model previously published for the US perspective [1] was adapted to follow the expected cohort of newborns in Italy in 2024 [9] during the first endemic season of RSV (**Figure 1**).
- The cohort of newborns was divided into two subpopulations to account for the differential risks of RSV-MA-LRTI: (1) palivizumab-eligible infants, representing newborns ≤35 weeks gestational age (wGA) or infants with congenital heart or chronic lung disease (4.4%, from CeDAP 2021[10], ORPHANET [11], SIP [12]); (2) late preterm and term infants, representing newborns with >35 wGA.
- The model considered that the epidemic season of RSV starts in late autumn (November), peaks in the winter (January) and has a variable end in early spring (April) ([5] and expert opinion).
- Currently, the coverage rate for palivizumab among eligible infants is assumed at 40% (estimate based on IQVIA sales data for season 2021/2022); in the cost-consequences analysis, a coverage rate of 60% was assumed for nirsevimab in all infants, similar to non-mandatory vaccines for infants.
- Monthly per-patient risks of RSV-MA-LRTI (**Figures 2, 3, 4**), risk of complications associated with an inpatient RSV infection and risk of death among RSV inpatient hospitalizations were obtained from the literature, and validated by clinicians involved in the study analysis.
- Direct costs were obtained using the available literature and by conducting a real-world analysis of National Hospital Discharge Records; indirect costs were estimated considering the productivity loss due to premature death among RSV inpatient hospitalizations. In particular, the average annual income lost due to premature death was calculated considering an average hourly income equal to € 11.40 [13], a number of working hours per day equal to 6.7 ([14], assuming 5.5 working day per week), an employment rate equal to 58.1% (ISTAT 2020) and considering an average age of exit from the labour market equal to 62 (OECD [15]). **Table 1** reports a comprehensive list of the parameters included in the model.

Figure 1. Model structure



* Infants with WGA ≤ 35 weeks and infants with congenital heart or chronic lung disease; ** Infants with WGA > 35 weeks; ICU = Intensive Care Unit; LRTI = Lower Respiratory Tract Infection; MA = Medically Attended; RSV = Respiratory Syncytial Virus

Figure 2. Hospitalization risk per month (ordinary and intensive care unit) of age (palivizumab-eligible infants: Feltes and Simoes 2005 [16]; late preterm and term infants: Heppe Montero et al. 2022 [17])

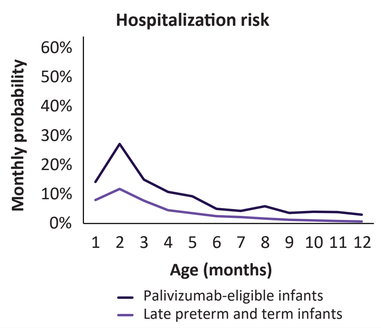


Figure 3. Risk of emergency room visits per month of age (Martinon-Torres et al. 2022, BARI study [18]→with application of gradient observed for hospitalizations)

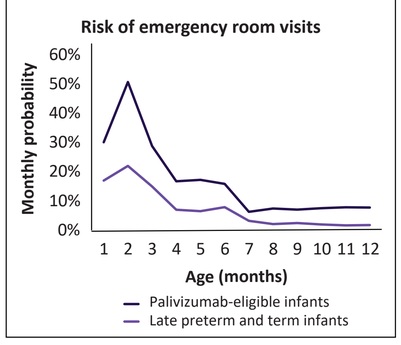


Figure 4. Risk of primary care visits by age among all infants (Martinon-Torres et al. 2022, BARI study [18])

