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ORIGINAL RESEARCH

Cost-Effectiveness of Bivalent Prefusion F Vaccine for Prevention of Respiratory Syncytial Virus Among Older Adults in Italy

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Background: Respiratory syncytial virus (RSV) represents a significant health threat for older adults and individuals with comorbidities. RSV infection is often underdiagnosed, limiting the understanding of its clinical and economic burden. The approval of the bivalent RSV prefusion F vaccine offers a new preventive strategy. This study evaluated its cost-effectiveness to optimize resource allocation in Italy.

Materials and Methods: A Markov cohort model was developed to assess the cost-effectiveness of vaccinating adults with a single dose of RSVpreF vaccine versus no vaccination, from the perspective of the Italian National Health Service (NHS). Two vaccination scenarios were analyzed: a base-case scenario assuming implementation of the vaccination strategy in the general population aged 75–99 years, and an alternative scenario focusing on adults aged 60–74 years with comorbidities. A vaccination coverage rate of 52.5% was assumed, according to the rate recorded among individuals over 65 years during the 2024/2025 season. Model outcomes included RSV cases, hospitalizations, deaths, direct medical costs, quality-adjusted life years (QALYs) and incremental cost-effectiveness ratio (ICER). To test the robustness of the results, deterministic sensitivity analysis (DSA) and probabilistic sensitivity analysis (PSA) were conducted.

Results: In base-case scenario, the analysis indicated that vaccination with RSVpreF vaccine could have prevented 314,486 RSV cases and 7163 deaths, resulting in gains of 41,638 LYs and 30,317 QALYs. The ICER was €10,662 per LY gained and €14,644 (range: €9021 to €21,740) per QALY gained. In the alternative scenario the model estimated the prevention of 221,600 RSV cases and 2567 deaths, resulting in gains of 28,429 LYs and 20,395 QALYs. The ICER was €11,211 per LY gained and €15,628 (range: €9597 to €21,965) per QALY gained. Both scenarios proved to be cost-effective.

Conclusion: Vaccinating with RSVpreF vaccine has shown substantial clinical and economic benefits. These findings support the inclusion of RSV vaccination in national immunization programs for older populations.

Keywords: RSV, economic evaluation, cost-utility, vaccination, RSVpreF vaccine, pharmacoeconomics

Introduction

Respiratory syncytial virus (RSV) has long been linked to infections in newborns and children, resulting in significant rates of hospitalization and mortality.[1,2]

However, RSV also significantly affects adults, especially older individuals and those with existing health issues like cardiorespiratory diseases, diabetes, and weakened immune systems.[1,3] RSV is classified into two subgroups, A and B, which are identified by the molecular structure of the G protein that facilitates viral attachment and entry into host cells.[1,2] Each year, the predominant circulating subgroup changes, but both typically circulate together during the same season.[2]

The effects of RSV on older adults and those with comorbidities are not as thoroughly documented as those on children.[1] Research by Fleming et al suggests that RSV infection poses a healthcare burden similar to that of influenza,

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with high hospitalization and mortality rates, particularly in older adults. A study in the United Kingdom estimated a significant number of RSV-related hospitalizations and deaths among individuals over 75 years, highlighting the considerable strain the disease places on healthcare systems.[4] Furthermore, RSV infection in this age group has been associated with a heightened risk of severe pneumonia, acute respiratory failure, and death, emphasizing the seriousness of its complications.[5] A similar investigation in Italy corroborated these results, estimating an annual incidence of RSV-related cardiorespiratory hospitalizations between 1064 and 1527 cases per 100,000 individuals aged 75 years and older.[6]

Early diagnosis is essential to improve clinical management and to avoid inappropriate hospitalizations and unnecessary antibiotic use. Molecular or rapid diagnostic tests, including multiplex assays for SARS-CoV-2, influenza, and RSV, may enhance diagnostic accuracy and support appropriate therapeutic decisions.[5] Currently, treatment in adults is mainly supportive, including oxygen therapy, close clinical monitoring, and management of exacerbations of chronic underlying conditions, as no specific antiviral therapies are routinely available for RSV in this population.[5]

Despite its significant impact, RSV infection in adults is frequently underdiagnosed due to delayed identification or the absence of specific diagnostic tests. This limitation, combined with the virus's nonspecific clinical presentation, contributes to the underestimation of RSV cases, complicating an accurate assessment of its clinical and epidemiological burden.[7]

RSV infection can show a wide range of clinical symptoms, from cases that show no symptoms at all to mild issues like fever, fatigue, and loss of appetite, or even severe respiratory infections that impact both the upper and lower airways.

Acute respiratory infections associated with RSV (RSV-ARI) are often indistinguishable from those caused by other respiratory viruses.[1] In addition to its clinical effects, RSV infection also creates a considerable socioeconomic burden. The rise in hospitalizations leads to direct costs, such as inpatient care, medications, and supportive therapies, as well as indirect costs like loss of independence, the need for home care, and increased frailty.[7]

Implementing vaccination programs could greatly lessen both the healthcare and economic impact of RSV, enhancing the quality of life for older adults while reducing the strain on the National Health Service (NHS).

