Unit No. 1

BRIDGING THE RISK GAPS ON THE VIRAL THREATS OF SHINGLES AND RSV

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ABSTRACT

Singapore's rapidly ageing population faces a growing threat from vaccine-preventable diseases (VPDs) such as respiratory syncytial virus (RSV) and herpes zoster (HZ), and this is driven by age-related decline in immunity (ARDI) and high rates of chronic comorbidities. Despite the success of Singapore's childhood immunisation programmes, adult immunisation rate remains poor. Emerging evidence highlights the long-term health and economic consequences of VPDs in older adults, underscoring the urgent need for proactive prevention. Adjuvanted vaccines, including novel RSV and HZ vaccines, have shown potential in enhancing immune responses, mitigating the effects of ARDI, extending protection duration, and restoring cellular immunity in older adults to levels observed in younger populations. With the availability of such vaccines and potential future government subsidies, adult immunisation should be integrated into routine care. Effective patient counselling and a standardised vaccination checklist can help to improve uptake and reduce the burden of VPDs in Singapore's ageing society.

Keywords: RSV, Shingles, Age-related decline in immunity, Adjuvants, Older adults

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INTRODUCTION

Singapore is one of the most rapidly ageing societies in Asia. Today, almost 1 in 2 (42.8 percent) adults in Singapore are 50 years or older and this proportion is only projected to increase significantly by 2035.[1] An increased risk and presence of comorbidities accompany advancing ages. In addition to this, a direct association between ageing and increased susceptibility to viruses has been established, and this has been in part, attributed to age-related decline in immunity (ARDI), resulting in reduced quality and quantity of immune cells.[2] This progressive decline in immune function increases the susceptibility to infections such as respiratory syncytial virus (RSV) and increases the risk of more severe complications of RSV, as has been observed for influenza and other non-respiratory infections such as herpes zoster (HZ).[2,3] To combat ARDI, adjuvant technology can be used in combination with a vaccine antigen to elicit a more robust immune response than with the antigen alone, leading to longer-lasting immunity.[4]

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There is a growing body of evidence demonstrating the long-term consequences of RSV and HZ infections. Severe outcomes such as increased risk of cardiovascular events, long-term morbidity, hospitalisation, and mortality beyond acute infection have been observed across multiple studies.[5-8] These infections, alongside influenza, pneumococcal, and COVID-19, contribute to a significant and growing burden among older adults. In view of our ageing population, there is a significant proportion of Singaporeans vulnerable to vaccine-preventable diseases (VPD). Adult immunisation must therefore be incorporated into our everyday counselling of patients to encompass holistic care for our older adults. Despite the success of childhood immunisation schemes, adult immunisation programmes in Singapore remain underutilised, which is important to address in order to ensure comprehensive public health protection across all age groups.

WHO IS AT RISK OF VPD

Beyond age, VPDs disproportionately affect adults with underlying chronic medical conditions.[9] There is a vicious cycle at play here, whereby the presence of comorbidities/risk factors augment the risk of contracting VPDs and vice versa, with VPDs potentially exacerbating underlying medical conditions beyond acute infection.[10-14] The following risk factors or conditions outlined by the Centres for Disease Control and Prevention (CDC) define some of the population at higher risk of severe VPD outcomes (Note: list may not be exhaustive)[15-17]:

1. Older adults

Chronic cardiovascular disease, chronic lung or respiratory disease, diabetes mellitus, severe obesity, end stage renal disease/dialysis dependence, chronic haematologic conditions, chronic liver disease, neurological or neuromuscular conditions, residence in a nursing home, moderate or severe immunocompromise, HIV, and other chronic medical conditions on risk factors that a provider determines would increase risk of severe disease due to viral infections (e.g., frailty)

2. Immunocompromised individuals

3. Socioeconomic disadvantage groups

THE SILENT THREAT OF RSV

A recent publication by Wee et al (2025) reported for the first time the severity of RSV infection and its associated factors amongst hospitalised adults from 2021 to 2023

in Singapore, compared to influenza and COVID-19.[5] Data from this study indicated that factors such as older age, immunocompromised status, and/or presence of comorbidities were independently associated with RSV disease severity.[5] 28-day mortality was five times higher and intensive care unit (ICU) admission was two times higher than patients hospitalised for RSV compared to adults hospitalised for influenza.[5]

Beyond the short-term impact of RSV observed in hospitalised older adults, it has been shown that approximately one-third of RSV patients experienced a decline in functional status at six months post-discharge, losing their previous independence before infection.[18] Another study showed that up to 24.5 percent of RSV patients required professional home care and up to 26.6 percent required re-admission within three months post-discharge.[19] A cumulative mortality rate of 25.8 percent has also been observed within one year of admission for RSV.[20]

