White Paper

Economic Burden of Respiratory Syncytial Virus (RSV) Infection Among Older Adults in Select Asia-Pacific Economic Cooperation (APEC) Countries*

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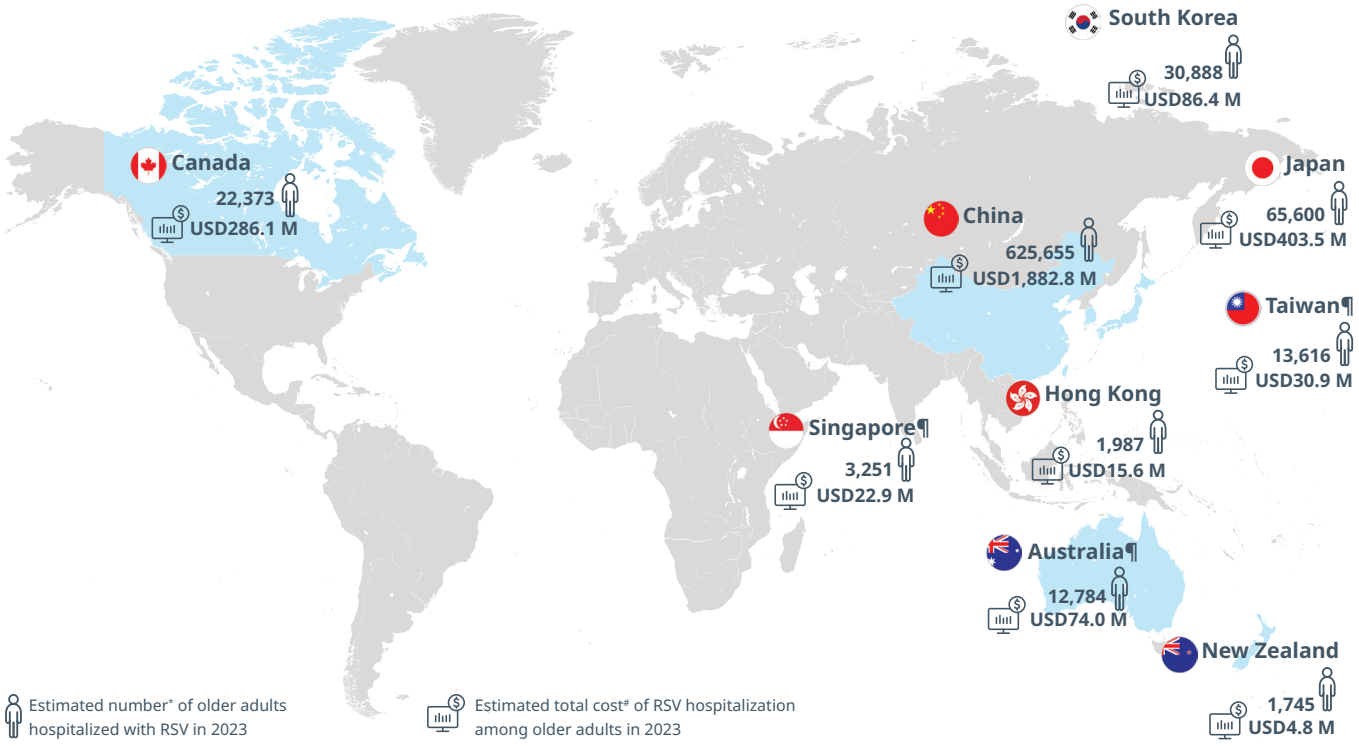
Executive summary

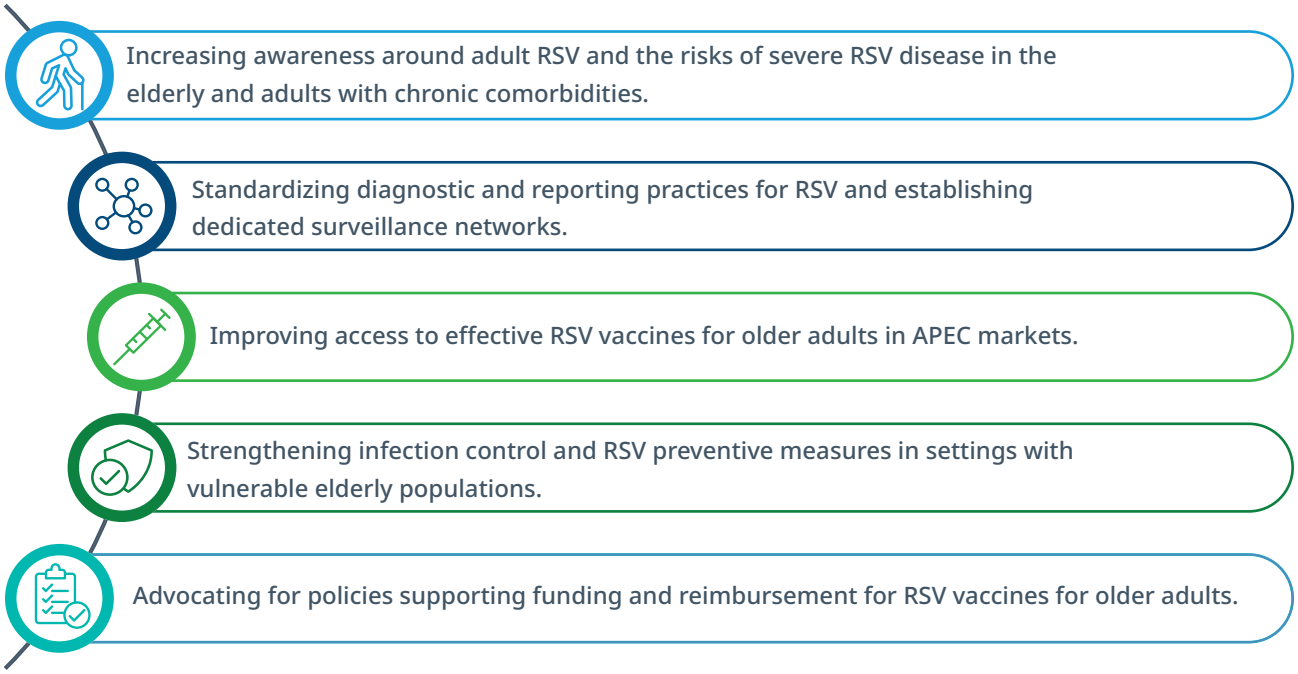
- Respiratory Syncytial Virus (RSV) is a common and contagious respiratory pathogen that can lead to lower respiratory tract disease, including pneumonia, and is responsible for approximately 5.2 million cases and 33,000 in-hospital deaths annually in older adults (age ≥60 years) in high-income countries.
- Older adults are at a higher risk of RSV infection due to immune decline, lung aging, and comorbidities like Chronic Obstructive Pulmonary Disease (COPD), asthma, and heart failure and are more likely to develop severe RSV disease leading to hospitalizations, intensive care unit admissions, and exacerbation of underlying chronic medical conditions.
- The economic burden of RSV on healthcare systems across countries of the Asia-Pacific Economic Cooperation (APEC) is expected to be substantial, however estimating the true clinical and economic burden is challenging due to the lack of epidemiological and healthcare resource use data in older adults.
- Leveraging published literature, we estimated that RSV was associated with **778,000 hospitalizations and 2.8 billion United States dollars (USD) in hospitalization costs in 2023** in select high-income APEC countries (China, Japan, South Korea, Canada, Singapore, New Zealand, Australia, Hong Kong, Taiwan). The highest estimated burden was seen in China (USD ~1.9 billion), followed by Japan (USD ~400 million) and Canada (USD ~290 million).
- Across the countries, an average of **one** in **500** older adults **were hospitalized annually** with RSV, and the estimated cost of a hospitalization episode varied across countries from USD 2,735 in New Zealand to USD 12,826 in Canada. A substantial clinical and economic burden was noted across all the countries.
- With the recent availability of safe and effective vaccines to protect older adults against RSV disease, policymakers, government agencies, and decision-makers should consider the significant impact of RSV preventive strategies on easing the burden on healthcare systems and economies.



APEC: Asia-Pacific Economic Cooperation; M: Million; Older adults refer to adults ≥60 years of age.
* RSV incidence estimates were adjusted for under-ascertainment using a x1.5 multiplier (McLaughlin, et al.; 2022) and extrapolated to the 2023 older adult population based on national statistics.
# Costs are adjusted for inflation till 2023, and where applicable, the local currency was converted to United States dollars (USD) based on the exchange rate of 2023.
¶ Country-specific adult RSV hospitalization costs were unavailable, and influenza hospitalization costs in adults aged ≥60 years was used as a proxy.

Urgent action is needed to address the growing impact of RSV infections in older adults on healthcare systems.

Strategies to address the growing burden of RSV in select APEC countries



It is the shared responsibility of healthcare practitioners, public health bodies, and policymakers to improve patient outcomes and promote preventive strategies for RSV in older adults.

List of abbreviations

APEC	Asia-Pacific Economic Cooperation
ARI	Acute Respiratory Infection
COPD	Chronic Obstructive Pulmonary Disease
EU	European Union
ICU	Intensive Care Unit
LRTD	Lower Respiratory Tract Disease
PLR	Pragmatic Literature Review
RSV	Respiratory Syncytial Virus
US	United States
USD	United States Dollars

Introduction

Communicable diseases account for approximately 414.7 million cases worldwide[1] and are a major cause of morbidity and mortality[2].

Acute Respiratory Infections (ARIs) form a significant portion of communicable diseases, with viral pathogens accounting for the majority of upper ARIs[3].