Recently, the development of vaccines specifically for RSV has provided new preventive options for the adults. In August 2023, the European Medicines Agency (EMA) approved a RSVpreF vaccine, based on the prefusion F protein, for adults aged 60 years and older, particularly targeting those over 75 years who are at the highest risk for complications.[8] This vaccine includes two stabilized recombinant RSV prefusion F antigens, which represent both the RSV-A and RSV-B subgroups. The prefusion F protein is the main target for neutralizing antibodies that prevent RSV infection. After being administered intramuscularly, the prefusion F antigens trigger a protective immune response against RSV-related lower respiratory tract disease.[8]

The efficacy, immunogenicity, and safety of this RSVpreF vaccine in older adults have been evaluated in the RENOIR clinical trial (RSV Vaccine Efficacy Study in Older Adults Immunized Against RSV Disease) (NCT05035212).[9]

This Phase III placebo-controlled study showed that RSVpreF vaccine significantly reduces RSV-associated lower respiratory tract disease, with a 65.1% reduction for cases with two or more symptoms and an 88.9% reduction for cases with three or more symptoms.[8,9] Additional follow-up through end of season 2 demonstrated that vaccine efficacy was sustained.[10]

However, to implement this on a large scale, it is necessary to evaluate its financial viability in Italy. Assessing the cost-effectiveness of vaccines is vital for the healthcare policy decisions of the NHS. With Italy's aging population and increasing healthcare demands, it is crucial to allocate resources optimally.

Pharmacoeconomic evaluations offer important insights into whether RSV vaccination is a cost-effective approach compared to other preventive and treatment options. Key considerations include the cost of the vaccine, the duration of immunity, the reduction in hospitalizations, and the associated cost savings.

This study evaluates the cost-effectiveness of the RSVpreF vaccine versus no vaccination in Italy, focusing on clinical and economic outcomes. The aim of analysis is providing evidence to guide immunization strategies for adults aged 60–74 years with comorbidities and for those aged ≥75 years.

The pharmacoeconomic model is applied to estimate the incremental cost-effectiveness ratio, highlighting the vaccine's potential value in preventing RSV disease in older adults.

Materials and Methods

Model Description

The cost-effectiveness analysis model used in this study is an adaptation of an international model previously applied to evaluate the RSVpreF vaccine in Greece and Germany.[11,12] The adaptation was carried out by integrating epidemiological and cost data specific to Italy to enhance its applicability within the NHS.

This study conducts a cost-effectiveness analysis to evaluate the impact of a single-dose RSVpreF vaccine against RSV in older adults, assessing both its public health implications and economic sustainability from the NHS perspective.

In the model, a base-case scenario was defined in which the vaccination strategy was implemented among the general population aged 75–99 years, assuming all cohorts included in that age range as a single risk group. In addition, an alternative scenario was explored, focusing on adults aged 60–74 years with comorbidities.

Both scenarios are compared with an alternative scenario without RSV vaccination.

A vaccination coverage rate of 52.5% was assumed in the analysis, corresponding to the influenza vaccination rate recorded for individuals over 65 years during the 2024/2025 season.[13]

The analysis is structured to estimate the disease burden in terms of RSV case incidence and RSV-related mortality, and to assess the cost-effectiveness of vaccination from the NHS perspective. The primary outcomes include direct costs and Quality-Adjusted Life Years (QALYs), calculated with a 3% discount rate, in accordance with Italian pharmacoeconomic evaluations. To determine the acceptability of the cost per QALY, the willingness-to-pay (WTP) threshold of €30,000 set by the Italian Medicines Agency (AIFA) was used. This value was selected based on a recent study analyzing 48 pricing negotiations, which reported an average incremental cost-effectiveness ratio (ICER) of €33,004 per QALY.[14]

The analysis uses a Markov cohort model, which helps illustrate how clinical outcomes and economic costs related to RSV infection and vaccination evolve over the lifetime of the population being studied, which can be up to 99 years. The overall structure of the model is presented in Figures 1 and 2.

The model includes three health states: general population (individuals without active RSV infection), RSV infection (active RSV infection during the cycle), and death (all-cause mortality). Arrows represent monthly transition probabilities between states. From the general population state, individuals may remain in the same state, develop RSV infection, or die. From the RSV Infection state, individuals may recover and return to the general population state or die. No transitions occur from the death state.

We project clinical outcomes on a monthly basis, corresponding to a model cycle length of one month, and continue estimating them until we reach the end of the specified time horizon. These outcomes encompass RSV cases that need medical attention, categorized by healthcare setting—whether that's hospitalization, emergency department visits, or outpatient care—as well as RSV-related deaths.

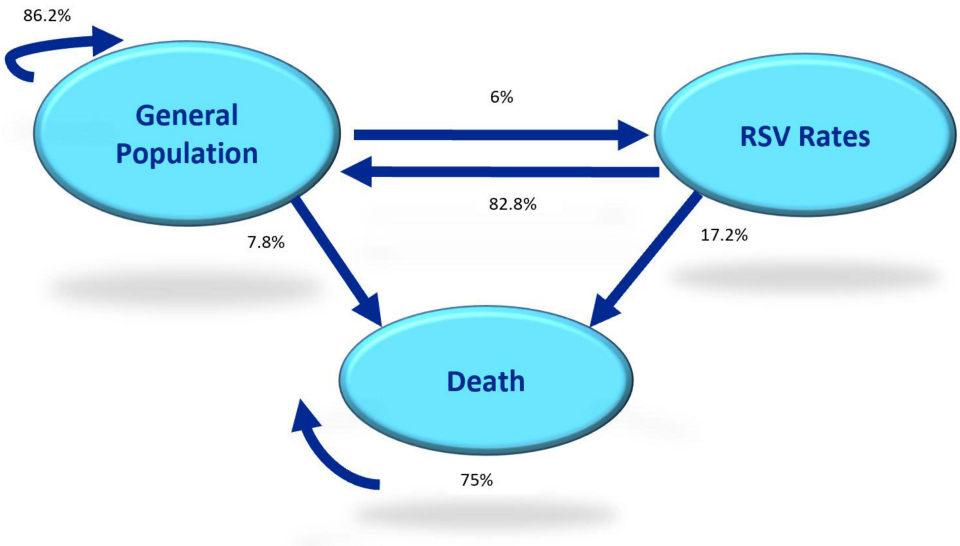

Figure 1 Structure of the model (base-case scenario).

