

Vaccines for the elderly

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Abstract

The size of the elderly population is increasing due to improved living standards and medical advancements. The elderly are typically vulnerable to infectious diseases, making them a particularly important target population for vaccination. In many countries, four vaccines are recommended for the elderly: influenza vaccine, pneumococcal vaccine, herpes zoster vaccine, and a vaccine combining tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis. This review briefly summarises the most recent relevant data regarding vaccination of the elderly.

Keywords: elderly, influenza, pneumococcal disease, herpes zoster, tetanus, diphtheria, pertussis, vaccination

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Background

Worldwide, the size of the elderly population (i.e. aged ≥ 60 years) is increasing due to medical advancements and improved living standards, with the number of elderly persons expected to increase from 962 million in 2017 to 2.1 billion in 2050.¹ In South Africa, life expectancy has increased tremendously since the inception of universal access to antiretroviral therapy for the management of HIV, to such an extent that the proportion of South Africa's elderly population will increase from approximately 8.4% in 2017 to 15.9% by 2050.^{1,2} This demographic shift will potentially present a challenge for South Africa's health system, as the elderly often suffer from chronic comorbidities, have more frequent and severe infections, and tend to experience serious complications and higher mortality rates in comparison to the younger population.³

Benefits and importance of vaccination in the elderly

One of the key strategies of the World Health Organization's (WHO) *Decade of Healthy Ageing (2020–2030)*, is a scale-up of vaccination in addition to other age-friendly primary health services for the elderly, such as screening, prevention, control and management of non-communicable and communicable diseases and age-related conditions.⁴

Vaccination is recognised as one of the most successful and cost-effective public health interventions ever, preventing an estimated 2.5 million deaths per year.⁵ While global infant vaccination coverage has steadily improved over the past 30 years, vaccination uptake amongst adults, and specifically the elderly, is low.⁶ Vaccine-preventable diseases (VPDs) including influenza, pneumococcal disease, herpes zoster (shingles) and pertussis, may cause illness, permanent disability or death amongst the elderly.^{7,8} Thus adopting a 'life-course' approach to vaccination can potentially play a major role in preserving the health and improving the quality of life of all ages, including the elderly.^{3,4} In addition, vaccination reduces antimicrobial use for the treatment

of infectious diseases, thereby supporting global efforts in antimicrobial resistance prevention.⁹

Ageing is accompanied by immunosenescence (a decline in innate and adaptive immune system responsiveness), resulting in increased incidence and severity of infectious diseases amongst the elderly. This is a major contributor to increased morbidity and mortality in the elderly.^{10,11} In South Africa, it is commonplace for the elderly to play a central role in the care and upbringing of their grandchildren,¹² putting them at risk of acquiring infectious diseases from the young in their care.⁸ Conversely, grandparents can transmit diseases like whooping cough to unvaccinated infants, which can often be fatal.⁸

Challenges with vaccination in the elderly

As happens during natural infections in the elderly, immunosenescence impairs local cell-mediated reactions thereby decreasing the effectiveness of vaccination, with antibody responses being weaker and declining faster.^{11,13,14} In addition, mostly because comorbidities, polypharmacy and frailty exclude the elderly from participating in vaccine trials, there is often a lack of pre-marketing safety and efficacy data in the elderly, resulting in under-prescribing of vaccination by healthcare providers (HCPs) treating the elderly.⁸ Apart from this lack of HCP confidence in vaccination of the elderly, the elderly tend to consult multiple HCPs, and the absence of a universal record including adult vaccination, makes it difficult to track their medical history, including which vaccinations have been received.^{6,8} Other significant barriers to vaccination amongst the elderly include their lack of access to information, decreased mobility, cost of vaccines, and health system bias towards childhood immunisation.^{6,8} For example, the Expanded Programme on Immunisation of South Africa (EPI-SA) has achieved considerable successes in the prevention of VPDs in children, through offering free universal infant immunisation against 10 VPDs.¹⁵ However, there is no comprehensive adult vaccination programme addressing the high burden of VPDs among the South African elderly population.