Clinical burden of Respiratory Syncytial Virus in older adults

Respiratory Syncytial Virus (RSV) is a common and contagious viral pathogen that causes ARI in individuals of all ages, with a notable disease burden among children (≤5 years) and older adults (≥65 years)[4].

In 2019, an estimated ~5.2 million cases, 470,000 hospitalizations, and 33,000 in-hospital deaths among older adults in high-income countries were due to RSV[5].

Older adults are at a greater risk of RSV infection due to age-related immune decline, lung aging, and higher rates of underlying chronic comorbidities such as Chronic Obstructive Pulmonary Disease (COPD), asthma, and heart diseases, particularly heart failure[6-10]. Older adults are more likely to develop RSV-related lower respiratory tract disease (LRTD), which often leads to hospitalizations and in some cases intensive care unit (ICU) admissions and death[9, 10]. RSV can also exacerbate underlying chronic conditions and lead to a cascading health decline, rehospitalizations, and loss of independence even after the acute episode has resolved[11].

RSV is particularly burdensome among older adults living in nursing homes or long-term care facilities[12-14]. In these environments, they are more vulnerable to infections and their complications due to higher rates of disease transmission, close quarters among residents, multimorbidity, and frailty. This further results in complex disease management and poorer health outcomes[15].

Economic burden of Respiratory Syncytial Virus in older adults

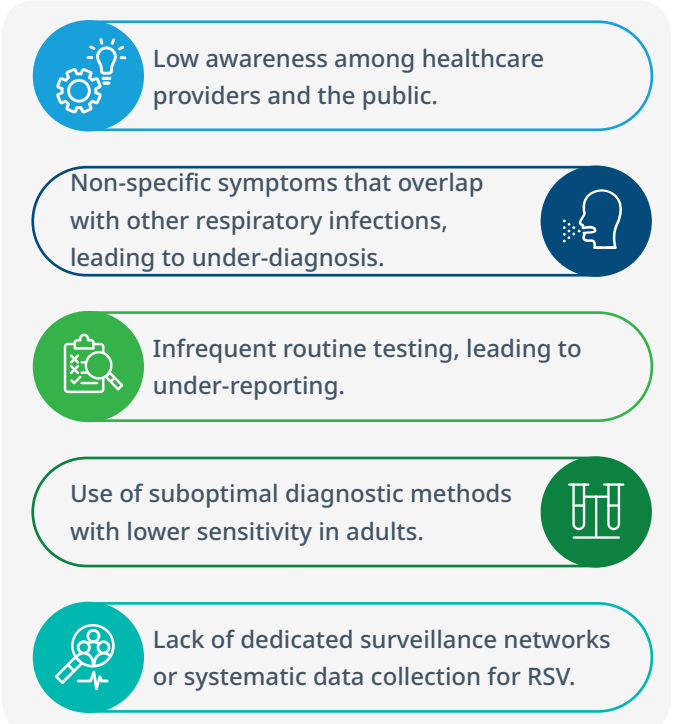
The burden of RSV on health systems is considerable, both on sustainability and capacity as well as on healthcare expenditures[16].

RSV-associated LRTD in older adults often requires extended hospital stays, intensive care, and significant resource use, which drives up healthcare costs[17]. Globally, the economic burden associated with RSV among older adults is significant. For instance, in the United States (US), the economic burden of RSV among high-risk older adults is estimated to be around United States dollars (USD) 6.6 billion annually[18].

Gaps in understanding the burden of RSV in Asia-Pacific region

The burden of RSV on healthcare systems across countries of the Asia-Pacific Economic Cooperation (APEC) is expected to be substantial; however, estimating the true clinical and economic burden is challenging due to the lack of epidemiological and healthcare resource use data in older adults. The reasons for under-recognition of RSV in older adults are listed in Figure 1[4, 19-22].

Figure 1: Low awareness of RSV in the selected APEC countries is attributed to a number of reasons



Abbreviation: RSV, Respiratory Syncytial Virus.

Routine testing for RSV is not done in clinical practice because clinical symptoms are non-specific and often overlap with those of other respiratory infections. Diagnosis is usually based on local epidemiology as opposed to laboratory testing. Consequently, RSV testing is not consistently performed in adults and, when performed, may employ suboptimal methods with lower sensitivity in adults[23]. Furthermore, there is a lack of specific treatment for RSV, which contributes to testing hesitancy. However, this situation is evolving as safe and effective vaccines to prevent RSV disease in older adults are now becoming available[24].

There is also a lack of dedicated surveillance systems for RSV in the APEC region as compared to countries in the European Union (EU) and the US where active RSV surveillance[25, 26] networks provide useful and timely insights to policymakers.

Studies on the economic impact of RSV in older adults in APEC countries are also limited.

With the recent availability of safe and effective vaccines to protect older adults against RSV disease, there is an urgent need for policymakers, government agencies, and other decision-makers to evaluate the potential positive impact of preventive RSV strategies on the healthcare systems and economies.

In this article, we have estimated the economic burden of hospitalization for RSV among older adults from select high-income APEC countries*.

The findings would facilitate formulation of data-driven policies to protect the vulnerable elderly and make decisions on effective healthcare resource allocation.

A Pragmatic Literature Review (PLR) was conducted to identify published evidence on the incidence and costs associated with RSV hospitalizations among older adults (aged ≥60 years) in select APEC countries.

Details of the PLR approach and the articles extracted can be found in the **Annexure 1**.

Annexure table 1 presents detailed information on the data extracted from the literature review.

RSV hospitalization incidence rate among older adults in select APEC countries

A lack of comprehensive data on RSV in older adults was observed across the countries. Published studies were limited to specific subpopulations or care settings, resulting in gaps in the overall understanding of the clinical and economic burden of RSV.

The RSV hospitalization incidence rate among older adults ranged from 57 to 146 per 100,000 population **(Table 1)**[5, 27-31]. The highest reported incidence rate was in Canada[28], while the lowest was in Hong Kong[27]. The lower observed rates in Hong Kong are likely due to utilization of antigen-based testing, which has shown lower sensitivity for RSV detection, particularly among adults[32]. Country-specific RSV hospitalization estimates were not available for Taiwan, South Korea, Singapore, and China, highlighting the critical need for epidemiological studies in these countries to understand the full burden of RSV disease in the elderly.

RSV-associated hospitalizations among older adults in select APEC countries in 2023

To estimate the number of RSV-associated hospitalizations, the RSV hospitalization incidence rates for each country were extrapolated to the older adult population of 2023 based on national statistics[33-41].

Due to the lack of country-specific RSV hospitalization incidence rates, pooled estimates from a recent meta-analysis were used for Taiwan, South Korea, Singapore, and China[5].

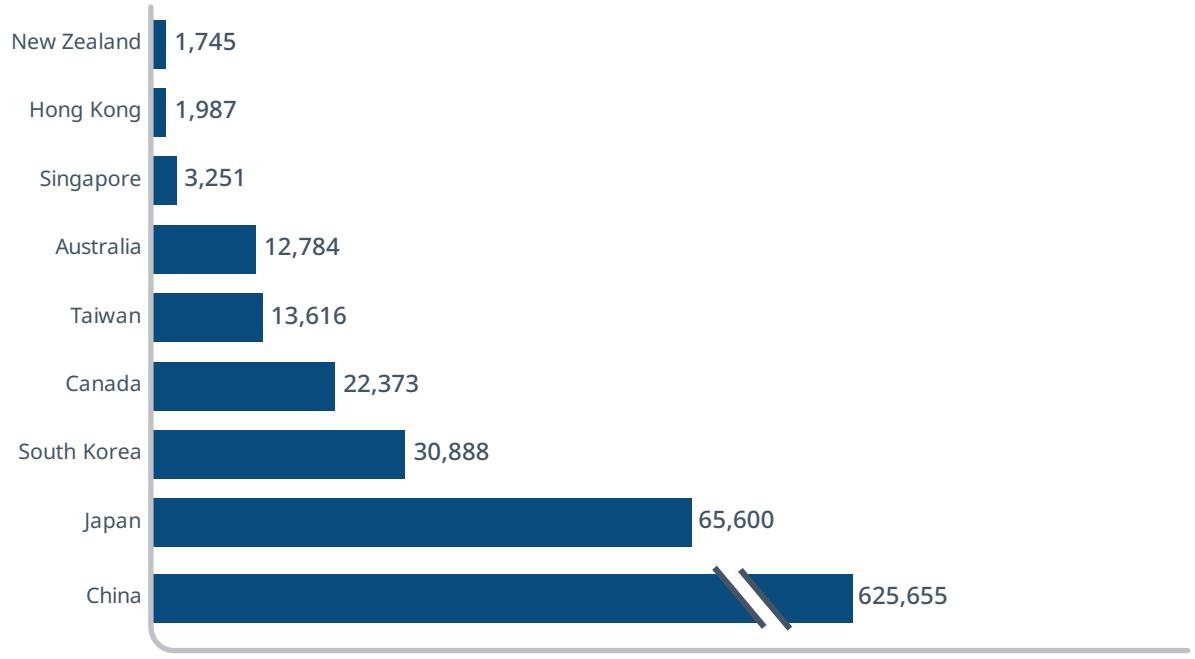
Economic evaluations for RSV often utilize a 'multiplier' to account for the under-reported incidence of RSV[42]. We used a similar approach with a ×1.5 multiplier to adjust for RSV under-reporting[43].

* China, Japan, South Korea, Canada, Singapore, New Zealand, Australia, Hong Kong, and Taiwan

Across select APEC countries, an average of 1 in 500 older adults were hospitalized annually with RSV, with an estimated 778,000 hospitalizations in 2023.