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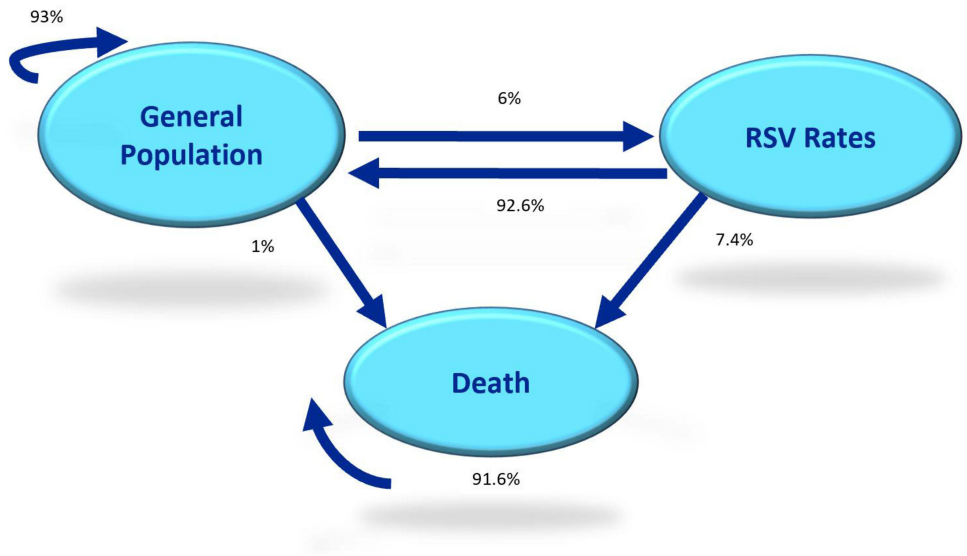

Figure 2 Structure of the model (alternative scenario).

Model Inputs

In this analysis, the incidence of RSV infection, overall and disease-specific mortality, direct medical costs, and vaccine efficacy were estimated by age group and healthcare setting, using data from published sources. The key parameters used in the model are summarized in Tables 1–3.

Population

This model considers a total population of 12,433,990 older individuals, defined according to ISTAT 2024 data.[15] Of these, 5,024,686 are adults aged 60–74 years with comorbidities, while 7,409,304 are aged 75–99 years.[16]

Table 1 Input

	Age and Population			***Reference***
	Alternative Scenario	***Base-Case Scenario***		
	60-74 Years[a]	**75-84 Years**	**85-99 Years**	
	5.024.686	5.110.728	2.298.576	[15,16]
RSV case rates (annual, per 100k)				
Hospital	520.7	520.7	520.7	[6]
Emergency Department	130.3	126.9	126.9	[20]
Outpatient Clinic	5090.7	4957.4	4957.4	[4]
Annual general population mortality (per 100)	0.9	3.7	13.2	[15]
Case fatality rate (per 100) for hospitalized RSV	7.4	13.6	21.9	[23]
Direct medical cost				
Vaccination		180.00 €		[29]
Administration		6.16 €		[30]
Hospital		5.834€		[21]
Emergency Department		344.26 €		[31]
Outpatient Clinic		96.45 €		[32]

Notes: [a]Adults with comorbidities.
Abbreviation: RSV, Respiratory Syncytial Virus.

Table 2 Seasonal RSV Trends

Calendar Month	Vaccine Uptake	RSV Cases
January	2.10%	29.30%
February	1%	31.70%
March	0%	21%
April	0%	0%
May	0%	0%
June	0%	0%
July	0%	0%
August	0%	0%
September	25%	0%
October	33.60%	0%
November	33.20%	0%
December	5.10%	18%

Abbreviation: RSV, Respiratory Syncytial Virus.

Table 3 Vaccine Effectiveness - VE

Time	Hospital	Emergency Department	Outpatient Clinic
Baseline – Month 6	84.60%	84.60%	65.10%
Month 12	77.90%	77.90%	55.50%
Month 18	69.90%	69.90%	43.90%
Month 24	61.80%	61.80%	32.30%
Month 36	45.70%	45.70%	9.20%
Month 42	0%	0%	0%

Comorbidities were identified according to the Passi d'Argento[16] surveillance system, a national program monitoring the health status of the older population coordinated by the Italian National Institute of Health (Istituto Superiore di Sanità). Chronic conditions included cardiovascular diseases (myocardial infarction, ischemic heart disease, coronary heart disease, or other heart diseases), stroke or cerebral ischemia, cancer (including leukemia and lymphoma), chronic respiratory diseases (chronic bronchitis, emphysema, respiratory failure, or bronchial asthma), diabetes, chronic liver disease and/or cirrhosis, and renal failure.

