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Unit No. 2

RESPIRATORY SYNCYTIAL VIRUS VACCINATION IN ADULTS: A BRIEF UPDATE FOR PRIMARY CARE PROVIDERS

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ABSTRACT

Respiratory syncytial virus (RSV) is a highly transmissible pathogen that poses a significant risk to older adults and individuals with chronic medical conditions. Two RSV vaccines, Arexvy® and Abrysvo®, are currently approved in Singapore. They are recommended for adults aged 75 years and older, as well as adults aged 60 years and above who have underlying risk factors such as cardiovascular disease, chronic lung disease, chronic kidney disease, diabetes mellitus, immunosuppression, frailty, or residence in long-term care facilities. Arexvy® is also indicated for adults aged 50 to 59 years with similar risk profiles in Singapore. Clinical trials have demonstrated approximately 80 percent efficacy in preventing lower respiratory tract infections in the first year following vaccination. This protection gradually declines to 70 percent at two years and 60 percent at three years. Mild local and systemic side effects are common, while serious adverse events remain rare. Guillain-Barré syndrome has been reported infrequently, with no confirmed causal relationship to the vaccine. Primary care providers play a critical role in improving vaccine uptake by educating patients, addressing concerns, and offering vaccination during routine visits. Year-round vaccination and co-administration with other adult vaccines, such as those for influenza, shingles, and COVID-19, are effective strategies to enhance coverage and protect high-risk populations.

Keywords: Immunisation Programmes; Guillain-Barre Syndrome; Preventive Health Services; Primary Healthcare; Vaccines, Subunit

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INTRODUCTION

Respiratory syncytial virus (RSV) is a pathogenic, single-stranded RNA virus and a leading cause of severe lower respiratory tract infections, particularly in infants and older adults.[1] Recent studies employing mathematical modelling estimate the basic reproductive number (R_0) of RSV to be approximately 3.0, highlighting its high transmissibility.[2] An R_0 of three indicates that, on average, each infected individual can transmit the virus to three others in a fully susceptible population, enabling rapid spread in the absence of preventive measures such as vaccination or social distancing.

Natural immunity is short-lived, and re-infection can occur as soon as two months after a prior infection.[3] Treatment is primarily supportive, and specific antiviral therapies are lacking. To reduce the burden of disease, preventive strategies include general measures such as hand hygiene and limiting transmission, as well as targeted approaches like monoclonal antibodies and vaccination.

Monoclonal antibody therapy provides immunoprophylaxis; however, its use is currently restricted to infants. Vaccination is available for infants through maternal immunisation and transplacental antibody transfer (passive immunisation), and for adults through direct vaccination. However, direct vaccination in children is not yet available due to the formation of non-neutralising antibodies that paradoxically leads to enhanced respiratory disease, a known immunological complication.

Primary care providers play a vital role in preventive healthcare and are well-positioned to lead adult vaccination efforts. This brief update summarises the current literature and key guidelines on RSV vaccination in adults, with a focus on its relevance to primary care practice in Singapore. Specifically, it addresses the following areas: recommendations from major medical organisations, vaccine efficacy and effectiveness, potential side effects, and strategies to enhance vaccine uptake.

RESPIRATORY SYNCYTIAL VIRUS VACCINATION RECOMMENDATIONS FOR ADULTS

RSV vaccines target the pre-fusion conformation of the RSV F protein. Although there are two major antigenic subtypes, known as RSV-A and RSV-B, the differences in their pre-fusion F proteins are small. As a result, targeting the pre-fusion F protein of one subtype can provide cross-protection against the other. Two RSV vaccines are currently available in Singapore. Both vaccines are administered as a single 0.5 ml intramuscular dose following reconstitution:

1. Abrysvo® (Pfizer Pte Ltd.) – an unadjuvanted bivalent protein subunit vaccine targeting both RSV-A and RSV-B pre-fusion F proteins

2. Arexvy® (GSK Pte Ltd.) – an adjuvanted monovalent protein subunit vaccine targeting the RSV-A pre-fusion F protein

According to the US Centers for Disease Control and Prevention (CDC), both vaccines are recommended for the active immunisation of adults aged 75 years and older, as

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well as adults aged 60 years and older who are at increased risk of severe RSV disease,[4] in alignment with vaccine indications in Singapore. In addition, in Singapore, Arexvy® is also indicated for adults aged 50 to 59 years who are at increased risk of RSV disease.[5]

Risk factors for RSV disease include chronic medical conditions such as cardiovascular disease, chronic lung diseases (including chronic obstructive pulmonary disease and asthma), and chronic kidney disease. Immunocompromised individuals – such as those undergoing cancer treatment, living with the human immunodeficiency virus, or receiving immunosuppressive therapy (e.g., organ transplant recipients) – are also at increased risk. Additional risk factors include frailty (a complex clinical syndrome involving reduced physiological reserves and a lowered ability to cope with physical or psychological stressors)[6] and long-term residence in nursing homes. Condition-specific guidelines also support RSV vaccination, including the Global Initiative for Asthma (GINA 2025), the Global Initiative for Chronic Obstructive Lung Disease (GOLD 2025), and the American Diabetes Association (ADA 2023) reports.