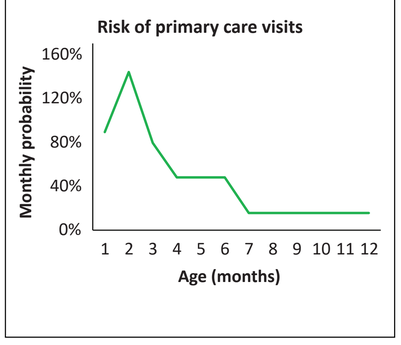


Table 1. Parameters included in the model

Complications due to RSV hospitalisation (%)	Palivizumab-eligible infants	Late preterm and term infants	Source
Risk of recurrent wheezing in the first year of life following a hospitalization due to RSV in the first year of life	31.0	31.0	Li et al. 2022 [19]
Risk of recurrent wheezing in the second year of life following a hospitalization due to RSV in the first year of life	27.0	27.0	Li et al 2022 [19]
Risk of recurrent wheezing in the third year of life following a hospitalization due to RSV in the first year of life	17.0	17.0	Li et al 2022 [19]
Risk of hospitalization due to asthma following a hospitalization due to RSV infection in the first two years of life (one-off probability)	25.2	25.2	Coutts et al. 2019 [20]
All-cause mortality among infants, by age	**Palivizumab-eligible infants**	**Late preterm and term infants**	**Source**
0-5 months	0.0002	0.0002	Mortality Table 2021 ISTAT [21]
6-11 months	0.0002	0.0002	
Risk of death among RSV inpatient hospitalizations, by age	**Palivizumab-eligible infants**	**Late preterm and term infants**	**Source**
0-5 months	0.0095	0.0005	Sanchez Luna et al. 2016 [22]
6-11 months	0.0095	0.0005	
Prophylaxis-related parameters	**Palivizumab-eligible infants**	**Late preterm and term infants**	**Source**
Coverage rate (%)			
Palivizumab	40.0	-	Assumption
Nirsevimab	60.0	60.0	
Efficacy (%)			
Nirsevimab (inpatient and outpatient)	79.5	79.5	Andabaka et al. 2013 [23],
Palivizumab (inpatient and outpatient)	51	-	Simoes et al. 2023 [8]
Cost parameters	**Cost**		**Source**
Health event costs – cost per event (€)			
Inpatient hospitalization	2,050.9		SDO Italia 2016-2019
ICU	5,484.2		SDO Italia 2016-2019
ER visit	305.6		Progetto Mattoni [24], actualized at 2021
Primary care visit	20.7		National tariff of outpatient visits [25]
Cost for the management of recurrent wheezing – annual cost (€)			
Recurrent wheezing (year 1)	1,538.0		National tariff of acute hospital care services [26] (DRG 98)
Recurrent wheezing (year 2)	110.3		Cost of 5,5 outpatient visits discounted considering an annual rate of 3% (Li et al. 2022 [19]; National tariff of outpatient visits [25])
Recurrent wheezing (year 3)	107.1		
Cost for the management of asthma – one-off cost (€)			
Hospitalization due to asthma	787.4		Calabria et al. 2021 [27] and Coutts et al. 2020 [20]. Annual costs up to 18 years of age, discounted considering an annual rate of 3%

RESULTS

- For 2024-2025 RSV season (birth cohort estimated equal to 405,299 infants [8]), the model estimated 223,639 RSV-MA-LRTIs, 15,760 associated complications and 19 deaths – corresponding to an economic burden of approximately € 52.7 million related to managing the RSV-MA-LRTIs, € 11.4 million associated to complications and € 3.5 million in lost productivity due to deaths. Universal immunization of all infants with nirsevimab is expected to prevent 103,398 RSV-MA-LRTIs, 7,226 complications and 7 deaths due to RSV infections, corresponding to an economic saving of approximately € 24.1 million, € 5.2 million, and € 1.4 million respectively (**Tables 2 and 3**).