RSV Infection Rates

Annual RSV incidence rates per 100,000 individuals, stratified by age group and healthcare setting, were primarily derived from Italian sources.[6] However, due to limited national epidemiological data, some values were supplemented with data from international sources (Table 1).[4] Both studies used statistical simulation models to account for underdiagnosis of RSV infection, which is often underestimated due to the low frequency of diagnostic testing and low-test sensitivity.[17–19]

For RSV hospitalization rates, the same values were assumed for the two age-groups, due to the absence of age-specific data differentiating the 60–74 and ≥75-year-old populations.[20] For RSV rates related to the emergency department, the model assumed that only 18% of patients presenting to the emergency department for RSV are not hospitalized, while the remaining 82% require hospital admission. Consequently, RSV hospitalization rates represent emergency department visits leading to hospital admission, whereas RSV emergency department rates correspond to visits that result in discharge without hospitalization.[21]

As for RSV rates in outpatient clinic settings, given the absence of italian-specific data, estimates were derived from a UK study that employed multiple linear time series regression modelling to quantify the burden of RSV in both the general population and adult subgroups, expressed in terms of general practitioner visits.[4]

RSV follows a seasonal infection pattern with annual recurrence. The analysis considers the monthly distribution of RSV cases[22] and the vaccine uptake rate across different months of the year, based on the use of the influenza vaccine among adults in 2018. (Table 2).

Mortality Rates

General population mortality rates per 100 individuals were obtained from ISTAT mortality tables for 2024.[15] Since the model considers age groups, mortality rates were calculated as weighted averages, accounting for age-specific mortality rates within each category.

A Danish study[23] reported case fatality rates per 100 hospitalized RSV patients during the acute phase of infection. The risk of death associated with RSV cases managed exclusively in outpatient settings, including emergency department and outpatient clinic consultations, was assumed to be zero.

Vaccine Efficacy

The vaccine efficacy (VE) data for RSVpreF vaccine used in the model were obtained from the RENOIR clinical trial[9] and extrapolation (Table 3). In the absence of direct clinical data on healthcare resource utilization, VE against medically attended RSV-associated lower respiratory tract infections (LRTIs) with three or more symptoms was adopted as a proxy for the prevention of hospitalizations and emergency department visits. Similarly, VE against medically attended RSV-ARI, defined by the presence of at least one symptom, was used as a proxy for outpatient cases (ambulatory care setting).[9,11,12]

Initial VE was assumed to be stable during the first six months following vaccination, consistent with the average follow-up duration for the first RSV season in the RENOIR trial.[9] The efficacy was then assumed to linearly decline to season 2 efficacy at month 16 based on average follow-up from the trial.[10] Thereafter, a linear decline in efficacy was assumed until the fourth season, at which point protection was set to zero to reflect waning immunity in the absence of long-term clinical evidence. Efficacy estimates were assumed to be age-invariant, based on trial data.[9]

Utility

General population utility values by age group were derived by Ara, Mangen, and Melegaro.[24,25,26] The model evaluates the impact of RSV infection using Quality-Adjusted Life Year (QALY) loss, which varies based on the severity of the disease and is categorized by healthcare setting and age group. It is estimated that the QALY loss is 0.0167[27] for patients who are hospitalized and 0.0054 for those treated in emergency departments or outpatient facilities.[28]

Direct Medical Costs

The direct costs considered in the model include the cost of the RSVpreF vaccine[29] (€180), vaccine administration costs (€6.16)[30] and RSV-related healthcare costs, assessed based on the healthcare setting. Vaccine price data were obtained from the Gallery Farmadati[29] database. The public price was considered; a 10% VAT was removed, and the resulting value was divided by two to estimate the maximum ex-factory price reimbursed by the NHS.

Regarding hospitalization-related costs, the average cost per hospitalized patient is €5834,[21] while the cost for an emergency department visit is €344,[31] which corresponds to the cost of a visit for an acute respiratory condition.

In ambulatory care settings, the average cost per RSV episode was assumed to be €96.45,[32] based on the cost of outpatient influenza management.

Sensitivity Analysis

A sensitivity analysis was conducted to evaluate the robustness of the results and assess the impact of parameter variability on the overall findings. Both Deterministic Sensitivity Analysis (DSA) and Probabilistic Sensitivity Analysis (PSA) were conducted as part of this evaluation.

For DSA, a ±25% variation was applied to the main model inputs to assess the impact of parameter uncertainty on the outcomes.

For PSA, 1000 Monte Carlo simulations were conducted, consistent with standard practice in health economic modelling. Different probability distribution curves were used to better capture the uncertainty in key parameters.

Specifically, a beta distribution was applied to disease rate, mortality rate, vaccine efficacy, and disutility, while a log-normal distribution was used for direct costs and vaccine costs. This approach ensures a more comprehensive evaluation of parameter variability.

Results

The analysis examined the clinical and economic effects of getting the RSVpreF vaccine compared to not getting any RSV vaccination throughout a person's lifetime. Two scenarios were considered. The base-case scenario assumed implementation of the vaccination strategy in the general population aged 75–99 years, treated as a single risk group. In addition, an alternative scenario was explored, focusing on adults aged 60–74 years with underlying comorbidities.

Outcomes were reported in terms of clinical endpoints, direct healthcare costs, and the cost-effectiveness of the vaccination strategy, as presented in Tables 4 and 5.

Base-Case Scenario

Clinical Outcomes

The clinical outcomes include the number of RSV cases, RSV-related deaths, life-years lost (LYs) and QALYs.

In the base-case scenario, RSVpreF vaccine significantly reduced the number of RSV infections. Overall, a total reduction of 314,486 cases was observed compared to the no-vaccination strategy. Specifically, hospitalizations decreased from 330,958 to 288,545 (−42,249), while emergency department visits declined from 242,629 to 217,611 (−25,018). The most significant reduction was observed in outpatient care, with 247,054 fewer RSV cases.