The number of RSV hospitalizations in older adults ranged between ~2,000 to ~3,000 in New Zealand, Hong Kong, and Singapore, to between ~13,000 to ~31,000 in Taiwan, Canada, and South Korea with the highest numbers estimated for Japan (~66,000) and China (~625,000) **(Table 1, Figure 2)**. While the higher number of hospitalizations in more populous countries is expected, it underscores the **significant impact RSV would have on healthcare systems with rapid aging** particularly as 1 in 2-3 individuals in APEC are projected to be aged 60 and above by 2050[44].

Figure 2: Estimated number of Respiratory Syncytial Virus-associated hospitalizations among older adults in Asia-Pacific Economic Cooperation region in 2023.



Abbreviation: APEC, Asia-Pacific Economic Cooperation.

Cost of RSV hospitalization episode among older adults in select APEC countries

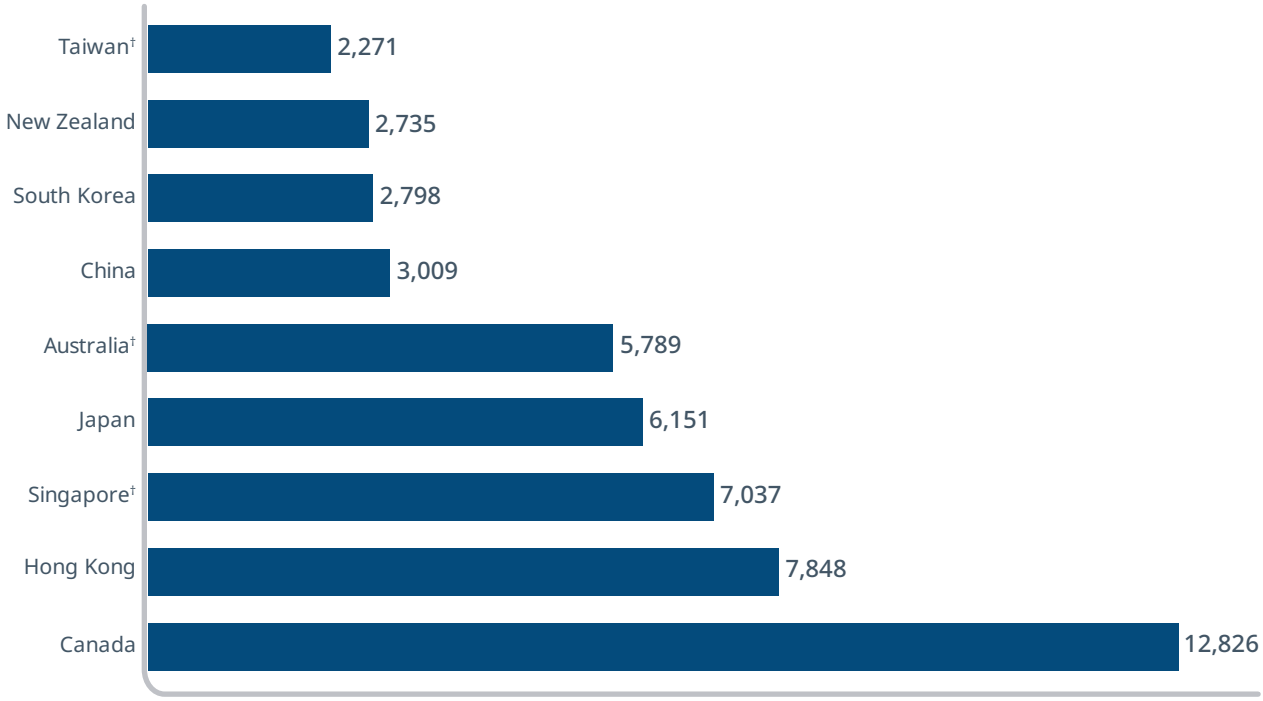
Publications on the economic burden and hospitalization costs of RSV in older adults in APEC were limited. For countries without adult RSV hospitalization costs, influenza hospitalization cost in adults aged ≥60 years was used as a proxy. Influenza was considered an appropriate proxy, given both these viruses exhibit comparable severity, mortality burden, and healthcare resource use[45-47]. Additionally, studies in the US have reported that the cost of RSV hospitalization in older adults was comparable to that of influenza[48].

Hospitalization costs were adjusted for inflation till 2023, and where applicable, the local currency was converted to United States dollars (USD) based on the exchange rate of 2023[49-61]. Details of the cost calculations can be found in the **Annexure 2**.

The RSV hospitalization cost across the countries ranged from ~USD 2,700 to ~USD 13,000, with New Zealand reporting the lowest and Canada reporting the highest costs[31, 62-66]. Several factors, including variability in healthcare systems, economic disparities, access to healthcare, health-seeking behaviors, and government policies, likely contributed to the variation in RSV hospitalization costs across countries[67, 68].

Due to the unavailability of country-specific RSV hospitalization costs in Taiwan, Australia, and Singapore, the influenza hospitalization cost was used as a proxy and ranged from ~USD 2,300 to ~USD 7,000 (Table 1, Figure 3)[69-71].

Figure 3: Respiratory Syncytial Virus-associated hospitalization cost per person among older adults in the APEC region in 2023

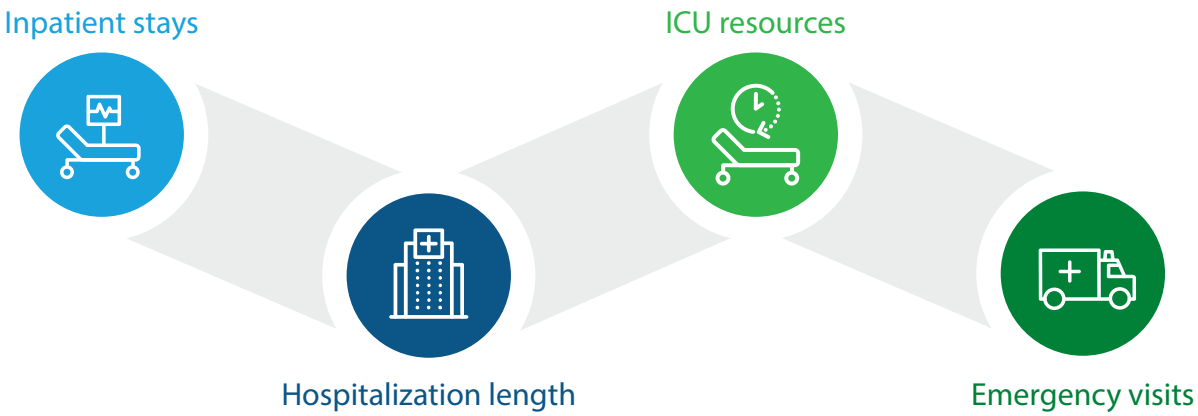


Respiratory syncytial virus-associated hospitalization cost per person among older adults in the APEC region in 2023.

Abbreviation: APEC, Asia-Pacific Economic Cooperation.
Note: †Country-specific adult RSV hospitalization costs were unavailable, and influenza hospitalization costs in older adults aged ≥60 years was used as a proxy.

In the articles chosen for this study, RSV was linked to a high per-person direct medical cost among older adults, considering the components presented in **Figure 4**.

Figure 4: Components considered for per-person direct medical cost of Respiratory Syncytial Virus

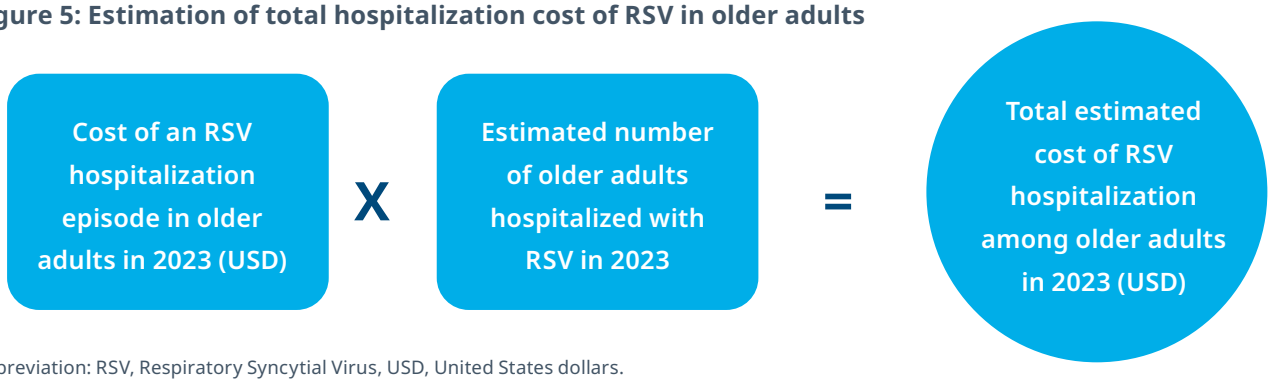


Abbreviation: ICU, intensive care unit.

Estimated total economic burden of RSV-associated hospitalizations among older adults in select APEC countries in 2023

To calculate the estimated total economic burden of RSV hospitalization, the cost of hospitalization for RSV (or influenza as a proxy) in the respective APEC countries, was multiplied by the number of estimated RSV hospitalizations among older adults in 2023 **(Figure 5)**.