Comorbidities such as diabetes, chronic pulmonary disease, and cardiac conditions are common in older adults,[21] and the combination of older age and certain underlying comorbidities may increase the risk of severe outcomes of infection.[3,7,22] Wee et al (2025) reported that adults with diabetes mellitus had greater odds of 28-day mortality in RSV hospitalisations.[5] Separately, it has also been demonstrated that one in 10 patients hospitalised for RSV had a concurrent cardiovascular event. In particular, individuals with preexisting cardiac conditions had higher odds of a concurrent acute cardiac event during RSV hospitalisation.[6] The odds of cardiac events were also significantly higher in RSV compared to COVID-19 hospitalisations.[6] Similar to influenza, RSV infection has also been shown to lead to cardiac complications such as heart failure, arrhythmia, and acute coronary and cerebrovascular events.[19,23-25]

There are currently no specific treatments for RSV in adults.[26] However, since May 2023, vaccines have become available to protect adults from the outcomes of RSV infection.[27-29] An adjuvanted vaccine, Arexvy, has been developed to overcome ARDI by augmenting the older adult's immune response to RSV vaccination.[27] The RSV AS01-adjuvanted versus non-adjuvanted RSV fusion protein (RSVPreF3) vaccine formulations has shown to induce broader neutralising antibody responses against diverse RSV strains in preclinical models and clinical studies, indicating the potential for broader protection against circulating and future RSV strains.[30] In addition, AS01-adjuvanted recombinant subunit prefusion RSVPreF3 antigen formulations induced significantly higher levels of cellular immune response versus the nonadjuvanted formulation and restored RSVPreF3 CD4+ T-cell levels in older adults to similar levels as found in young adults aged 18-40 years.[31] In view of the growing elderly Singaporean population and the availability of novel RSV vaccines, it is crucial that our older adults are protected from the short- and long-term consequences of RSV, along with other respiratory illnesses such as influenza and COVID-19.[5]

THE SILENT THREAT OF HERPES ZOSTER: BEYOND THE RASH

Systematic reviews have reported that the lifetime risk of having HZ is approximately 1 in 3 in the general population, with the risk increasing sharply from the age of 50 years old.[32,33] With age-related decline in immunity and/or immunocompromising conditions, the decline in cellular immunity is also associated with an increased risk of HZ.[34]

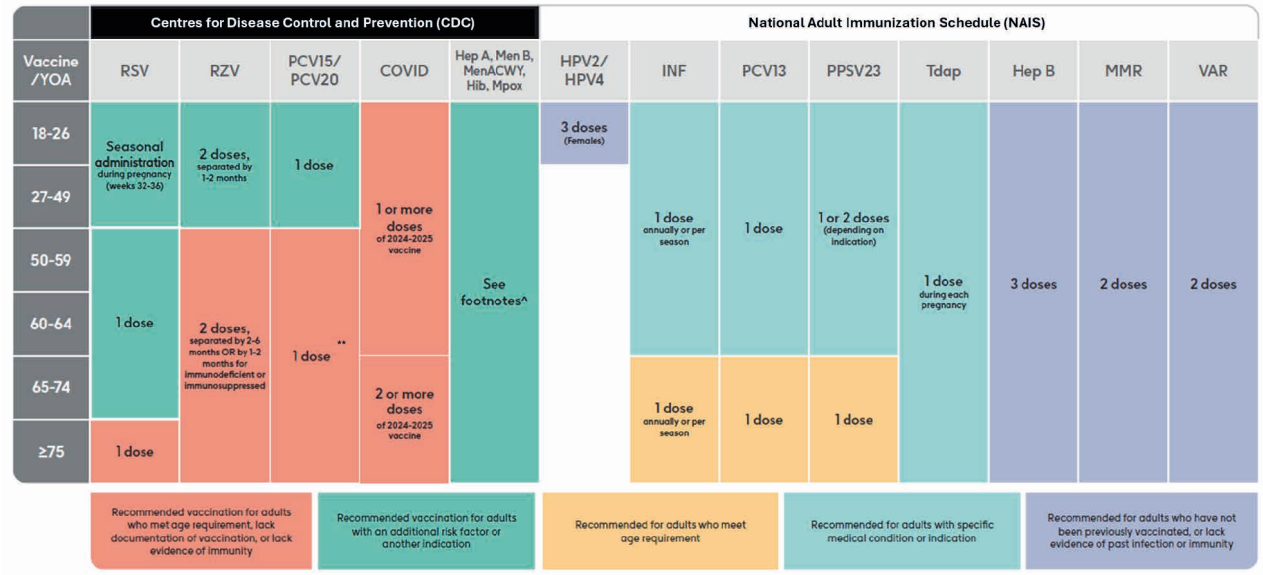
The risk of HZ and PHN is further augmented among patients with chronic medical conditions as outlined in above and ageing. With Singapore's high prevalence of chronic diseases such as diabetes, cardiovascular disease, and chronic kidney disease, a significant proportion of Singaporeans might suffer worsened disease outcomes if infected with HZ.[9,35-37] Studies have shown that patients with diabetes have a 27 percent increase in the risk of diabetes-related hospitalisation.[35] In those with cardiovascular diseases, there is a 19 percent increase in the risk of MI in the first year following HZ infection.[38] Beyond this, it has also been demonstrated that patients with chronic kidney disease have a 36 percent increase in risk of end-stage renal disease progression post shingles infection.[36]