Table 4 Results of Base-Case Scenario

	No Vaccine	RSVpreF Vaccine	Difference
Clinical Outcomes			
Number of RSV cases			
Hospital	330.958	288.545	−42.249
Emergency Department	242.629	217.611	−25.018
Outpatient Clinic	3.157.169	2.910.115	−247.054
Total cases	3.730.756	3.416.270	−314.486
RSV-related deaths	64.455	57.292	−7.163
Life-years (LYs)			
Undiscounted	63.000.467	63.051.503	51.033
Discounted	52.805.777	52.847.415	41.638
Quality-Adjusted Life-Years (QALYs)			
Undiscounted	44.108.779	44.154.502	36.723
Discounted	37.138.650	37.168.967	30.317
Cost in million, EUR			
Direct cost			
Medical care	1.887.73 €	1.626.47 €	−261.26 €
Vaccine	0.00 €	681.88 €	681.88 €
Administration	0.00 €	23.34 €	23.34 €
Total	1.887.73 €	2.426.22 €	484.37 €
Cost-effectiveness analysis (discounted values, €)			
Cost per LY		10,662	
Cost per QALY		14,644	

Abbreviation: RSV, Respiratory Syncytial Virus.

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Table 5 Results of Alternative Scenario

	No Vaccine	RSVpreF Vaccine	Difference
Clinical Outcomes			
Number of RSV cases			
Hospital	496.559	465.499	−31.061
Emergency Department	366.217	347.567	−18.650
Outpatient Clinic	4.736.910	4.565.021	−171.890
Total cases	5.599.687	5.378.086	−221.600
RSV-related deaths	67.391	64.824	−2.567
Life-years			
Undiscounted	96.313.346	96.352.690	39.345
Discounted	70.784.187	70.812.616	28.429
Quality-Adjusted Life-Years (QALYs)			
Undiscounted	65.263.084	65.290.607	27.522
Discounted	48.562.675	48.583.070	20.395
Cost in million, EUR			
Direct cost			
Medical care	2.472.09 €	2.281.97 €	−190.12 €
Vaccine	0.00 €	492.01 €	492.01 €
Administration	0.00 €	16.84 €	16.84 €
Total	2.472.09 €	2.790.82 €	318.73 €
Cost-effectiveness analysis (discounted values, €)			
Cost per LY		11,211	
Cost per QALY		15,628	

From a mortality perspective, the number of RSV-related deaths decreased from 64,455 to 57,292, corresponding to a reduction of 7163 deaths.

The life-year analysis shows an increase in both LYs and QALYs following RSVpreF vaccination. The total life-years gained (discounted LYs) was 41,638, while the increase in QALYs (discounted) was 30,317.

Cost Analysis

The costs associated with RSV infection management vary significantly depending on the chosen strategy. Without vaccination, total medical care expenditure was €1887.73 million. With vaccination, medical care costs decreased to €1626.47 million (- 261.26 million). Including vaccine acquisition (€681.88 million) and administration (€23.34 million), total direct costs increased to €2426.22 million, €484.37 million higher than no vaccination. No indirect costs associated with productivity, whether due to morbidity or mortality, were analysed in either of the strategies analyzed.

Cost-Effectiveness Analysis

The cost-effectiveness analysis indicates a cost per LY gained of 10,662 and a cost per QALY gained of 14,644, which falls within the accepted threshold.

Alternative Scenario

Clinical Outcomes

In the alternative scenario, the RSVpreF vaccine demonstrated a substantial reduction in the number of RSV infections. Overall, a total decrease of 221,600 cases was observed compared to the no-vaccination strategy. Specifically, hospitalizations declined from 496,559 to 465,499 (−31,061), while emergency department visits decreased from 366,217 to 347,567 (−18,650). The most notable reduction occurred in outpatient care, with 171,890 fewer RSV cases reported.

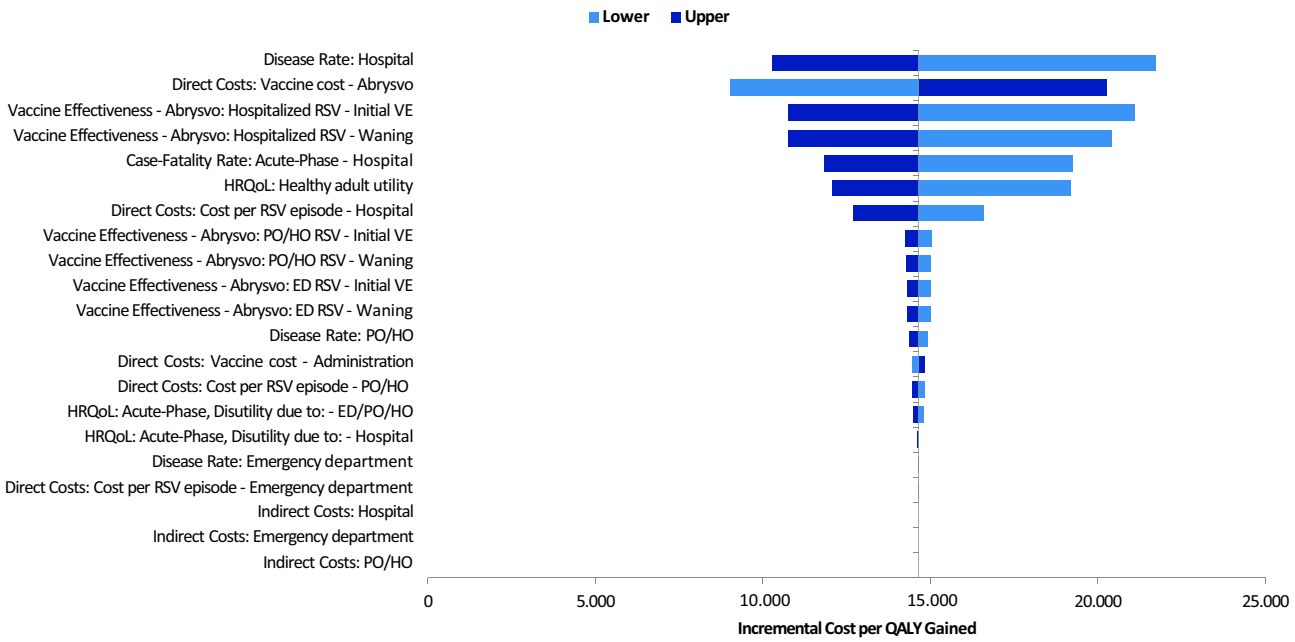

Figure 3 Results of DSA (base-case scenario).