All data presented in this brief update will be based on studies involving these two protein subunit vaccines. Although an mRNA-based vaccine targeting the RSV-A pre-fusion F protein (mResvia®, Moderna Inc.) is available in other countries (e.g., the United States and European Union), it is not currently available in Singapore.

RESPIRATORY SYNCYTIAL VIRUS VACCINATION FOR ADULTS: EFFICACY AND EFFECTIVENESS

The primary clinically meaningful outcomes of vaccination include the prevention of infection and the reduction of severe complications from breakthrough infections, such as respiratory failure, hospitalisation, intensive care admission, and death. Investigators in well-controlled randomised trials can measure the extent to which vaccines prevent these outcomes, yielding a percentage known as vaccine efficacy. However, the controlled conditions of such trials may not fully reflect real-world settings and might overestimate the vaccine's protective effect. Therefore, it is also important to evaluate vaccine performance in certain open-label randomised trials or real-world observational studies, which provide a measure known as vaccine effectiveness. When efficacy and effectiveness are similar, clinicians and patients can be more confident that the benefits observed in controlled trials are applicable to routine clinical practice.

Clinical trials have demonstrated that RSV vaccination provides high efficacy – approximately 80 percent – in preventing lower respiratory tract infections within the first year after vaccination.[7] Real-world observational studies have reported similar levels of effectiveness in healthy older adults and in individuals with comorbid conditions, including chronic cardiovascular and respiratory diseases.[8,9] For comparison, the annual influenza vaccine showed an effectiveness of 30-60 percent.[10]

In immunocompromised individuals, vaccine effectiveness is expected to be lower, especially in those with severe immunosuppression.[9,11] Although clinical outcome data are not yet available for severely immunocompromised populations, such as organ transplant recipients receiving immunosuppressive therapy, immunogenicity studies suggest that vaccines containing adjuvants might produce higher antibody levels compared to unadjuvanted formulations.[12] It is still unknown whether alternative dosing strategies, such as multiple priming doses, could further enhance the immune response in these patients.

Long-term data on the adjuvanted RSV vaccine in older adults indicate that it maintains efficacy against severe lower respiratory tract disease for up to three years. However, cumulative protection wanes over time, declining to approximately 70 percent at two years[13] and 60 percent at three years.[14] Current evidence suggests that re-vaccination within this three-year period does not enhance efficacy, and the optimal timing for booster doses remains uncertain. Additionally, long-term data for the unadjuvanted RSV vaccine suggest a comparable level of protection over a two-year period,[15] although further evidence is needed to confirm its durability beyond that time period.

RESPIRATORY SYNCYTIAL VIRUS VACCINATION FOR ADULTS: SIDE EFFECTS

The benefits of RSV vaccination outweigh its known risks. Mild local adverse effects are common, with up to 60 percent of vaccine recipients experiencing pain at the injection site. Mild systemic side effects – such as fatigue, headache, and myalgia – occur in up to 30 percent of individuals.[16] Fortunately, severe adverse events remain exceedingly rare.

Neuroinflammatory disorders, primarily Guillain-Barré syndrome, have been reported within 42 days of RSV vaccination, occurring at a rate of fewer than 10 cases per million doses administered.[17] In comparison, the incidence associated with the influenza vaccine is approximately one case per million doses. While a causal link to RSV vaccination has not been definitively established, the US CDC has updated the prescribing information for Abrysvo® and Arexvy® to include a warning about a potential increased risk of Guillain-Barré syndrome within this time frame. This potential risk should be weighed alongside the risk of Guillain-Barré syndrome following RSV infection itself.[18]