Taking into consideration the risk of HZ among adults 50 years and above, all eligible Singaporeans should be offered vaccination. In Singapore, there is only one locally approved HZ vaccine, Shingrix, an adjuvanted recombinant zoster vaccine. Shingrix provides long-lasting protection with a two-dose regimen, maintaining high efficacy levels of 87.7 percent over 11 years. To date, no booster is required due to evidence demonstrating sustained vaccine efficacy up to 11 years post-vaccination.[39]

ADULT VACCINATION AS PART OF HOLISTIC CARE

In Singapore, the National Adult Immunisation Schedule (NAIS) offers a list of vaccines subsidised by the government, providing valuable support for adult immunisation. However, incorporating the latest recommendations from global health authorities such as the CDC can further enhance the programme. By considering international adult vaccination recommendations, we can ensure a more comprehensive approach to preventive care, particularly benefiting the elderly, individuals with chronic conditions, and those with immunocompromised states. This holistic approach supports the well-being of at-risk groups and strengthens overall public health. **Figure 1** combines the latest adult vaccination recommendations from CDC and the NAIS.

Figure 1. Adult vaccination recommendations from CDC and NAIS*†[40-45]



*NAIS is for vaccines subsidised in Singapore only. RZV and PCV20 will be under NAIS effective 1 September 2025. GSK RSVPreF3 OA is indicated for active immunisation for the prevention of LRTD caused by RSV in adults 50 through 59 YOA who are at increased risk for RSV disease. These vaccines are not repeated in the CDC-recommended vaccines section of the table. The CDC-recommended vaccines include vaccines not recommended by NAIS. CDC recommendation as of 16 April 2025.

†For a more comprehensive list of vaccine and dosing schedule, special situations, contraindications and precautions, etc., please refer to CDC schedule and Society of Infectious Diseases (Singapore) handbook.

**Based on shared clinical decision-making, adults ≥65 YOA have the option to get PCV20 if they have received both PCV13 (but not PCV15 or PCV20) at any age and PPSV23 at or ≥65 YOA.

^Hep A: 2, 3, or 4 doses depending on vaccine; MenACWY: 1 or 2 doses depending on indication; MenB: 2 or 3 doses depending on vaccine and indication; Hib: 1 vaccines or 3 doses depending on indication. Please refer to CDC schedule for detailed information.

Hep B = hepatitis B
Hib = Haemophilus Influenzae type B
HPV = human papillomavirus
Mpox = monkeypox
INF = influenza
MenACWY = meningococcal ACWY
MenB = Meningococcal B
MMR = Measles-Mumps-Rubella
PCV = pneumococcal conjugate vaccine
PPSV = pneumococcal polysaccharide vaccine
RSV = respiratory syncytial virus
RZV = recombinant zoster virus
Tdap = Tetanus-Diphtheria-Pertussis
VAR = varicella
YOA = years of age

Beyond CDC and NAIS, professional medical societies such as the American Diabetes Association, American College of Rheumatology, Global Initiative for Asthma, and Global Initiative for Chronic Obstructive Lung Disease have also recommended several vaccinations for patients with certain underlying conditions. The consistent recommendation for adult vaccination across societies reinforces the importance of embedding vaccination as standard of care for all patients aged 50 years and older.

To help promote vaccination counselling as part of daily practice, a vaccination checklist may be useful as a quick reference tool to assist in identifying immunisations that might be due or missing during routine consultations (refer to **Table I**). Especially for high-risk adults, this checklist promotes a proactive, regular approach to the monitoring of immunisation status. Additionally, if widely implemented, it minimises lost opportunities by standardising care across the different specialties and clinics (such as general care, pharmacies, and hospitals).

This checklist will not only support healthcare providers but also empower patients to take charge of their preventive health by serving as a personal health record. Incorporating it into yearly health evaluations or reviews of chronic illnesses can potentially improve the nation's vaccination rates, reduce the local burden of VPDs, and facilitate effective communication between patients and healthcare professionals. Immunisation rates may be further augmented by considering co-administration of vaccines to ensure that at-risk populations are protected in a timely manner.