In terms of mortality, RSV-related deaths decreased from 67, 391 to 64,824, corresponding to a reduction of 2567 deaths.

The life-year analysis revealed an increase in both LYs and QALYs following RSVpreF vaccination. The total life-years gained (discounted LYs) amounted to 28,429, while the increase in QALYs (discounted) was 20,395.

Cost Analysis

The analysis of direct healthcare costs indicates that, in the absence of vaccination, total medical care expenditure was estimated at €2472.09 million. Following the introduction of vaccination, medical care costs decreased to €2281.97 million, corresponding to savings of €190.12 million. However, the vaccination program incurred an additional €508.85 million, including €492.01 million for vaccine acquisition and €16.84 million for administration. As a result, the total direct costs under the vaccination scenario reached €2790.82 million, representing an incremental cost of €318.73 million compared with the no-vaccination scenario.

Cost-Effectiveness Analysis

The cost-effectiveness analysis indicated a cost per LY gained of 11.211 and a cost per QALY gained of 15.628, both within the commonly accepted willingness-to-pay threshold.

Sensitivity Analysis

DSA and PSA confirmed the robustness of the results, indicating that variations in key parameters did not significantly alter the overall conclusions of the study.

The results of the base scenario are illustrated in Figures 3 and 4, while those of the alternative scenario are shown in Figures 5 and 6.

Discussion

This study demonstrates that the introduction of the RSVpreF vaccine has the potential to significantly reduce RSV-associated disease cases, including hospitalizations and RSV-related deaths, in a cost-effective manner. In the base-case scenario, implementing a vaccination strategy for adults aged ≥75 years resulted in an ICER of approximately €14,600/QALY, well below the commonly accepted WTP thresholds in Italy. The alternative scenario, targeting adults aged 60–74 years with comorbidities, yielded a comparable ICER (€15,600/QALY), further confirming the economic sustainability of this intervention.

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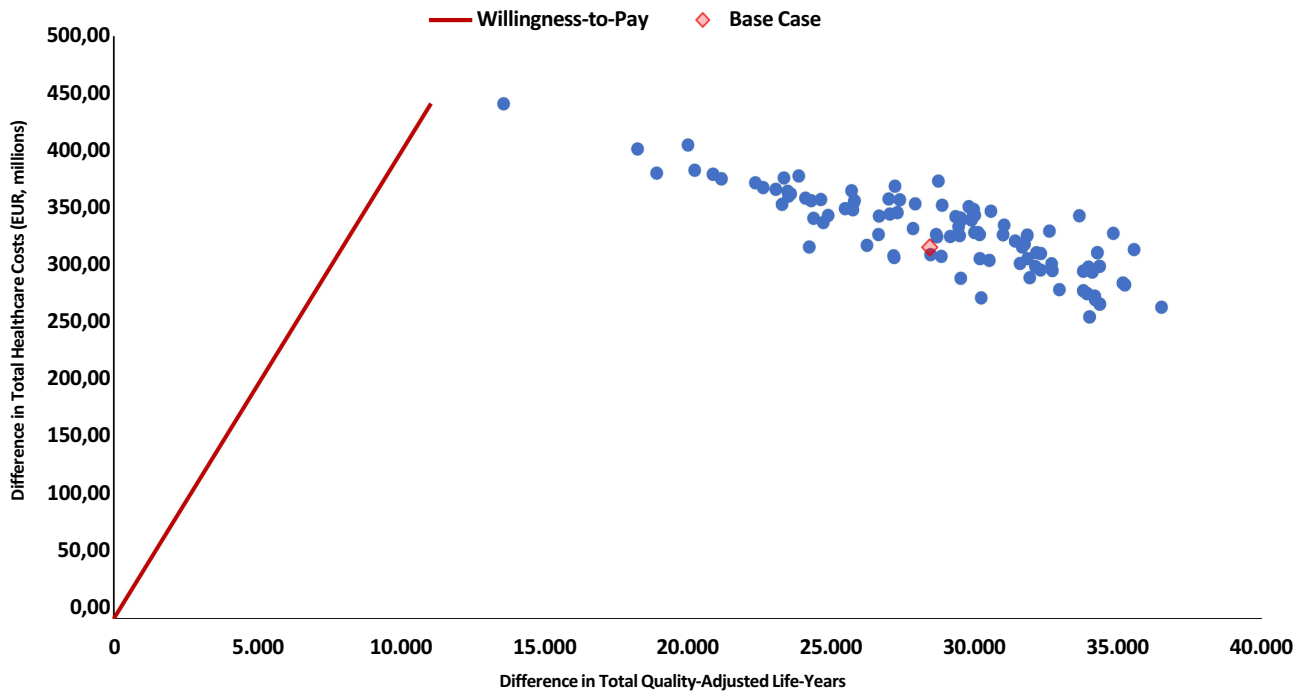

Figure 4 Results of the PSA (base-case scenario).