STRATEGIES TO IMPROVE VACCINE UPTAKE

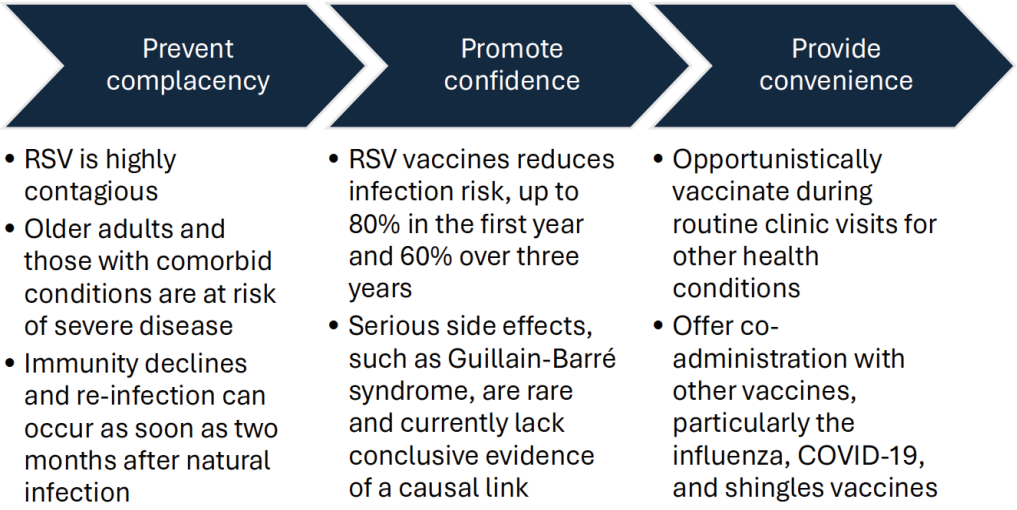
To improve vaccine uptake, the World Health Organisation's Strategic Advisory Group of Experts on Immunisation (SAGE) recommends focusing on three key domains: complacency, confidence, and convenience, commonly referred to as the 3C model (refer to **Figure 1**).[19]

To address complacency, primary care providers should inform individuals about their risk of severe RSV infection.

This includes not only acute complications such as respiratory failure and acute heart failure, but also long-term outcomes like functional decline and loss of independence. To build confidence in vaccination, providers should engage in open and balanced conversations about the benefits and potential risks. As for COVID-19 vaccination, these discussions can be supported by various patient decision aids, including printed materials or digital tools such as web-based applications and mobile chatbots.[20]

Primary care providers can enhance convenience by offering RSV vaccination during routine healthcare visits and by co-administering it with other recommended vaccines. Although RSV infections display seasonal patterns worldwide, these patterns vary considerably within and between regions, making it difficult to predict peak periods accurately.[21] As a result, in Singapore, primary care providers can administer RSV vaccination year-round to individuals who meet the eligibility criteria. Co-administration with other vaccines, such as those for influenza,[22] shingles (ClinicalTrials.gov ID NCT05966090), and COVID-19,[23] has been shown to be safe and effective. To minimise local side effects when multiple vaccines are given at the same visit, each vaccine should be administered at a different anatomical site (e.g., deltoid region of the upper right and left arms).

Figure 1. A stepwise approach to adult respiratory syncytial virus (RSV) vaccination for primary care providers



CONCLUSION

RSV is a common yet potentially severe respiratory pathogen in older adults and those with comorbidities. The availability of two effective vaccines, Abrysvo® and Arexvy®, offers a promising opportunity to reduce the burden of disease in these populations. Clinical and real-world evidence supports their use, demonstrating robust protection against lower respiratory tract infections and favourable safety profiles. Although rare, the potential for neuroinflammatory events such as Guillain-Barré syndrome necessitates continued surveillance and informed clinical decision-making.

Primary care providers are well-positioned to lead adult RSV vaccination efforts. By addressing patient complacency, building confidence in vaccine safety and efficacy, and enhancing access and convenience, they can play a pivotal role in improving vaccine uptake. Routine health visits provide valuable opportunities for patient education, risk assessment, and co-administration with other vaccines. As RSV vaccination becomes integrated into adult immunisation programmes, ongoing research and real-world data will be essential in refining booster strategies and optimising long-term protection.

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LEARNING POINTS

- **RSV is a significant cause of severe respiratory illness in older adults and high-risk populations, with an estimated basic reproductive number (R_0) of three, indicating high transmissibility.**
- **Two protein-based RSV vaccines, Arexvy® and Abrysvo®, are approved for adults aged 60 years and above in Singapore, with Arexvy® also indicated for at-risk individuals aged 50-59 years.**
- **Vaccine efficacy is high in the first year (around 80 percent) and remains moderately protective for up to three years, although booster schedules and longterm durability are still being studied.**
- **Mild local and systemic side effects are common, while serious adverse events like Guillain-Barré syndrome are rare and not causally established, prompting precautionary labelling rather than strict warnings.**
- **Primary care providers are essential in improving RSV vaccine uptake by educating patients, addressing vaccine hesitancy, and integrating RSV vaccination into routine care, including co-administration with other adult vaccines.**