Table I: Routine vaccine checklist for adults

Vaccine	NAIS/CHAS Coverage/ Subsidised	Recommended Age Group/ Dose	Completed?	Uptodate
Influenza	≥65 years ≥18 years with specific medical condition or indication	All Adult Age Group – Yearly or per season Seasonal availability	☐	
Pneumococcal*	≥65 years ≥18 years with specific medical condition or indication	≥50 years ≥18 years with specific medical condition or indication	☐	
COVID-19	All Adult Age Group	All Adult Age Group – Yearly or per season Seasonal availability	☐	
Herpes Zoster*	≥60 years Immunocompromised ≥18 years	≥50 years/2 doses (0, 2-6 m) Immunocompromised ≥18 years/2 doses (0, 1-2 m)	☐	
Respiratory Syncytial Virus (RSV)	N/A	≥75 years 50-74 years at increased risk	☐	
Tetanus, reduced diphtheria, and acellular pertussis (Tdap)	During each pregnancy	During each pregnancy/ 1 dose Every 10 years/1 booster dose	☐	

***Note:** Herpes Zoster Vaccine and Pneumococcal 20-valent conjugate vaccine will be subsidised by the Singapore government from 1 September 2025.

In addition to evidence-based guidelines, patient counselling plays a critical practical role in promoting vaccine uptake; **Table II** provides strategies that may help facilitate conversations with vaccine-hesitant individuals based on barriers commonly faced by local physicians.

Table II: Proposed strategies to navigate conversations with patients

Barrier	Patient Perception	Assessment	Proposed Strategies
Pain/Fear of Injection/ Needle Phobia/Anxiety	"Injections are painful." "I'm scared of needles."	Gauge if fear is psychological or from past negative experience.	Reassure patients that vaccine needles are small, and vaccination is quick. Offer vaccinations in a calming environment.
Perceived Inconvenience	"I don't have time."	Understand the patient's daily schedule, mobility, work hours, and ability to access clinics.	Offer co-administration with other vaccines or during existing appointments. Provide reminders (SMS, WhatsApp). Reinforce benefits of prevention vs time lost to illness.
Cost Concerns	"It's too expensive."	Explore financial status and awareness of subsidy schemes.	Educate about vaccine subsidy options, MediSave usage, and long-term cost savings. Compare vaccine cost vs cost of hospitalisation for VPDs.

Lack of Knowledge	"I'm not sure if I need this."	Check literacy level, awareness of VPDs and prior health education.	Provide simple visuals or infographics. Use analogies (e.g., vaccines as insurance). Schedule time for Q&A. Engage family caregivers.
Low Perceived Risk	"I'm healthy."	Assess understanding of adult immunity and risk factors (e.g., age, comorbidities).	Share statistics about adult disease burden. Personalise with case examples of patients affected. Highlight ARDI and risk factors that are applicable to them.
Misinformation	"Vaccines cause disease."	Ask about sources of belief (e.g., online forums, friends/ family).	Provide evidence-based information. Reassure using safety data available. Debunk misinformation respectfully. Direct to credible resources (CDC, WHO, MOH).
Fear of Side Effects	"I'll get sick from the vaccine."	Assess knowledge of side effects.	Explain that normal vaccine response (pain, fatigue, etc.) and side effects are mild and transient. Reassure about close monitoring and adverse event reporting systems.
Belief that Vaccines Are Only for Kids	"Vaccines are for children only, not adults."	Assess knowledge of adult vaccine recommendations.	Educate on ARDI. Explain risk factors like ageing, chronic disease, and lifestyle.

CONCLUSION

Given the rising prevalence and consequences of RSV and HZ in older adults, it is imperative that all healthcare professionals play an active role in protecting our population against VPDs. Redefining preventive care is of utmost importance, especially with the recent availability of novel vaccines such as pneumococcal 20-valent conjugate vaccine, adjuvanted recombinant zoster vaccine, and RSV vaccines. Together, we can replicate the success of our childhood immunisation programme for Singaporean adults.

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LEARNING POINTS

- **Adult immunisation should mirror the success of childhood immunisation programmes and integrated into daily practice.**
- **Older adults are at increased risk of vaccine-preventable diseases and associated long-term outcomes, but with advancements in vaccine technology, adjuvants can help to combat ARDI to elicit robust immune response similar to levels observed in younger adults.**
- **Co-administration strategies should be adopted as it will accelerate vaccine coverage.**
- **HCPs should continue to advocate for preventive health through vaccination, recognising that patient hesitancy is common, but consistent, evidence-based engagement can lead to increased acceptance over time.**