Table 1: Recommended immunisation for the elderly^{17,28}

Vaccine	Dosing schedule	Route of administration	Special precautions and contraindications	Side-effects
Trivalent influenza e.g. Vaxigrip®, Influvac®, or Quadrivalent influenza* e.g. Vaxigrip Tetra®	1 dose (0.5 ml) annually	Intramuscular or deep subcutaneous	<ul style="list-style-type: none"> Vaccine SHOULD NOT be administered by intravascular injection and SHOULD NOT penetrate a blood vessel. Defer vaccine in persons with fever or with moderate or severe acute illness without fever. Psychogenic response to vaccination may cause syncope. Take necessary precautions to manage patients at risk. Persons with a history of Guillain-Barré syndrome following 6 weeks of a previous dose of influenza vaccine should generally not be vaccinated with influenza unless the benefits of vaccination outweigh any risks to the person. <p>Contraindicated: History of anaphylaxis or severe allergic reaction to any component of the vaccine including egg proteins and chicken proteins.</p>	<p>Mild: Pain/tenderness at the site of injection, malaise, low grade fever and chills, myalgia, headache.</p>
Pneumococcal conjugate (PCV13)* e.g. Prevenar®13	1 dose (0.5 ml) if vaccine naïve, followed by PPSV23 12 months later	Intramuscular	<ul style="list-style-type: none"> Persons with altered immunity e.g. asplenic adults or persons with HIV infection, malignancy, hematopoietic stem cell transplant, nephrotic syndrome, may have reduced antibody responses to the vaccine. If PPSV23 has already been administered, a single dose of PCV13 should be given at least 12 months after PPSV23. <p>Contraindicated: Hypersensitivity to a previous dose or to any vaccine component including diphtheria toxoid.</p>	<p>Mild: Pain at the site of injection, fatigue, headache, myalgia, loss of appetite, chills.</p>
Pneumococcal polysaccharide (PPSV23)* e.g. Pneumovax®23	1 dose (0.5 ml) 12 months after PCV13	Intramuscular or deep subcutaneous	<ul style="list-style-type: none"> Defer vaccine in persons with moderate or severe acute illness. Exercise caution in persons with severely compromised cardiovascular and/or pulmonary function. Reduced response to zoster live vaccine when administered concurrently (Recommendation: administer the two vaccines at least four weeks apart). <p>Contraindicated: History of anaphylaxis or severe allergic reaction to any component of the vaccine.</p>	<p>Mild: Pain/swelling/redness at the site of injection, fatigue, headache and myalgia.</p>
Zoster live vaccine* e.g. Zostavax®	1 dose (0.65 ml)	Subcutaneous	<ul style="list-style-type: none"> Persons who test negative for immunity to varicella zoster virus (VZV) should rather get the VZV vaccine*. Vaccine should be deferred in persons with acute illness and persons with active untreated tuberculosis. Possibility of transmission of vaccine virus between vaccinees and susceptible contacts. <p>Contraindicated: Severely immunocompromised individuals e.g. persons with leukaemia, lymphoma or other malignant neoplasms affecting the bone marrow or lymphatic system, AIDS and those on immunosuppressive therapy. History of severe reaction to gelatin, neomycin or any other component of the vaccine.</p>	<p>Mild: Pain, swelling and tenderness at the injection site, headache and muscle pain.</p>
Tetanus, diphtheria and acellular pertussis* (Tdap or Td) e.g. Boostrix®/Adacel®	1 dose (0.5 ml) Tdap, then Td or Tdap booster every 10 years	Intramuscular	<ul style="list-style-type: none"> Vaccine should be deferred in persons with progressive or unstable neurological conditions. A period of at least 10 years should have elapsed in persons who experienced an Arthus-type hypersensitivity reaction following a prior dose of a tetanus toxoid-containing vaccine. Psychogenic response to vaccination may cause syncope. Take necessary precautions to manage patients at risk. Immunosuppressive therapies may reduce the immune response to the vaccine. Increased risk of Guillain-Barré syndrome with subsequent dose of tetanus toxoid-containing vaccine if Guillain-Barré syndrome occurred within 6 weeks of receipt of a prior vaccine containing tetanus toxoid. <p>Contraindicated: Severe allergic reaction to any component of the vaccine. Encephalopathy (e.g. coma, decreased level of consciousness, prolonged seizures) within 7 days of administration of a previous pertussis antigen-containing vaccine.</p>	<p>Mild: Pain/swelling/redness at the site of injection, headache, body ache and myalgia.</p>

* Currently available only in the private sector

Vaccine recommendations for the elderly

Many developed countries have established vaccination recommendations for adults, with four vaccines commonly being recommended for the elderly: influenza vaccine, pneumococcal vaccine, herpes zoster vaccine, and a vaccine combining tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis.^{7,16,17} Of these vaccines, the South African public healthcare sector Standard Treatment Guidelines and Essential Medicines List (STGs/EML) recommends only free influenza vaccination for the elderly.¹⁸ However, South Africa also has disease-specific guidelines such as those from the National Institute of Communicable Diseases and the Federation of Infectious Diseases Societies of Southern Africa which complement the STGs/EML, which recommend other vaccines for the elderly.^{19,20} These additional vaccines can only be accessed through the private sector, which is unaffordable for the majority of elderly South Africans. See Table I for further details.