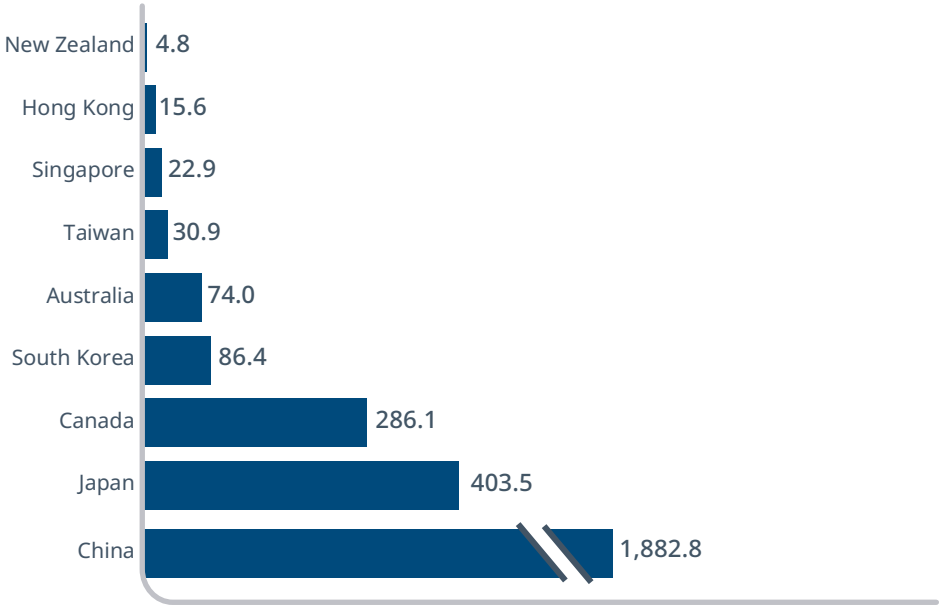
Figure 5: Estimation of total hospitalization cost of RSV in older adults



Abbreviation: RSV, Respiratory Syncytial Virus, USD, United States dollars.
Note: Country-specific adult RSV hospitalization costs were unavailable for Taiwan, Australia, and Singapore, and influenza hospitalization costs in older adults aged ≥60 years was used as a proxy.

A substantial clinical and economic burden was noted across all the countries. The highest estimated burden was seen in China (USD ~1.9 billion), followed by Japan (USD ~400 million) and Canada (USD ~290 million) (Table 1, Figure 6).

Figure 6: Estimated economic burden (in millions) of RSV-associated hospitalization among older adults in select APEC countries in 2023.



Estimated economic burden (in millions) of respiratory syncytial virus-associated hospitalizations among older adults in APEC countries in 2023.

Abbreviation: APEC, Asia-Pacific Economic Cooperation.

Overall, RSV in older adults was associated with 2.8 billion USD in hospitalization costs in select APEC countries in 2023.

Table 1: Respiratory Syncytial Virus-associated hospitalization incidence rate, number, and cost among older adults aged ≥60 years in 2023

COUNTRY	RSV HOSPITALIZATION INCIDENCE IN ADULTS AGED ≥60 YEARS (PER 100,000 POPULATION)	ESTIMATED NUMBER* OF ADULTS AGED ≥60 YEARS HOSPITALIZED WITH RSV IN 2023	COST# OF RSV HOSPITALIZATION IN ADULTS AGED ≥60 YEARS IN 2023 (USD)	TOTAL COST OF RSV HOSPITALIZATION AMONG ADULTS AGED ≥60 YEARS IN 2023 (USD)
China	150[1]	625,655	3,009[7]	1,882.8 M
Japan	100[2]	65,600	6,151[8]	403.5 M
Canada	146[3]	22,373	12,826[3]	286.1 M
South Korea	150[1]	30,888	2,798[9]	86.4 M
Australia	139[4]	12,784	5,789[10¶]	74.0 M
Taiwan	150[1]	13,616	2,271[11¶]	30.9 M
Singapore	150[1]	3,251	7,037[12¶]	22.9 M
Hong Kong	57[5]	1,987	7,848[13]	15.6 M
New Zealand	99[6]	1,745	2,735[6]	4.8 M

Older adults refer to adults ≥60 years of age, APEC: Asia-Pacific Economic Cooperation.

* RSV incidence estimates were adjusted for under-ascertainment using a x1.5 multiplier (McLaughlin, et al.; 2022) and extrapolated to the 2023 older adult population based on national statistics.

Costs are adjusted for inflation till 2023, and where applicable, the local currency was converted to United States dollars (USD) based on the exchange rate of 2023.

¶Country-specific adult RSV hospitalization costs were unavailable, and influenza hospitalization costs in adults aged ≥60 years was used as a proxy.

1. Savic, et al. Influenza and other respiratory viruses (2023)
2. Kurai, et al. Influenza and other respiratory viruses (2022)
3. ElSherif, et al. Open Forum Infect Dis (2023)
4. Foley, et al. Viruses. (2024)
5. Chan, et al. Medicine. (2015)
6. Prasad, et al. PloS one (2020)
7. Chen, et al. Eur J Clin Microbiol Infect Dis (2021)
8. Igarashi, et al. Future Virol. (2023)
9. Yoon, et al. Sci Rep. (2020)
10. Newall, et al. Vaccine (2008)
11. Peasah, et al. Vaccine (2013)
12. Yue, et al. Value Health. (2019)
13. Wang, et al. Vaccines (2023)

Insights

Challenges in Asia

EXISTING HEALTHCARE LANDSCAPE

Pressure on healthcare systems across APEC is increasing due to the rapidly aging population and increasing prevalence of chronic comorbidities. This is further aggravated by inadequate medical staff to attend to the patients, long waiting times to access the right care providers, increasing cost of treatment and manpower, and lack of investments in preventive health[72].

AGE IS A CRUCIAL FACTOR IN THE CLINICAL BURDEN OF RSV INFECTION

RSV clinical burden is expected to rise as the population ages[15]. Most APEC countries had a high percentage of older adults, ranging from ~23% to 30% in 2023[73], and the older adult population is projected to increase significantly, ranging from ~30% to 50% by 2050[73].

This demographic shift presents substantial societal and financial challenges for these countries, including reduced savings rates and worsening government finances[74].

Accurate data on the RSV clinical and economic burden among older adults is valuable for guiding future prevention programs and crucial for regulatory decision-making and healthcare system planning. Consequently, these preventive measures will help reduce hospitalization among older adults, enabling healthier longevity.

EFFECTIVE INTERVENTIONS FOR RSV LOWER RESPIRATORY TRACT DISEASE WILL REDUCE THE BURDEN ON HEALTHCARE SYSTEMS

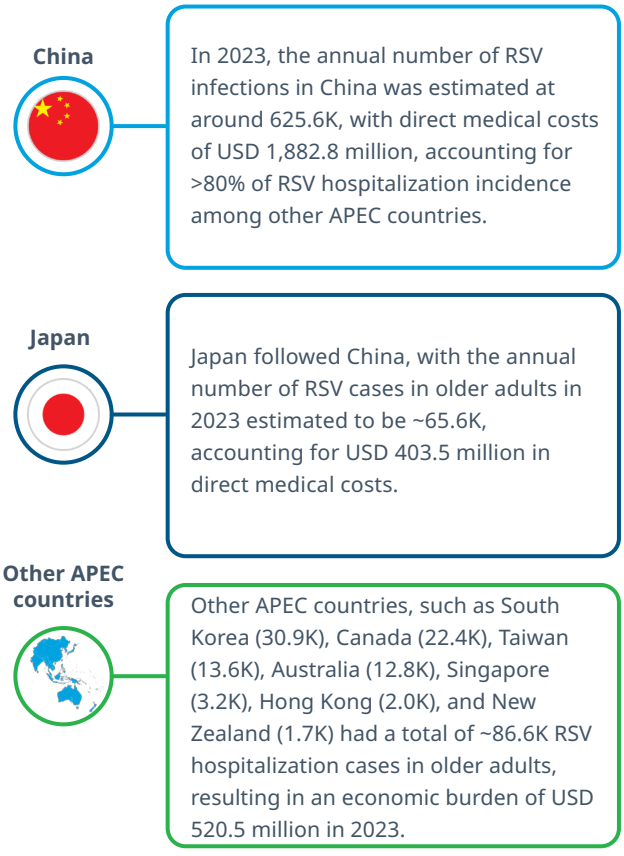
For the first time, as the culmination of over 50 years of research and development, safe and effective RSV vaccines to protect older adults are available[75]. RSV vaccination among older adults could reduce the burden of RSV by lowering health complications and hospitalization costs and is proven to be cost-effective[76].

Key Findings

RSV is associated with a substantial economic burden in select APEC countries.

Our study quantified the already published clinical and economic burden of RSV in select APEC countries, focusing on older adults. Key findings observed from our analysis are presented in **Figure 7**.

Figure 7: RSV hospitalizations and associated cost in older adults in Asia-Pacific countries



Abbreviations: APEC, Asia-Pacific Economic Cooperation; K, thousand; RSV, Respiratory Syncytial Virus; USD, United States dollars.

The direct medical cost related to RSV hospitalization rose significantly for patients with more severe outcomes, which were more frequently observed in older adults, especially those with pre-existing comorbidities[21].

Additionally, with the population of older adults in these APEC countries ranging from ~20% to ~36%, these estimates indicate increased pressure on healthcare systems, especially in future seasons when RSV may co-circulate with influenza and possibly SARS-CoV-2.

