

ABSTRACT

The “Healthier SG Initiative”, a new healthcare reform plan announced by the Singapore government focuses on promoting healthy living to tackle the challenges of an ageing population. As part of this initiative, free vaccinations against influenza and pneumococcus will be offered to the elderly. Vaccination is a powerful public health tool in the prevention of infectious diseases. The implementation of National Childhood Immunisation Programme in many countries has led to improvement in child health and mortality from preventable infectious diseases. Many who have benefitted from such programmes are now adults and experiencing waning immunity. The ageing adult population is also vulnerable to many infectious disease threats due to immunosenescence. There is much that we can do to bolster take up rates for adult immunisation. We need to understand the patterns of vaccine preventable infections in this population, their needs, barriers to immunisation, access and further develop ways to scale up adult vaccination programmes.

Key Words: Adult vaccination, Healthier SG, vaccine update, elderly

SFP2023; 49(2): 10-13

INTRODUCTION

In July 2023, Singapore will transition to an ambitious multi-year healthcare reform entitled Healthier SG. The key components of this strategic reform focus on keeping the population healthy and disease-free for as long as possible and to identify health problems through regular health screening. Promoting healthy lifestyles and preventive care are at the core of this ambitious reform. In this article, we will discuss how adult vaccinations will form an important component of preventive care in Healthier SG.

National immunisation programmes in Singapore and many other developed countries have traditionally been targeted at infants and children. These programmes have been successful in increasing vaccine coverage and conferring herd

immunity, reducing the burden of infectious diseases such as tetanus, measles, mumps, rubella, tuberculosis, Hepatitis B, and pneumococcal infections. Adult immunisation has been underutilised as a public health measure and it is now appreciated that vaccinations should be recommended throughout life to prevent certain infections and their sequelae.

Vaccines are recommended for adults on the following bases:

1. Age
2. Prior vaccination status and vaccination history
3. Co-morbidities
4. Lifestyle
5. Occupation
6. Travel destination

In this article, we will focus on the “routine” adult vaccines that family practitioners can incorporate into their practice. In Singapore, we have two adult immunisation recommendations, one from MOH (the National Adult Immunisation Schedule [NAIS]) (from 2017) and the other a joint effort from Academy of Medicine, College of Family Physicians, and Society of Infectious Diseases published in 2020.¹ Besides these two, many of the references and recommendations that we will discuss come from the United States (including from the Advisory Committee on Immunisation Practices [ACIP]),² where such recommendations have been in existence for many years. Travel vaccinations will be considered separately and do not form part of Healthier SG. Whilst there are many reasons why vaccine coverage in adults is low, the recommendation by family physicians and other healthcare providers is a strong motivator for patients to receive their recommended vaccines. Assessing gaps in vaccine needs for adults will be part of the individual health plan in Healthier SG and will be an important opportunity for family physicians to enhance their doctor-patient relationship. Nationally recommended adult vaccinations such as influenza and pneumococcal will be fully subsidised.

INFLUENZA

Recommendations: All adults annually

Routine annual influenza vaccinations have been advocated for many years. The indications have been broadened so extensively that any person above the age of six months should possibly receive the influenza vaccine on an annual basis. From October 2021 to June 2022, it has been estimated by the Centres for Disease Control and Prevention (CDC), United States that influenza infection resulted in 8 to 13 million symptomatic illnesses; 3.7 million to 6.1 million medical visits; 82,000 to 170,000 hospitalizations; and 5,000 to 14,000 deaths.³ Tropical

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countries such as Singapore have a different seasonal influenza pattern compared to the developed countries in the Northern Hemisphere. However, influenza epidemics in Singapore do result in increased hospitalisations⁴ and excess mortality.⁵ Incorporating annual influenza vaccinations for the at-risk groups will reduce our outpatient attendances and hospitalisations for respiratory tract infections.

Under “book.health.gov.sg/flu”, patients can schedule influenza vaccinations with family physicians who are under the patient-care network scheme. Presently, eligible patients under various government subsidy schemes will pay a subsidised rate. With the rollout of Healthier SG from July 2023, patients aged 60 years and above who are registered with their family physicians may receive their annual influenza vaccinations free of charge.

Newer formulations that may allow us to improve our fight against influenza viz Recombinant influenza vaccines (RIV) have been registered in numerous countries and in Singapore. The main advantage of RIV is that it does not contain egg protein and it can be safely administered in those who have egg allergy. In the US, ACIP and CDC preferentially recommends certain influenza vaccine formulations⁶ for those who are >65 years. These have higher antigen dose (four times more in Fluzone High Dose Quadrivalent) or are adjuvanted. Several studies have demonstrated that in those aged > 65 years, these “higher dose and/or adjuvanted” vaccines are potentially more effective in reducing influenza morbidity and mortality. In areas where such high dose or adjuvanted influenza vaccines are not available (such as in Singapore), the latest available “standard” quadrivalent vaccines should continue be administered annually.