Influenza vaccination

Influenza is a highly contagious respiratory infection, caused by influenza viruses. Most global influenza pandemics are caused by influenza A virus, while influenza A and B cause seasonal influenza epidemics. Symptoms range from mild to severe, and include chills, fever, myalgia, headache, arthralgia, pharyngitis, cough and rhinitis/coryza. Infection is spread through respiratory droplets up to approximately seven days after symptoms have subsided.²⁹ Recovery usually occurs within one week; however, severe illness requiring hospitalisation occurs in high-risk populations. Influenza is the leading viral cause of community acquired pneumonia (CAP) in adults,²⁰ and increases the risk of secondary bacterial infections (including pneumococcal pneumonia, which is the leading cause of bacterial CAP²⁰ requiring antimicrobial treatment), with the elderly being especially prone to the risks of complications, hospitalisation and death due to influenza.^{20,29} In South Africa, influenza (and pneumonia) are among the five leading natural causes of death in adults in 2013,²⁰ while currently > 10 million influenza-associated illnesses are estimated to occur annually, resulting in > 11 000 deaths, with the highest burden amongst the elderly.^{30,31}

Vaccination is the most effective strategy currently available for the prevention of influenza. Effectiveness varies according to age, immune status and the circulating strain/vaccine strain match. Although influenza vaccination effectiveness is lower in the elderly, it substantially reduces influenza-related hospitalisation and death in the elderly.^{19,32} The relationship between the influenza virus and cardiac disease is well established, thus the influenza vaccine may potentially protect against cardiac events such as acute myocardial infarction.³³

Since the circulating influenza strains vary each year, the vaccine strains vary each year. Also, the neutralising antibody titres produced in response to the vaccine gradually wane within a year. Thus the vaccine must be administered annually, as early as possible before the influenza season starts, in order to provide sufficient protection.¹⁹ In South Africa, two types of inactivated influenza vaccines are licensed and recommended for use in the elderly.¹⁹ The inactivated trivalent vaccine is available in both public and private sector healthcare facilities and contains two strains of influenza A virus (H3N2 and H1N1) and one influenza B

virus. An inactivated quadrivalent formulation is currently available in the private sector only and contains an additional strain of influenza B. The quadrivalent form of the vaccine is especially beneficial for adults who are naïve to the influenza vaccine and lack pre-vaccination immunity to influenza B lineage.¹⁹

Pneumococcal vaccination

Pneumococcal disease is caused by *Streptococcus pneumoniae* and manifests through a range of illnesses, the most serious being pneumonia and invasive diseases such as bacteraemia and meningitis. More than 90 pathogenic pneumococcus serotypes have been isolated, some of which cause severe disease.³⁴ *S. pneumoniae* associated infections are a leading cause of illness and death worldwide, particularly in children under two years, and the elderly.³⁵ *S. pneumoniae* is the leading cause of CAP in adults,²⁰ with 6.8 million hospitalisations and 1.13 million deaths globally among the elderly being due to CAP in 2015.³⁶ South Africa bears a high burden of CAP, with over a quarter of adult CAP cases being caused by *S. pneumoniae* before the introduction of infant vaccination against pneumococcal disease.²⁰ The high incidence of CAP in South Africa is possibly driven by the high rates of HIV infection, although the rate of disease is decreasing as an indirect effect of childhood vaccination.²⁰

Worldwide, vaccines have substantially reduced the burden of pneumococcal disease and death.^{37,38} Over the past few years, there has been an increase in antibiotic resistant strains of *S. pneumoniae*,³⁴ making vaccination an important strategy in antimicrobial stewardship.^{20,37,39,40} There are currently two pneumococcal vaccines recommended for the elderly; a 13-valent pneumococcal conjugate vaccine (PCV13), and a 23-valent pneumococcal polysaccharide vaccine (PPSV23).^{17,20} PCV13 offers protection against 13 serotypes of *S. pneumoniae*, with pneumococcal polysaccharides being conjugated (bound) to a highly immunogenic non-toxic diphtheria protein called CRM 197 to improve their immunogenicity.⁴¹ An advantage of PCV13 is that it also reduces nasopharyngeal carriage, thereby reducing transmission, resulting in herd immunity.⁴⁰ PPSV23 on the other hand is a pneumococcal polysaccharide vaccine targeting 23 serotypes.³⁷