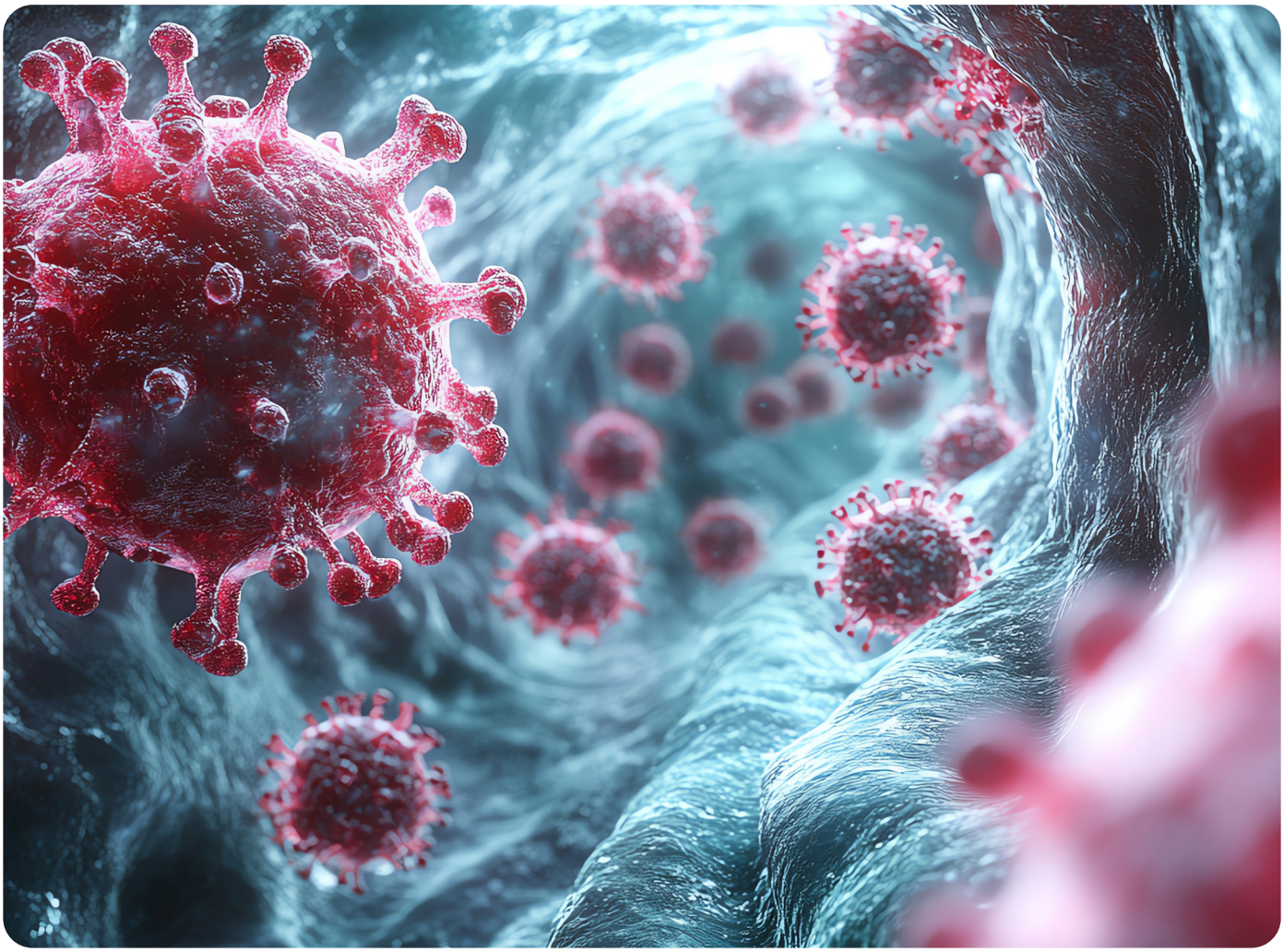
Burden of RSV in older adults of long-term care facilities

Older adults residing in long-term care settings such as nursing homes are particularly at risk of RSV, due to housing in close quarters which allows infections to spread more quickly. This, together with advanced age and multimorbidity, predisposes older adults to infections and associated complications. Among APEC countries, studies from Japan and South Korea reveal substantial RSV attack rates between ~24% to ~73% during outbreak situations in long-term care settings[13, 14].

Limitations

There were significant variations in results across regions, most likely due to differences in study designs, populations, and geographies. Several data gaps were discovered, including a lack of robust epidemiological data on clinical burden in Taiwan, South Korea, Singapore, and China. Data were insufficient to stratify analyses further, for example by age groups or comorbidity types.

The lack of data and heterogeneity of published studies limited the comparability and feasibility of a meta-analysis. Significant heterogeneity in cost estimation was also noted across studies, as many studies were unable to quantify the actual economic cost, making direct comparisons difficult.



Key Takeaways

There has been an increasing burden of vaccine-preventable respiratory diseases in terms of incidence, severity, and mortality rates, particularly among the aging population and those with chronic health issues such as asthma and COPD in the APEC region.

There is a significant need to establish strong foundations by enhancing primary, acute, and long-term care settings to lessen the burden of respiratory diseases across the APEC region. These could be crucial for:

- Vaccination and management of disease
- Managing chronic conditions more effectively and reducing the incidence of severe respiratory diseases
- Early detection and timely treatment

RSV is an established vaccine preventable respiratory disease that causes LRTD, resulting in ICU admission, hospitalization, and death. However, the true burden of RSV is under-reported in the APEC region.

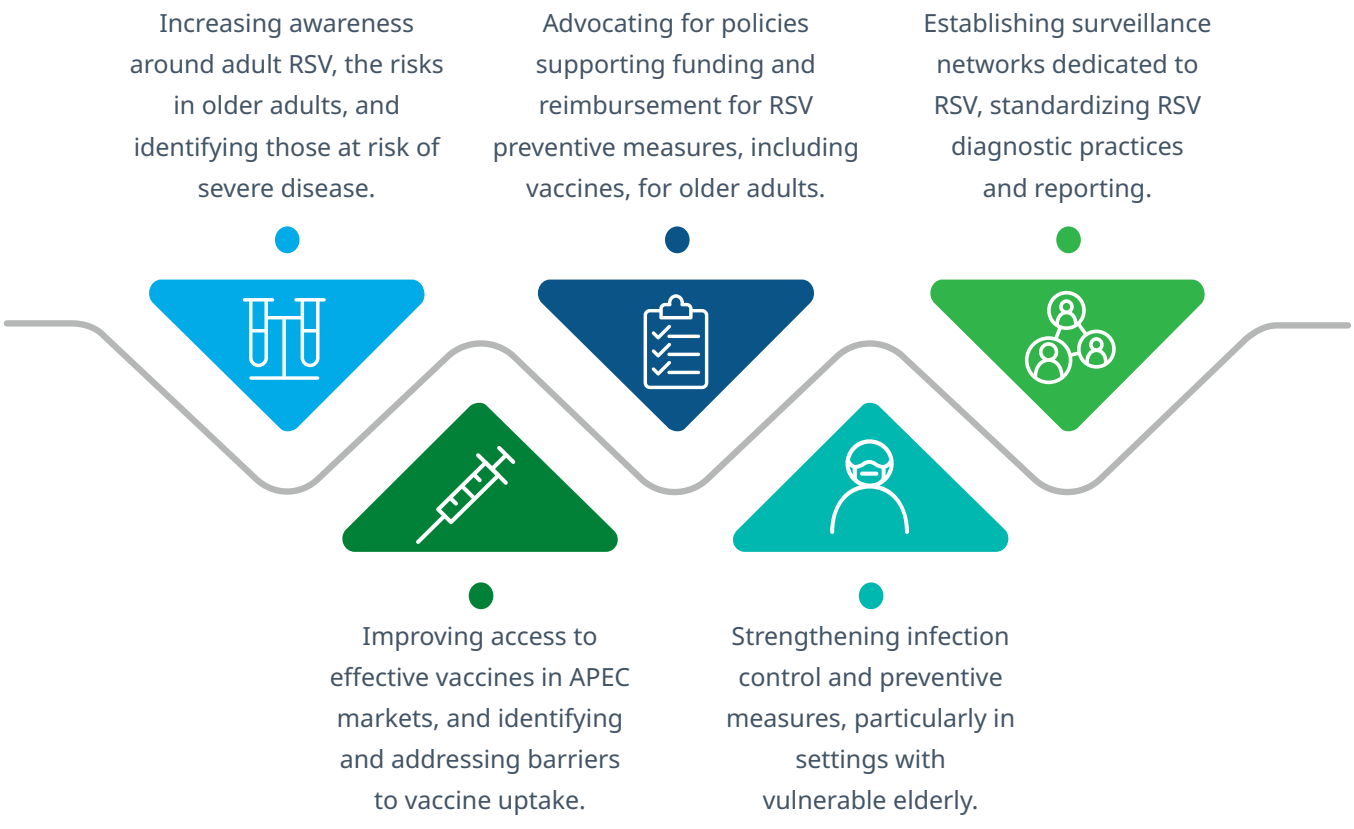
Leveraging published literature, we projected the burden of RSV among older adults in select APEC countries and uncovered a significant clinical and economic burden across all the countries, particularly in China and Japan.

With an estimated total hospitalization cost of USD 2.8 billion, the burden of RSV disease among older adults in select APEC countries is a major concern.

The high per-person medical cost of hospitalization underscores the strain on healthcare systems.

Hence, there is a need for an urgent strategic mitigation plan to address the growing burden of RSV infection among older adults in APEC countries. A few of these are listed in **Figure 8**.

Figure 8: Strategic mitigation plan to prevent Respiratory Syncytial Virus infection among older adults.



Abbreviations: APEC, Asia-Pacific Economic Cooperation; RSV, Respiratory Syncytial Virus.

These proposed strategies can aid policymakers and governing bodies in making informed decisions to mitigate the burden of RSV-related infections in the APEC countries.

To conclude, healthcare practitioners, public health bodies, and policymakers need to come together to improve RSV patient outcomes in APEC countries and prevent RSV infection in older adults.