PNEUMOCOCCAL INFECTION

Recommendations: One or two doses in adulthood. Recommended for adults aged >65 years, younger if they have underlying medical conditions that put them at risk for pneumococcal disease

Adult pneumococcal disease has been a persistent health problem that should lend itself to vaccine intervention. There are two formulations of pneumococcal vaccine licensed in Singapore for use in adults, i.e., conjugate pneumococcal 13 valent vaccine (PCV 13) and pneumococcal polysaccharide 23 valent vaccine (PPV 23). The indications for use are for all adults above aged 65 years and younger for those with underlying diseases including cardiovascular and respiratory diseases. In the US, approximately 60 percent of adults >65 years have received pneumococcal vaccination, whereas only 20 percent of adults between the ages 19 years to 64 years who were at high risk for pneumococcal disease received the vaccine. Prevention of pneumococcal disease got a huge boost in Singapore as deduction through Medisave is now allowed for adults taking pneumococcal vaccines. Conjugated pneumococcal vaccines covering more serotypes (15 and 20) have been registered for use in the United States for the elderly population⁷ and these are expected to be

available in Singapore in the first or second quarter of 2023. These are further elaborated on at a later section.

TETANUS DIPHTHERIA AND ACCELLULAR PERTUSSIS (TD AND TDAP)

Recommendations: Td once every 10 years and substitute Tdap once for Td booster

After the primary series of five doses in childhood, these vaccines should be administered once every 10 years. In the past, the focus was administration of tetanus and/or diphtheria (Td). However, pertussis has become a re-emerging infection recently due to waning immunity in adults. The current recommendation is that adults should have one dose of Tdap (tetanus, diphtheria, and acellular pertussis) in place of the Td booster. Thereafter, only Td (preferred) LEA or TT (tetanus toxoid) needs to be given every 10 years.

HERPES ZOSTER (HZ)

Recommendations: For persons >60 years, two doses of Shingrix vaccine 2-6 months apart

With our ageing population, we expect to see more cases of HZ infection. The first HZ vaccine, Zostavax, was registered in 2013. This is a live attenuated virus vaccine that is moderately effective. Increasing awareness of the morbidity of zoster has prompted more of the elderly population to come forward for the vaccine. A second HZ vaccine, Shingrix, became available in 2020. Shingrix is an adjuvanted recombinant viral glycoprotein vaccine with improved efficacy. Shingrix is the preferred HZ vaccine; in the US, Shingrix has replaced Zostavax in the ACIP guidelines.² Under the MOH’s 2017 NAIS, vaccination against varicella is in the schedule but not vaccination against HZ.

HUMAN PAPILLOMA VIRUS

Recommendations: 3-dose schedule for all females up to 26 years

There are two vaccines against HPV licensed for use in females: the bivalent (HPV2) and the nonavalent (HPV9). For females, a 2-dose series is recommended from ages 9-14 years and three doses until 45 years. The costs of HPV vaccines are claimable through Medisave (HPV2). In Australia, HPV vaccine take-up is 80 percent in females <18 years of age and 76 percent in males. These results are indeed remarkable and will hopefully be replicated in Singapore. Australia is projected to be the first developed country to eliminate cervical cancer (defined as <4 per 100,000 women). There is emerging data that a 2-dose HPV vaccine schedule is sufficient in reducing the burden of HPV-related disease.

HEPATITIS VACCINES

Recommendations: Hepatitis B: all adults with 3-dose schedule if not done in childhood

Hepatitis A: 2-dose vaccine for all adults

Hepatitis A and B co-formulation (Twinrix) requires a 3-dose schedule for adults.

Routine childhood hepatitis B vaccine was incorporated into our national childhood immunisation programme starting 1987. Seroprevalence data in 2010 has shown reduction in anti-HBc and HBsAg compared to other surveys in 2004 and 1996. In addition, there has been reduction in age-specific incidence of hepatocellular carcinoma in Singapore. There continue to be a small group of adults who have yet to be vaccinated. In Singapore, 28 cases of acute hepatitis B were notified in 2022 (compared with 17 cases in 2021).

Hepatitis A vaccination is strongly advised in view of the high endemicity of Hepatitis A in the region. In 2012, there were 108 cases of acute hepatitis A notified and the number of notifications has steadily decreased to a median of 66 between the years 2017 to 2021. In 2021 and 2022, the number of notifications has reduced to 19 and 25 respectively. The possible reasons could be the reduction in travel during the COVID-19 pandemic and/or the rise in vaccination rates of Hepatitis A. Interestingly, acute Hepatitis E, another food and waterborne viral hepatitis, had more notifications in 2021 (50) and 2022 (38) than hepatitis A in the corresponding periods. We also continue to have cases of acute hepatitis A acquired “locally”. It is estimated that 59 percent of acute hepatitis A were acquired overseas whilst the rest were “local”.