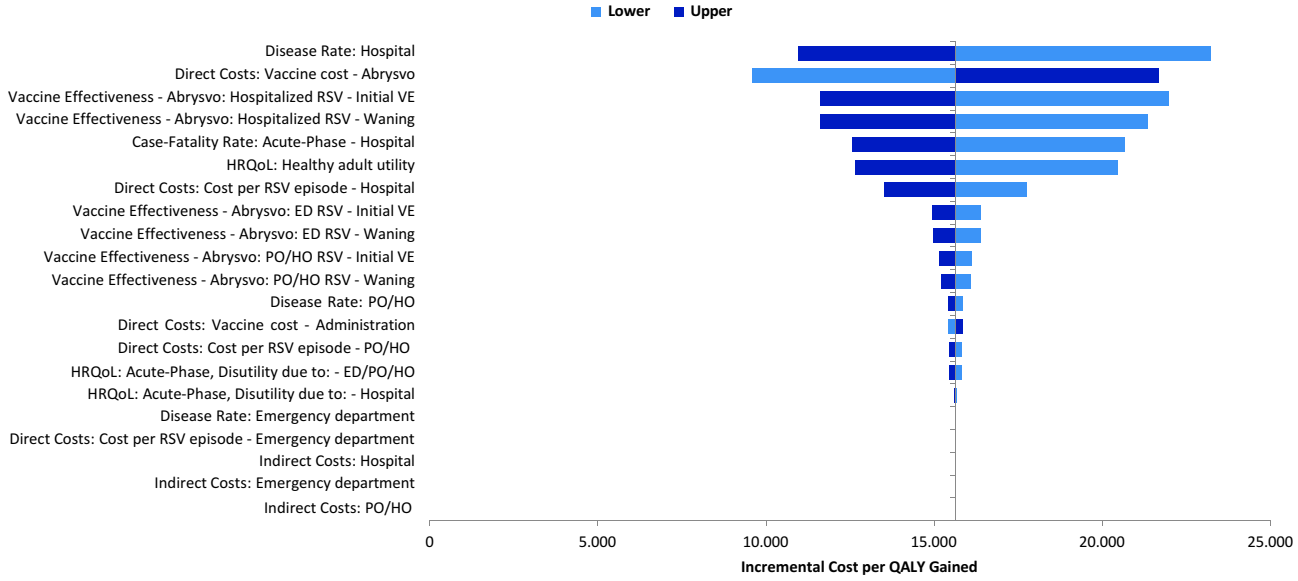

Figure 5 Results of DSA (alternative scenario).

These findings highlight the importance of establishing an effective preventive strategy in which vaccination plays a central role in mitigating both the clinical and economic burden of RSV infection. In our analysis, introducing RSVpreF vaccination in adults ≥75 years was associated with more than 314,000 fewer RSV cases and over 7000 fewer deaths, generating a reduction of approximately €261 million in direct medical costs—primarily driven by the reduction in hospitalizations and outpatient visits due to acute disease episodes, partially offset by vaccination program costs.

RSV infection has long been underestimated in adults, despite its clinical severity and high healthcare resource use. Comparative analyses with influenza suggest that RSV is associated with longer and more complex clinical courses, an average hospital stay of 6 days[33] versus 3.6[33] for influenza, reflecting a greater morbidity and healthcare burden. The

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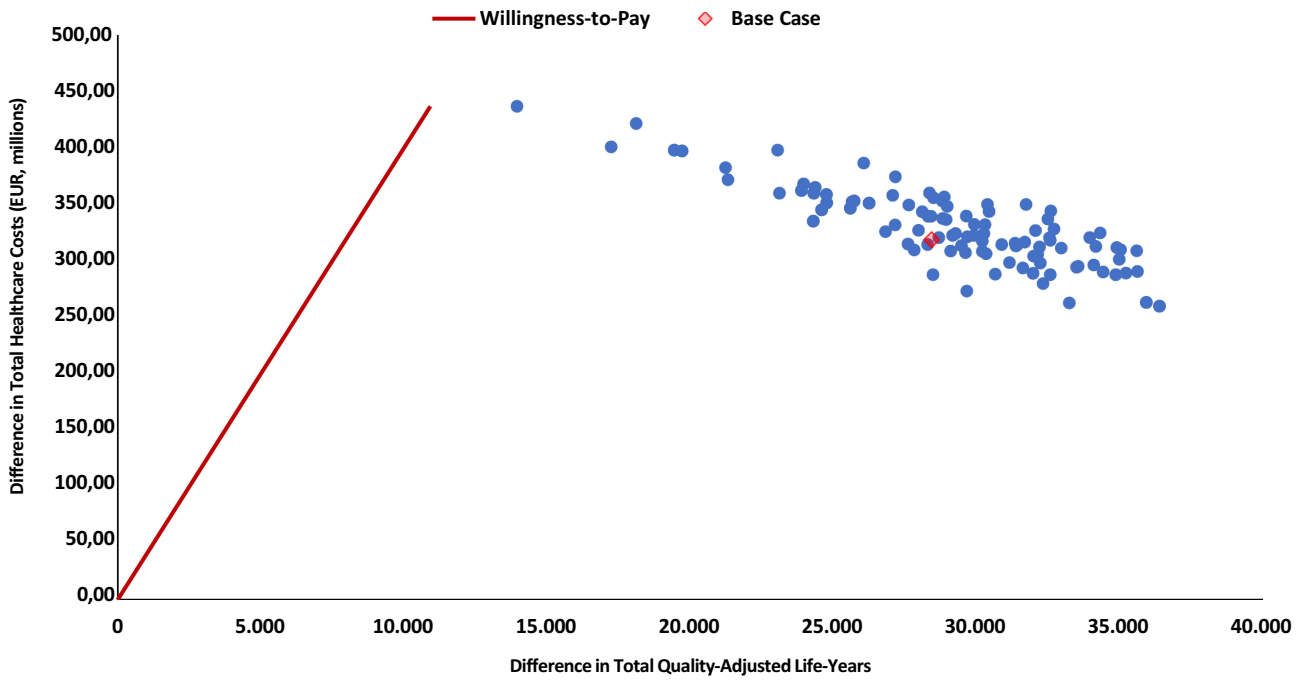