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Annexures

Annexure 1

SEARCH METHODOLOGY

A Pragmatic Literature Review (PLR) was conducted to identify published evidence on Respiratory Syncytial Virus (RSV) hospitalization incidence, number, and cost in adults, with a defined scope, inclusion criteria, and data identification and extraction methods. Once the criteria were defined, they were converted into strategies, which were then used to search relevant databases for identifying pertinent evidence. The selected articles were assessed according to the established inclusion and exclusion criteria.

Publicly available sources (PubMed, Google Scholar) were used to search for English language articles, in addition to manual searches for gray literature. Gray literature included information produced by government agencies and academic institutions that was not typically made available by academic publishers. The PLR focused on published clinical and economic data; published cost and resource use; and other inputs, including the cost of drugs and resources.

Keywords for the PLR included RSV economic burden, RSV hospitalization incidence, RSV hospitalization cost, influenza hospitalization cost, adult, older adult, Japan, China, Canada, South Korea, Singapore, Hong Kong, Taiwan, Australia, and New Zealand. Searches were first restricted to the last 10 years, and for countries where relevant articles were not identified within this time frame, search was extended to older articles.

For RSV incidence estimates, modeling studies were excluded because they provide projected numbers rather than the actual burden of RSV. Studies describing vaccine usage for the prevention of RSV were also excluded, as these were out of scope of our objective.

Table 1: Summary of publications reviewed in the pragmatic literature review

SR. NO.	AUTHOR/ WEBSITE, YEAR	COUNTRY	AGE CUT-OFF IN YEARS	STUDY DETAILS	REFERENCE
RSV Incidence (articles)					
1	Leung, 2019[77]	China	60–89	RSV incidence in community: 1,088/100,000 person-years.	Leung NHL, Shen J, Zhang J, et al. Incidence of influenza virus and RSV infections in older adults in eastern China: Findings from the China Ageing REspiratory infections Study (CARES) [Poster]. 2019. Available at: https://isirv.org/site/images/conferences/Optionsx/Options%20X_Abstracts%20_Oral%20and%20Poster.pdf
2	Luo, 2022[78]	China	≥60	RSV positivity rate in hospitalized adults with acute respiratory infection (ARI): 1.57%.	Luo M, Gong C, Zhang Y, et al. Comparison of infections with Respiratory Syncytial Virus between children and adults: a multicenter surveillance from 2015 to 2019 in Beijing, China. Eur J Clin Microbiol Infect Dis. 2022;41(12):1387-1397. doi:10.1007/s10096-022-04492-7.
3	Li, 2024[79]	China	>60	• RSV positivity rate before pandemic (Jul 2015–Jun 2019): 1.55%. • 2019–2020 season: 1.05%. • 2020–2021 season: 0.45%. • 2021–2022 season: 1.51%. • 2022–2023 season: 0.15%.	Li M, Cong B, Wei X, et al. Characterising the changes in RSV epidemiology in Beijing, China during 2015-2023: results from a prospective, multi-centre, hospital-based surveillance and serology study. Lancet Reg Health West Pac. 2024;45:101050. doi:10.1016/j.lanwpc.2024.101050.
4	Wang, 2022[80]	China	≥60	The annual mean incidence rates of infections, symptomatic illness, and medically attended illness per 1000 person-seasons were 2.37 (95% UI, 1.32–4.57), 1.57 (95% UI, 0.89–2.98), and 1.12 (95% UI, 0.65–2.08), respectively.	Wang Q, Yang L, Liu C, Jin H, Lin L. Estimated Incidence of Seasonal Influenza in China From 2010 to 2020 Using a Multiplier Model. JAMA Netw Open. 2022;5(4):e227423. doi:10.1001/jamanetworkopen.2022.7423.
5	Kurai, 2022[30]	Japan	≥65	RSV acute respiratory disease in community adults: 24/1,000 (2.4%).	Kurai D, Natori M, Yamada M, Zheng R, Saito Y, Takahashi H. Occurrence and disease burden of Respiratory Syncytial Virus and other respiratory pathogens in adults aged ≥65 years in community: A prospective cohort study in Japan. Influenza Other Respir Viruses. 2022;16(2):298-307. doi:10.1111/irv.12928.
6	Nguyen-Van-Tam, 2022[81]	Japan	≥60	Among older adults, RSV caused 4.37 (3.56–5.35) symptomatic respiratory infections in annual studies.	Nguyen-Van-Tam JS, O'Leary M, Martin ET, et al. Burden of Respiratory Syncytial Virus infection in older and high-risk adults: a systematic review and meta-analysis of the evidence from developed countries. Eur Respir Rev. 2022;31(166):220105. Published 2022 Nov 15. doi:10.1183/16000617.0105-2022.

SR. NO.	AUTHOR/ WEBSITE, YEAR	COUNTRY	AGE CUT-OFF IN YEARS	STUDY DETAILS	REFERENCE
7	Savic, 2023[5]	Canada	≥60	0.67%–1.6% attack rate Attack rate was defined as the number of new cases of RSV-associated ARI during a specified time interval divided by the size of the population at risk. Modeled as attack rate (defined as the number of new hospitalizations of RSV-associated ARI during a specified time interval divided by the size of the population at risk). Hospitalization rate: 0.03%–0.316%	Savic M, Penders Y, Shi T, Branche A, Pirçon JY. Respiratory Syncytial Virus disease burden in adults aged 60 years and older in high-income countries: A systematic literature review and meta-analysis. Influenza Other Respir Viruses. 2023;17(1):e13031. doi:10.1111/irv.13031.
8	Kim, 2018[82]	South Korea	≥65	RSV positivity rate from influenza-like illness (ILI) surveillance: 1.6%.	Kim JM, Jung HD, Cheong HM, et al. Nation-wide surveillance of human acute respiratory virus infections between 2013 and 2015 in Korea. J Med Virol. 2018;90(7):1177-1183. doi:10.1002/jmv.25069.
9	Kim, 2024[83]	South Korea	Not specified	Overall, current estimates indicate that the annual RSV attack rate in the general adult population ranged from 1% to 7%, increasing to approximately 4%–10% among elderly and high-risk groups. RSV was responsible for 7.3%–9.0% of the viruses detected in samples from patients hospitalized with ARTIs.	Kim T, Choi SH. Epidemiology and Disease Burden of Respiratory Syncytial Virus Infection in Adults. Infect Chemother. 2024;56(1):1-12. doi:10.3947/ic.2024.0011.
10	Kim, 2022[84]	South Korea	Not specified	Clinical surveillance data of inpatients with ARI (4075550) suggested that 15.5% (62968) of patients were RSV positive.	Kim JH, Kim HY, Lee M, et al. Respiratory Syncytial Virus Outbreak Without Influenza in the Second Year of the Coronavirus Disease 2019 Pandemic: A National Sentinel Surveillance in Korea, 2021-2022 Season. J Korean Med Sci. 2022;37(34):e258. doi:10.3346/jkms.2022.37.e258.
11	Ang, 2020[85]	Singapore	≥65	RSV positivity rate from ILI surveillance: 5.3%.	Ang LW, Mak TM, Cui L, Leo YS, Lee VJM, Lin RT. Characterisation of Respiratory Syncytial Virus activity in children and adults presenting with acute respiratory illness at primary care clinics in Singapore, 2014-2018. Influenza Other Respir Viruses. 2020;14(4):412-419. doi:10.1111/irv.12730.
12	Caini, 2024[86]	Singapore	≥65	RSV positivity rate: 3.6%.	Caini S, Casalegno JS, Rodrigues AP, et al. Change in Age profile of Respiratory Syncytial Virus disease over the course of annual epidemics: a multi-national study. J Infect. 2024;88(5):106154. doi:10.1016/j.jinf.2024.106154.
13	Saravanos, 2010[87]	Australia	≥65	RSV hospitalization incidence: 19/100,000.	Saravanos GL, Sheel M, Homaira N, et al. Respiratory Syncytial Virus-associated hospitalisations in Australia, 2006-2015. Med J Aust. 2019;210(10):447-453. doi:10.5694/mja2.50159.