CATCH-UP VACCINATIONS

For adults who have missed the childhood immunisations for MMR (two doses at least one month apart) and Varicella (two doses at least two months apart), they should be “updated” as soon as possible.

Hepatitis B catch-up vaccination is for those who either did not seroconvert after completing the primary series or “lose” their HBs antibody levels. It is estimated that up to 30 percent of adults of adults may be seronegative despite childhood immunisation.

COVID-19 VACCINES

At the time of writing at this article, the bivalent COVID-19 mRNA (incorporating the original SARS-CoV2 strain and the Omicron variant) is recommended for those aged five years and above. After three years, while COVID-19 has become endemic, the SARS-CoV2 virus continues to persist and evolve. There has been a recent spike in numbers in mainland China since December 2022. This potentially has a knock-on effect on countries like Singapore through travel-related infections as border restrictions have eased. The genetic evolution of SARS-CoV2 poses huge challenges

and the newer bivalent vaccines currently being used are likely to be at best a temporary solution. Whether regular “annual” booster COVID-19 vaccinations (like annual influenza vaccination) will be required remains to be determined. Hopefully, a “next-generation” pancoronavirus vaccine can be developed and deployed effectively to keep COVID-19 under control.⁸

NEWER VACCINES IN THE PIPELINE WITH A FOCUS ON RESPIRATORY INFECTIONS

Recent years have brought further attention to vaccine-preventable respiratory infections in adults. In the Northern Hemisphere, the 2022 winter season has brought fears of a “tripledemic” of circulating respiratory viruses, which include RSV, influenza, and SARS-CoV2. These respiratory viral infections then pre-dispose to bacterial pneumonias with *Staphylococcus aureus* and *Streptococcus pneumoniae*. There have been recent advances in the prevention of pneumococcal lower respiratory tract infections with conjugated vaccines covering more serotypes.

Pneumococcal Vaccines

Two new formulations of conjugated pneumococcal vaccines incorporating more serotypes have been available in the US since 2021 and are likely to be registered in Singapore in 2023. In the US, the ACIP have reviewed the available trials and their recent 2022 recommendation for adults >65 years is either a single dose of PCV20 or a dose of PCV15 followed by PPV 23.⁷ When these newer conjugated pneumococcal vaccines become available in Singapore, they will likely prompt revisions to the current recommendations.

Respiratory Syncytial Virus (RSV) Vaccine

There has been better appreciation in the role of RSV causing “winter pneumonias”. There are several RSV vaccines in advanced stages of registration with the US Food and Drug Agency (FDA).^{9,10} It is expected that an RSV vaccine will become available for immunisation of adults within the next 2-5 years. The strategy is prevention of RSV in the elderly through direct vaccination and prevention of RSV-associated infant bronchiolitis through vaccinating pregnant women in the third trimester.

Pancoronavirus Vaccine

We have transited to bivalent vaccines for COVID-19 infection. In the short term, it is likely that there will be further tweaks to the current mRNA vaccines and incorporate “newer” variant constructs. There may be further development to “trivalent” or “quadrivalent” COVID19 vaccines.⁸ We look forward to the “next generation” of COVID-19 vaccines that will cover all SARS-CoV2 strains and possibly even one that covers all coronaviruses.

Combination Respiratory Viral Vaccines for Adults

There are numerous respiratory viruses circulating in the community that result in significant morbidity and

mortality in the older adults. These viruses such as influenza and coronaviruses (including SARS-CoV2) are known to evolve frequently, requiring “regular updates” to the vaccine formulation. There has been research by several vaccine groups to incorporate both influenza and SARS-CoV2 strains into a single annual vaccine “booster”.

DIGITAL HEALTH PLAN, VACCINE REMINDERS, AND HEALTHHUB

With incorporation of the individual health plan and further enhancements to the HealthHub app, it is expected that regular vaccine reminders to individuals will be made available via the HealthHub app.

The challenge for many is to overcome the fear and unfamiliarity of digital health. Educating the elderly to use these mobile health apps will be key to implementation success. The family physician can certainly reinforce the use of such mobile apps.

CONCLUSION

Adult vaccination should no longer be considered a luxury for developed countries. Instead, we must view how lifelong immunisation can have an important public health role in reducing vaccine-preventable diseases and their sequelae.

Despite having well-established recommendations for adult immunisation in the US, vaccine coverage varies considerably. Clearly, we can do much better by assessing and engaging our patients to help close their immunisation gaps. The government can incentivise the elderly and/or those at high risk to get vaccinated and improve awareness, public education, and funding.

Finally, guidelines for adult immunisation are living documents that need to be regularly updated.

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LEARNING POINTS

- It is important to maintain vaccinations in adults due to waning immunity.
- Vaccinations remain the most effective public health tool against vaccine-preventable infections in the population.
- Family practitioners' involvement in patient education and engagement are important factors in the successful implementation of the adult immunisation programme.
- There are existing guidelines on adult immunisation both locally and internationally. These need to be updated regularly.