Table 2. Epidemiological impact of nirsevimab during 2024-2025 RSV season

Clinical outcomes	Standard of care			Nirsevimab			Difference		
	Palivizumab-eligible infants	Late preterm and Term infants	Total	Palivizumab-eligible infants	Late preterm and Term infants	Total	Palivizumab-eligible infants	Late preterm and Term infants	Total
Hospitalizations (incl. ICU)	1,210	14,519	15,729	801	7,717	8,517	-410	-6,802	-7,212
ICU admissions	238	1,938	2,176	157	1,030	1,187	-80	-908	-988
ER visits	2,301	27,989	30,290	1,524	14,891	16,415	-777	-13,098	-13,875
Primary care visits	6,338	171,283	177,621	4,194	91,116	95,309	-2,144	-80,167	-82,311
RSV-MA-LRTIs	**9,849**	**213,791**	**223,639**	**6,518**	**113,724**	**120,242**	**-3,331**	**-100,067**	**-103,398**
Recurrent wheezing	908	10,889	11,797	601	5,787	6,388	-307	-5,102	-5,409
Asthma	305	3,659	3,964	202	1,945	2,146	-103	-1,714	-1,817
Complications	**1,213**	**14,548**	**15,760**	**802**	**7,732**	**8,534**	**-410**	**-6,816**	**-7.226**
RSV-related deaths	11	7	19	8	4	12	-4	-3	-7

Table 3. Economic impact of nirsevimab during 2024-2025 RSV season

Cost outcomes	Standard of care			Nirsevimab			Difference		
	Palivizumab-eligible infants (€)	Late preterm & Term infants (€)	Total (€)	Palivizumab-eligible infants (€)	Late preterm & Term infants (€)	Total (€)	Palivizumab-eligible infants (€)	Late preterm & Term infants (€)	Total (€)
Hospitalizations (standard ward only)	1,994,579	25,801,722	27,796,301	1,319,681	13,713,518	15,033,199	-674,898	-12,088,204	-12,763,102
ICU admissions	1,304,523	10,627,995	11,932,518	863,116	5,648,740	6,511,856	-441,407	-4,979,256	-5,420,662
ER visits	703,023	8,553,154	9,256,178	465,573	4,550,663	5,016,237	-237,450	-4,002,491	-4,239,941
Primary care visits	130,940	3,538,702	3,669,642	86,640	1,882,447	1,969,087	-44,300	-1,656,255	-1,700,556
RSV-MA-LRTIs	**4,133,065**	**48,521,574**	**52,654,640**	**2,735,010**	**25,795,368**	**28,530,379**	**-1,398,055**	**-22,726,206**	**-24,124,261**
Recurrent wheezing	635,192	7,619,005	8,254,197	420,264	4,049,472	4,469,737	-214,927	-3,569,532	-3,784,460
Asthma	240,175	2,880,854	3,121,029	158,908	1,531,163	1,690,071	-81,267	-1,349,691	-1,430,958
Complications	**875,367**	**10,499,859**	**11,375,226**	**579,172**	**5,580,635**	**6,159,808**	**-296,195**	**-4,919,223**	**-5,215,418**
RSV-related deaths	2,152,902	1,383,905	3,536,807	1,424,433	735,540	2,159,973	-728,469	-648,365	-1,376,834

LIMITATIONS AND CONCLUSIONS

- This study presents several limitations, principally due to absence of data referred to the national context. Where it was not possible to obtain granular data about the per-patient risk of RSV per month and per subpopulation, data were obtained from the international literature. Also, the risk of contracting recurrent wheezing and asthma due to RSV infection and the in-hospital mortality probabilities were obtained from international literature.
- The new immunization strategy with Nirsevimab targeting all infant could substantially reduce the RSV-related health events (hospitalizations, ER visits, PC visits, complications, and inpatient deaths), with an important reduction in the costs associated with the management of RSV infections and associated events.
- In this perspective, as already recommended by Italian Scientific Societies [28], the inclusion of monoclonal antibodies in the national immunization calendar as a newborn cohort prevention strategy may support the implementation and the equity of RSV prevention for all infants during their first RSV season.

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COMPETING INTERESTS:

- Bini C, Marcellusi A, Mennini FS declare no competing interest.
- Muzii B, Soudani S, Kieffer A, Beuvelet M are employees of Sanofi and may hold shares and/or stock options in the company.

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