SR. NO.	AUTHOR/ WEBSITE, YEAR	COUNTRY	AGE CUT-OFF IN YEARS	STUDY DETAILS	REFERENCE
14	Nazareno, 2017[88]	Australia	<5	The estimated all-age average annual rate of respiratory hospitalizations attributable to RSV was 54.8 (95% confidence interval [CI]: 20.1, 88.8) per 100,000.	Nazareno AL, Muscatello DJ, Turner RM, Wood JG, Moore HC, Newall AT. Modelled estimates of hospitalisations attributable to Respiratory Syncytial Virus and influenza in Australia, 2009-2017. Influenza Other Respir Viruses. 2022;16(6):1082-1090. doi:10.1111/irv.13003.
15	Foley, 2024[29]	Australia	≥60	RSV detections rose annually between 2017 and 2023, reaching 50.7 per 100,000 in 2023 (95% CI, 47.9–53.8). Detection rate in 2023 among those aged ≥75 years (199.5 per 100,000; 95% CI, 180.5–220).	Foley DA, Minney-Smith CA, Tjea A, et al. The Changing Detection Rate of Respiratory Syncytial Virus in Adults in Western Australia between 2017 and 2023. Viruses. 2024;16(5):656. doi:10.3390/v16050656.
16	Yang, 2015[89]	Hong Kong	≥65	RSV incidence: 64.2 per 100,000.	Yang L, Chan KH, Suen LK, et al. Impact of the 2009 H1N1 Pandemic on Age-Specific Epidemic Curves of Other Respiratory Viruses: A Comparison of Pre-Pandemic, Pandemic and Post-Pandemic Periods in a Subtropical City. PLoS One. 2015;10(4):e0125447. Published 2015 Apr 30. doi:10.1371/journal.pone.0125447.
17	Chan, 2015[27]	Hong Kong	≥65	RSV hospitalization incidence: 5.7 per 10,000.	Chan PKS, Tam WWS, Lee TC, et al. Hospitalization Incidence, Mortality, and Seasonality of Common Respiratory Viruses Over a Period of 15 Years in a Developed Subtropical City. Medicine (Baltimore). 2015;94(46):e2024. doi:10.1097/MD.0000000000002024.
18	Shih, 2015[90]	Taiwan	≥60	RSV positivity rate from ILI surveillance: 3.6%.	Shih HI, Wang HC, Su IJ, et al. Viral Respiratory Tract Infections in Adult Patients Attending Outpatient and Emergency Departments, Taiwan, 2012-2013: A PCR/Electrospray Ionization Mass Spectrometry Study. Medicine (Baltimore). 2015;94(38):e1545. doi:10.1097/MD.0000000000001545.
19	Chang, 2023[91]	Taiwan	≥65	Total RSV positivity rate was 0.9 %. RSV positivity rate was 0.7% (15/2149).	Chang WC, Huang RC, Perng CL, Shang HS, Yu CM, Wang CH. Epidemiology and clinical characteristics of hospitalized adults with Respiratory Syncytial Virus infection at a medical center in northern Taiwan. J Formos Med Assoc. doi:10.1016/j.jfma.2023.12.004.
20	ElSherif, 2023[28]	Canada	≥60	Estimated Respiratory Syncytial Virus hospitalization rates among Canadian adults: 145.5.	ElSherif M, Andrew MK, Ye L, et al. Leveraging Influenza Virus Surveillance From 2012 to 2015 to Characterize the Burden of Respiratory Syncytial Virus Disease in Canadian Adults ≥50 Years of Age Hospitalized with Acute Respiratory Illness. Open Forum Infect Dis. 2023;10(7):ofad315. doi:10.1093/ofid/ofad315.

SR. NO.	AUTHOR/ WEBSITE, YEAR	COUNTRY	AGE CUT-OFF IN YEARS	STUDY DETAILS	REFERENCE
RSV Incidence (gray literature)					
1	Global epidemiology of RSV, 2018[92]	Singapore	Not available	Data for 2011–2018: Median cases per season (IQR) = 1786 (1647–2076).	The Global Epidemiology of RSV in Community and Hospitalized Care: Findings From 15 Countries [Internet]. Available at: https://academic.oup.com/view-large/306774107. Accessed Jul 25, 2024.
2	NCIRS, 2024[93]	Australia	≥50	Between 2016 and 2019, the hospitalization rate in adults aged 65 years and older was estimated at 123 per 100,000 population. The rate was greater in those aged 75 years and over (194 per 100,000 population) compared with those aged 50–64 years (26 per 100,000 population).	Respiratory Syncytial Virus (RSV): Frequently asked questions (FAQs) [Internet]. Available at: https://ncirs.org.au/ncirs-fact-sheets-faqs-and-other-resources/respiratory-syncytial-virus-rsv-frequently-asked. Accessed Jul 25, 2024.
3	CHP, 2024[94]	Hong Kong	Not available	Not specifically provided.	Centre for Health Protection: Influenza virus subtyping [Internet]. Available at: https://www.chp.gov.hk/en/statistics/data/10/641/643/2275.html. Accessed Jul 25, 2024.
4	NIDSS, 2024[95]	Taiwan	Not available	Not specifically provided.	Taiwan National Infectious Disease Statistics System [Internet]. Available at: https://nidss.cdc.gov.tw/en/nndss/Cdcwnh07?id=487a. Accessed Jul 25, 2024.
5	Xiong, 2021[96]	Hong Kong	≥65	Annual rates of RSV-associated respiratory hospitalization: 330 (95% CI: 230, 430) per 100,000 person-year, which contributed 53% of all RSV-associated respiratory hospitalizations.	Xiong, Q. Comparative epidemiology of Respiratory Syncytial Virus (RSV) and influenza viruses. (Thesis). 2021. University of Hong Kong, Pokfulam, Hong Kong SAR. Available at: https://hub.hku.hk/handle/10722/300405. Accessed Jul 25, 2024.
RSV incidence and hospitalization cost (articles)					
1	Kurai, 2023[15]	Incidence: China, Japan, South Korea	≥60	China: The median proportion of elderly patients with RSV with ARI or community-acquired pneumonia was 48.00% (3.64%–80.00%). Japan: The median proportion of elderly patients with RSV with ARI or community-acquired pneumonia was 79.78% (71.43%–88.12%). South Korea: The median proportion of elderly patients with RSV in all adult patients with ARI or community-acquired pneumonia was 28.57% (22.76%–33.33%).	Kurai D, Song J, Huang YC, et al. Targeted Literature Review of the Burden of Respiratory Syncytial Infection among High-Risk and Elderly Patients in Asia Pacific Region. Infect Dis Ther. 2023;12(3):807-828. doi:10.1007/s40121-023-00777-2.
2	Yoon, 2020[64]	South Korea	Adults (19–49 years, 50–64 years, and ≥65 years)	Incidence: The median proportion of elderly patients with RSV among all adult patients with RSV was 64.7%. Cost: The median (IQR) cost of RSV hospitalization in those aged >65 years was USD 2,933.17 (1,748.26–6,339.93).	Yoon JG, Noh JY, Choi WS, et al. Clinical characteristics and disease burden of Respiratory Syncytial Virus infection among hospitalized adults. Sci Rep. 2020;10(1):12106. doi:10.1038/s41598-020-69017-8.

SR. NO.	AUTHOR/ WEBSITE, YEAR	COUNTRY	AGE CUT-OFF IN YEARS	STUDY DETAILS	REFERENCE
3	Prasad, 2020[31]	New Zealand	≥60	Incidence: RSV hospitalization incidence: 99 per 100,000. Cost: Median (IQR) cost of RSV hospitalization in adults: NZD 3,723.84 (2500.44–5,028.44).	Prasad N, Newbern EC, Trenholme AA, et al. The health and economic burden of Respiratory Syncytial Virus associated hospitalizations in adults. PLoS One. 2020;15(6):e0234235. doi:10.1371/journal.pone.0234235.
4	Wang, 2023[62]	Hong Kong	≥60	Cost: Cost of RSV inpatient care (per day): USD 654.	Wang Y, Fekadu G, You JHS. Comparative Cost-Effectiveness Analysis of Respiratory Syncytial Virus Vaccines for Older Adults in Hong Kong. Vaccines (Basel). 2023;11(10):1605. Published 2023 Oct 17. doi:10.3390/vaccines11101605.
RSV hospitalization cost (articles)					
1	Chen, 2021[66]	China	≥50	Median (IQR) cost of RSV hospitalization in adults: USD 2,919.10 (1,172.10, 15,627.40).	Chen L, Han X, Li Y, Zhang C, Xing X. Comparison of clinical characteristics and outcomes between Respiratory Syncytial Virus and influenza-related pneumonia in China from 2013 to 2019. Eur J Clin Microbiol Infect Dis. 2021;40(8):1633-1643. doi:10.1007/s10096-021-04217-2.
2	Sruamsiri, 2018[97]	Japan	≤5	Mean total health care cost of JPY 365,583 (USD 3,344) per hospitalization.	Sruamsiri R, Kubo H, Mahlich J. Hospitalization costs and length of stay of Japanese children with Respiratory Syncytial Virus: A structural equation modeling approach. Medicine (Baltimore). 2018;97(29):e11491. doi:10.1097/MD.0000000000011491.
3	Igarashi, 2023[65]	Japan	≥60	The mean cost among those hospitalized was USD 6,609.	Igarashi A, Togo K, Kobayashi Y, Kamei K, Yonemoto N, Ishiwada N. Inpatient and Outpatient Costs Associated with Respiratory Syncytial Virus in Japanese Infants and Older Adults. Future Virol. (2023) 18(10), 643–657. doi.org/10.2217/fvl-2023-0069.
4	ElSherif, 2021[63]	Canada	50-59 ≥80	Mean resource utilization and direct medical cost per case was CAD 13,315 (95% CI: 12,846; 13,785), ranging provincially from CAD 12,093 to CAD 24,830.	El Sherif M, McNeil S, Andrew M, et al. Prevalence, severe outcomes, and costs associated with Respiratory Syncytial Virus (RSV) in adults ≥ 50 years of age hospitalized with respiratory illness in Canada, 2012-2015; abstract no. E&E-17. 6th ReSViNET conference. Virtual; 2021.
5	Rafferty, 2022[98]	Canada	65–79	RSV-attributable costs for laboratory-confirmed cases were CAD 12,713 at 30 days following diagnosis. RSV-attributable costs for laboratory-confirmed cases in the age group of 65–79 years were CAD 17,507 at 30 days following diagnosis.	Rafferty E, Paulden M, Buchan SA, et al. Evaluating the Individual Healthcare Costs and Burden of Disease Associated with RSV Across Age Groups. Pharmacoeconomics. 2022;40(6):633-645. doi:10.1007/s40273-022-01142-w.