Both PCV13 and PPSV23 are recommended for all adults aged ≥ 65 years.^{17,20} PCV13 and PPSV23 should be given at separate time points (≥ 1 year apart) to help ensure that protective antibodies to each vaccine develop.³⁷ Studies in adults have found that the efficacy of PPSV23 is enhanced when administered after a dose of PCV13.³⁷ The South African guidelines for the management of CAP recommend that adults ≥ 65 years who are vaccine naïve should first receive a single dose of PCV13 followed by PPSV23 one year later.²⁰ However, the elderly who are PCV13 naïve may already have received PPSV23 as children or adults if they have comorbid conditions predisposing them to severe pneumococcal disease. These include immunocompromising conditions (HIV infection; congenital or acquired immunodeficiency; receiving immunosuppressive treatments [chemotherapy, radiation, post-transplant treatment]; chronic renal failure; nephrotic syndrome; congenital or acquired asplenia; sickle cell disease or other haemoglobinopathies; malignancies), cerebrospinal fluid leak, cochlear implant, and other chronic conditions (alcoholism;

diabetes; chronic heart, lung or liver disease).¹⁷ Although administering a dose of PPSV23 before a dose of PCV13 may reduce the immune response to PCV13, PCV13 is still recommended in PCV13 naïve adults who have already received PPSV23, at least one year after the PPSV23 dose.^{17,20,37,38}

Herpes zoster vaccination

Herpes zoster (shingles) occurs when latent varicella zoster virus (VZV) becomes reactivated. Initial infection with the VZV causes chickenpox, which is more common in children. After recovery, VZV remains dormant for life in the dorsal spinal ganglia and can be reactivated as shingles when immunity declines (immunosenescence). The incidence of shingles increases around four-fold in persons over 80 years when compared to persons under 50 years.⁴²

Shingles presents as a painful rash which is initially maculopapular and then becomes vesicular.⁴² The rash is distributed unilaterally, being confined to a single dermatome.⁴³ The most common complication of shingles is postherpetic neuralgia (PHN), with pain persisting for several months or indefinitely, after the rash has resolved.^{8,43} The pain can be severe, and can significantly diminish quality of life. In addition, studies have shown a possible link between shingles and cerebrovascular and cardiovascular events. For example, a 127% increased risk of stroke in the first two weeks post herpes zoster reactivation has been documented.⁴⁴ Disturbances of vision or complete blindness can occur in severe cases where reactivation occurs in the ophthalmic nerve (herpes zoster ophthalmicus).⁴³

There are currently two vaccines licenced for the prevention of shingles in adults aged ≥ 50 years.^{17,45} The first is a live attenuated virus vaccine (Zostavax[®]), which is available in South Africa. It is administered as a single dose and has been shown to reduce shingles incidence by 51.3%, and PHN by 66.5%, in adults aged ≥ 60 .^{25,43} However, as with most other live attenuated vaccines, vaccination in the severely immunocompromised is contraindicated.^{17,25} The second is an inactivated recombinant vaccine (Shingrix[®]), which is not yet available in South Africa. This vaccine is administered in two doses, with 97% and 90% efficacy at preventing shingles in those aged ≥ 50 and ≥ 70 years respectively, and a longer duration of protection than Zostavax[®].⁴⁵⁻⁴⁷ Despite the greater efficacy and longer duration of protection, Shingrix[®] is associated with a higher chance of adverse events at the injection site when compared with Zostavax[®]. Also, it still remains to be determined if the recombinant vaccine is cost-effective since it is administered in two doses.⁴⁵

Tetanus, diphtheria and pertussis vaccination

Tetanus, commonly known as "lockjaw," is a life-threatening non-communicable (i.e. it is not transmitted from person-to-person) disease caused by neurotoxins of *Clostridium tetani*. These bacteria commonly occur in the soil and animal faeces, being introduced through a break in the skin.^{48,49} Tetanus neurotoxins affect the nervous system, most commonly causing generalised tetanus, with muscle spasms starting in the jaw and spreading to the rest of the body.⁴⁸ Generalised tetanus is considered a medical emergency with respiratory failure being the most common cause of death in the developing world, where ventilators are often not

widely available.⁴⁸ Infants and the elderly are at the greatest risk of death, with up to 100% case fatality rates reported in untreated patients, dropping to 10–20% in patients receiving appropriate treatment.⁴⁹ Although tetanus has become less frequent as a result of successful vaccination programmes, it cannot be eradicated since *C. tetani* spores are ubiquitous in the environment.^{48,49}