Figure 6 Results of the PSA (alternative scenario).

results of this analysis underscore the significant public health value of RSVpreF vaccination in improving clinical outcomes and preserving healthcare sustainability.

RSVpreF vaccine represents a highly effective vaccination strategy with a bivalent formulation, which includes antigens derived from both RSV A and RSV B subgroups.[1,2] The bivalent nature may be an advantage should significant mutations appear in the future that would render cross-protection more labile. As a matter of fact, a study on sequence variability of the RSV fusion gene (F) showed that, although antigenic sites of RSV F are generally well conserved, differences are observed. Discrepancies are accented in the antigenic sites in pre-fusion F genes of RSV/B isolates.[34]

RSVpreF vaccine has been approved in Europe for several populations. It is currently indicated for pregnant women to protect infants from birth to 6 months, as well as for individuals aged 60 years and older. More recently, it has also been approved for adults aged 18 and above. This broader applicability underscores the vaccine's versatility and its potential to offer extended protection across various demographic groups.

At the European level, several countries, including Germany, Greece, France, Belgium, and Spain, have already recommended RSV vaccination for pregnant women and older adults. Cost-effectiveness analyses conducted in Germany[11] (ICER: €32,335/QALY) and Greece[12] (ICER: €19,723/QALY) confirm our findings, supporting the value of RSVpreF vaccination in populations at risk.

The main difference between the Italian and the German study concerns the population analyzed. In the present study, adults aged 60–74 years with comorbidities were evaluated in the alternative scenario, while the entire cohort aged 75–99 years was considered as a single risk group in the base-case scenario. In contrast, the German study stratified the population by age classes and comorbidity profile. This different segmentation influences the estimated RSV incidence, hospitalization, and mortality rates and, consequently, the resulting ICER.

Moreover, although both studies applied the same QALY losses for hospitalized and non-hospitalized RSV cases, the differences primarily stem from the cost components, including vaccine price, administration costs, and case management costs. These elements reflect the structural and tariff-specific characteristics of the respective healthcare systems and ultimately affect the final ICER estimates.

In Italy, although awareness of RSV is increasing, the current National Immunization Plan (PNPV 2023–2025)[35] does not yet include RSV vaccination for adults. Based on the evidence presented here, the integration of RSVpreF into the

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Italian vaccination calendar could represent a crucial step toward reducing RSV-related morbidity, mortality, and healthcare expenditure. This is particularly relevant in a demographic context characterized by rapid population aging and the high prevalence of chronic diseases. Beyond the general population, particular attention should be given to adults with comorbidities. Vaccination against RSV would be especially advantageous for individuals with chronic illnesses, who represent a large share of RSV-related hospitalizations. Even when the infection shows mild symptoms, these patients face a higher risk of severe complications and higher mortality rates.[36]

Our analysis is consistent with the current Italian epidemiological landscape and includes two key population groups: individuals aged ≥75 years and those aged 60–74 years with comorbidities, accounting for approximately 48% of the older adult population, as reported by the PASSI d'Argento surveillance system.[16] This 48% represents a relatively high value, as it encompasses a wide range of chronic conditions of varying severity, not all of which necessarily constitute a risk factor for RSV infection. Nevertheless, this estimate was adopted to reflect a pragmatic and adaptable approach, allowing policymakers to adjust the target population based on specific epidemiological and healthcare priorities.

A vaccination coverage rate of 52.5%[13] was assumed in the model, based on influenza vaccination rates in adults aged ≥65 years. Although this value may overestimate coverage in the 60–74 age group and underestimate it in individuals aged ≥75 years, the model's results are independent of vaccination coverage, and therefore this parameter does not influence the overall cost-effectiveness outcomes.

Despite these promising findings, our analysis has several important limitations, mainly related to uncertainty surrounding input values. Due to the limited availability of scientific literature on RSV in adults, it was not always possible to rely on Italian sources to estimate RSV incidence across different healthcare settings. Specifically, hospitalization rates were derived from a study conducted in the United Kingdom, while mortality data came from a Danish study. Moreover, because of the scarcity of RSV-specific data, some parameters were extrapolated from influenza-related evidence, such as vaccination coverage rates and outpatient management costs. An additional limitation concerns vaccine efficacy estimates, which were based on the RENOIR clinical trial. To this analysis, a duration of protection of four years was assumed. Vaccine efficacy waning was modeled as gradual over time, although this assumption is not currently supported by robust empirical data. Overall, while further research is warranted to refine these estimates and validate assumptions, the introduction of RSVpreF vaccine appears to be a promising and sustainable strategy for reducing the clinical and economic burden of RSV in older adults.

Conclusions

The results of this evaluation suggest that the use of RSVpreF in older adults in Italy, compared with no vaccination, could reduce both the health and economic burden associated with RSV representing a valuable and cost-effective public health investment.

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