SR. NO.	AUTHOR/ WEBSITE, YEAR	COUNTRY	AGE CUT-OFF IN YEARS	STUDY DETAILS	REFERENCE
6	Shoukat, 2024[99]	Canada	≥60	• ED visit: CAD 562 per visit. • Hospital stay in GW: CAD 1,052 per day. • Intensive care unit (ICU) stay without mechanical ventilation: CAD 2,612 per day. • ICU stay with mechanical ventilation: CAD 3,426 per day.	Shoukat A, Bawden CE, Röst G, et al. Impact and cost-effectiveness analyses of vaccination for prevention of Respiratory Syncytial Virus disease among older adults in Ontario: A Canadian Immunization Research Network (CIRN) study. Vaccine. 2024;42(7):1768-1776. doi:10.1016/j.vaccine.2024.02.041.
7	Crawford, 2024[100]	Canada	≥18	The range of direct medical costs per RSV hospitalization ranged from USD 27,055 to USD 28,329, USD 16,564 to USD 33,128, and USD 15,220 to USD 48,484 for the UM-CDC, RSVPreF3 (Arexvy) industry-funded, and RSVpreF (Abrysvo) industry-funded economic evaluations, respectively.	Crawford R, Bailey S, Cornelissen T. Cost-Effectiveness of Respiratory Syncytial Virus Vaccines for Adults: Technology Review. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; February 2024.
Influenza as a proxy hospitalization cost (articles)					
1	Gong, 2021[101]	China	Not available	The total economic burden was 26.38 billion Chinese yuan renminbi (CNY), accounting for 0.266% of the gross domestic product (GDP) in 2019, of which the hospitalization-related economic burden accounted for the highest proportion (86.4%, 22.79 billion CNY), followed by the outpatient-related economic burden (11.3%, 2.97 billion CNY). The indirect economic burden of productivity loss of premature deaths was the lowest (2.4%, 0.62 billion CNY).	Gong H, Shen X, Yan H, et al. [Estimating the disease burden of seasonal influenza in China, 2006-2019]. Zhonghua Yi Xue Za Zhi. 2021;101(8):560-567. doi:10.3760/cma.j.cn112137-20201210-03323.
2	Zhou, 2013[102]	China, Hong Kong	All age groups (≤15 years, 16–64 years, and ≥65 years)	China: The mean (range) direct medical cost was USD 1,797 (80–27,545) for all hospitalizations, and the median (IQR) direct medical costs were USD 231 (164), USD 854 (890), and USD 2,263 (7,803) for children, adults, and elderly, respectively. Hong Kong: Hospitalization due to influenza-related illness incurred a high cost to patients. The overall direct medical cost in Hong Kong constituted 1.9% of the GDP per capita (USD 31,758) in 2010.	Zhou L, Situ S, Huang T, et al. Direct medical cost of influenza-related hospitalizations among severe Acute Respiratory Infections cases in three provinces in China. PLoS One. 2013;8(5):e63788. doi:10.1371/journal.pone.0063788.
3	Yue, 2019[71]	Singapore	≥65	Total hospitalization cost: USD 6,116 (SGD 8,252) per admission. Cost per bed: USD 701 (SGD 946) per stay.	Yue M, Dickens BL, Yoong JS, I-Cheng Chen M, Teerawattananon Y, Cook AR. Cost-Effectiveness Analysis for Influenza Vaccination Coverage and Timing in Tropical and Subtropical Climate Settings: A Modeling Study. Value Health. 2019;22(12):1345-1354. doi:10.1016/j.jval.2019.07.001.

SR. NO.	AUTHOR/ WEBSITE, YEAR	COUNTRY	AGE CUT-OFF IN YEARS	STUDY DETAILS	REFERENCE
4	Raina McIntyre, 2023[103]	Australia	≥65	Between 2002 and 2017, the average cost of hospitalization among older people during the influenza season (April–November) was AUD 7,175 per admission. The average circulatory plus respiratory hospitalization cost was AUD 7,829 per admission.	Raina MacIntyre C, Kevin Yin J, Felter C, et al. Estimated health and economic impact of using high-dose influenza vaccine on respiratory and circulatory plus respiratory hospitalizations of older adults in Australia. Vaccine X. 2023;15:100365. doi:10.1016/j.jvacx.2023.100365.
5	Newall, 2008[70]	Australia	≥65	There was an annual average of 310,000 general practitioner consultations for influenza/influenza-like illness and 18,400 hospitalizations attributable to influenza over the period of review. The estimated cost to the Australian health care system for these events was AUD 115 million annually.	Newall AT, Scuffham PA. Influenza-related disease: the cost to the Australian healthcare system. Vaccine. 2008;26(52):6818-6823. doi:10.1016/j.vaccine.2008.09.086.
6	Peasah, 2013[69]	Hong Kong, Taiwan	All age groups	Hong Kong: The costs of hospital admission, an outpatient visit, and loss of productivity per day in Hong Kong were USD 529, USD 16, and USD 4, respectively. Taiwan: The hospitalization cost per stay in Taiwan was USD 2,376 for the elderly.	Peasah SK, Azziz-Baumgartner E, Breese J, Meltzer MI, Widdowson MA. Influenza cost and cost-effectiveness studies globally--a review. Vaccine. 2013;31(46):5339-5348. doi:10.1016/j.vaccine.2013.09.013.
7	Chan, 2017[104]	Hong Kong	≥65	Patients with ICU admission reported longer IR-LOS (12.7 ± 6.0 days versus 5.5 ± 2.7 days; P<0.001) and higher direct costs (36,588 USD ± 21,482 versus 5,773 USD ± 2,017; P<0.001; 1 USD = 7.8 HKD).	Chan YK, Wong RY, Ip M, Lee NL, You JH. Economic outcomes of influenza in hospitalized elderly with and without ICU admission. Antivir Ther. 2017;22(2):173-177. doi:10.3851/IMP3102.
Influenza as a proxy hospitalization cost (gray literature)					
1	NCGM, 2023[105]	Japan	Not available	General cost is mentioned for all diseases, but nothing specific on respiratory infections.	Estimation of medical expenses for hospitalization: National Center for Global Health and Medicine Hospital [Internet]. Available at: https://www.hosp.ncgm.go.jp/inpatient/070/index.html. Accessed Jul 25, 2024.
Other respiratory infections cost (gray literature)					
1	Portal site of Official Statistics of Japan[106]	Japan	Not available	• JPY 10,940–185,681 for URTD. • JPY 50,302–185,681 for LRTD.	Portal site of Official Statistics of Japan (e-STAT). Statistics of Medical Activities in Public Health Insurance 2021 Available at: https://www.e-stat.go.jp/stat-search/files? page=1&layout= datalist & toukei= 00450048&tstat=000001029602 &cycle=7&tclass1=000001166295&tclass2= 000001166326&tclass3= 000001166327 &tclass4val=0. Accessed Jul 25, 2024.
2	Japan health system review, 2018[107]	Japan	Not available	Per-capita health expenditure was lower than the median OECD per-capita expenditure until 2010, but it officially reached USD 4435.6 in 2015, which is higher than the OECD median.	Japan health system review [Internet]. Available at: https://iris.who.int/bitstream/handle/10665/259941/9789290226260-eng.pdf. Accessed Jul 25, 2024.

SR. NO.	AUTHOR/ WEBSITE, YEAR	COUNTRY	AGE CUT-OFF IN YEARS	STUDY DETAILS	REFERENCE
3	Ninkatec, 2024[108]	Singapore	Not specified	The mean annual treatment cost for a respiratory patient in Singapore was almost SGD 8,500, with additional annual work impairment and productivity loss of SGD 10,000 and SGD 9,000, respectively. That is a total cost of SGD 27,500 per year per case for a working adult patient.	Common Lung Diseases In Singapore: All You Need To Know [Internet]. Available at: https://ninkatec.com/most-common-lung-diseases-singapore/. Accessed Jul 25, 2024.

Note: References that were ultimately chosen for the calculations are shaded in blue.

Annexure 2

DETAILS OF COST CALCULATION

To calculate RSV or influenza as a proxy hospitalization cost, four scenarios were considered:

Scenario 1 for Japan:

- The RSV or influenza as a proxy hospitalization cost was presented in a 2023 published article[65] in the local currency of Japan.
- The local currency was directly converted to United States dollars (USD) based on the exchange rate of 2023, as per the World Bank[58].

Scenario 2 for Australia, Canada, and New Zealand:

- The articles[31, 63, 70] presented costs of RSV or influenza as a proxy hospitalization in the local currency of the respective countries before the year 2023.
- The local currency costs were first converted to 2023 by adjusting to 2023 inflation rates based on the respective countries' World Bank data[50, 51, 54].
- The 2023 local currency costs were then converted to USD based on the exchange rate of 2023, as per the World Bank[49, 56, 60].

Scenario 3 for Hong Kong:

- The article[62] stated costs of RSV hospitalization in USD for 2023; thus, no further conversions were undertaken.

Scenario 4 for China, South Korea, Singapore, and Taiwan:

- The articles[64, 66, 69, 71] stated costs of RSV or influenza as a proxy hospitalization in USD prior to 2023.
- USD was first converted to the local currency of the respective country for the stated year in the article[57, 59, 61, 109].
- Post-conversion to local currency, the inflation rate till 2023 was applied based on respective countries' World Bank data[52, 53, 55, 110].
- After calculating the cost in local currency for 2023, the local currency was then converted to USD based on the exchange rate of 2023, as per the World Bank[57, 59, 61, 111].

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About IQVIA

IQVIA (NYSE:IQV) is a leading global provider of clinical research services, commercial insights and healthcare intelligence to the life sciences and healthcare industries. IQVIA's portfolio of solutions are powered by IQVIA Connected Intelligence™ to deliver actionable insights and services built on high-quality health data, Healthcare-grade AI™, advanced analytics, the latest technologies and extensive domain expertise. With approximately 88,000 employees in over 100 countries, including experts in healthcare, life sciences, data science, technology and operational excellence, IQVIA is dedicated to accelerating the development and commercialization of innovative medical treatments to help improve patient outcomes and population health worldwide.

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