Respiratory diphtheria is a life-threatening disease caused by toxigenic *Corynebacterium diphtheriae* strains infecting the nasopharynx. It is characterised by a grey-coloured pharyngeal pseudomembrane, which can dislodge and cause fatal respiratory obstruction.⁴⁹ Diphtheria toxins may also enter the bloodstream reaching all organs including the heart, with myocarditis being a common complication leading to heart failure and death.⁵⁰ Diphtheria was largely eradicated globally by successful vaccination programmes; however, there is presently global concern as recent outbreaks show that diphtheria is re-emerging because of sub-optimal vaccination coverage.^{49,50} Older adults are at risk of diphtheria as immunity from childhood vaccination wanes over time.^{49,50}

Pertussis (whooping cough) is an acute and highly contagious respiratory disease caused by *Bordetella pertussis*.⁵¹ In children aged < 5 years, pertussis is characterised by prolonged paroxysmal coughing, with significant associated morbidity and mortality, particularly in infants aged ≤ 2 months.^{49,51} Although pertussis vaccines have been administered routinely to infants and children for many decades, immunity wanes over time. While pertussis is commonly asymptomatic or mild in adults, the elderly remain susceptible to the disease because of waning immunity, and should be protected.^{49,51} In addition, theoretically, unvaccinated elderly persons in close contact with infants may risk spreading pertussis to infants in their care.⁸ However, there is insufficient evidence to support recommendations for vaccinating the elderly based solely on "cocooning" their grandchildren.⁴⁹

Adults whose tetanus vaccination history is unknown should complete their initial vaccine series which includes a Tdap (tetanus toxoid, reduced diphtheria toxoid, acellular pertussis) dose.⁴⁹ Booster vaccines containing tetanus toxoid and reduced diphtheria toxoid (Td) or Tdap are recommended every 10 years throughout the entire lifetime due to waning immunity of childhood vaccines.⁴⁹

Other vaccines

The United States Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices (ACIP) offers one of the most comprehensive guidelines for adult (> 19 years) vaccination, including vaccines for older adults.¹⁷ The ACIP provides evidence-based guidelines for vaccination of high-risk elderly patients against additional diseases, including hepatitis A, hepatitis B, *Haemophilus influenzae* type b (Hib) and meningococcal infection.¹⁷ In addition, the elderly who travel internationally, may require vaccination against hepatitis A, hepatitis B, typhoid and cholera, although optimal protection may not be achieved because of immunosenescence.^{17,52,53} Also, yellow fever vaccination, which may be required for travel to some countries, should be used with caution in the elderly because of the higher risk of multiple organ failure from viscerotropic disease seen in those aged > 60 years.⁵³

Role of healthcare providers in promoting vaccines for the elderly

HCPs are trusted sources of advice on health matters amongst the elderly. The elderly are already physically and psychologically vulnerable due to their advanced age and failing health status. Often, the HCP's advice is an important factor associated with vaccination decisions.^{54,55} HCPs can engage in a number of advocacy and communication activities to make recommendations and create more general awareness of the importance of vaccination of the elderly, and instil confidence in vaccination.⁵⁴⁻⁵⁶ Implementation of an alert system for patients to remind them to get their annual influenza vaccine also has the potential to increase uptake.⁸

Pharmacists specifically have an important role in promoting vaccines for the elderly.^{56,57} The elderly are often plagued with multi-morbidities and regularly interact with pharmacists when their chronic medicines are dispensed.⁵⁶ These interactions are an opportunity for pharmacists to provide information on the increased risk of the elderly to infections as well as education and advocacy on the importance of vaccines to prevent such infections.⁵⁶ In their role as educators and advocates for health, pharmacists can reduce complacency and instil confidence in vaccine efficacy and safety.⁵⁷ Convenience and access to vaccines can be increased by ensuring that pharmacies are located in close proximity to the communities they serve, including rural areas, as well as ensuring that they have sufficient stocks of vital vaccines.^{56,57}

Although not protective against SARS-CoV-2, HCPs should encourage the elderly to be vaccinated against influenza and pneumococcal disease, to lessen the burden on the healthcare system due to the current COVID-19 pandemic.¹⁹

Conclusion

Vaccination programmes in many countries focus mostly on childhood vaccination, although many vaccines are recommended for adults. The elderly in particular, are vulnerable, suffering more frequent episodes of illness with disease severity often being higher due to immunosenescence. These VPDs result in increased expenditure and reduced quality of life among the elderly. The increased susceptibility to illness makes the elderly an important target population for vaccination in order to facilitate healthy aging. Modern public health policies should therefore transition from *childhood vaccination programmes* to *vaccination programmes for all ages and all groups* and HCPs should proactively promote vaccines in order to prevent VPDs and their sequelae in the elderly.

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