Immunizations in Older Adults

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Abstract

The age-related decline in immunity known as immunosenescence means that older adults are at increased risk of infection, as well as at higher risk of severe forms, complications, and poor outcomes. In parallel, the burden of infectious diseases is highest among older adults, with the inherent risk of hospitalization, aggravation of pre-existing diseases, frailty, increased disability, and ultimately death. Vaccination is the most effective means to prevent against common infectious diseases, yet vaccine uptake in adults remains consistently below target. We discuss here the physiopathological rationale for vaccination in older adults, focusing on the three main diseases that account for the greatest morbidity and/or mortality in this population, namely, seasonal influenza, pneumococcal disease, and herpes zoster. We discuss the burden of each disease and the available vaccines. We also briefly review other vaccines recommended in older adults. The role of the family physician in promoting vaccination among older adults is key

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and can actively drive efforts to improve vaccine uptake in this population, thereby reducing the burden of infectious disease and contributing to healthy aging.

Keywords

Older people · Vaccinations · Vaccine-preventable disease · Immunosenescence Vaccine hesitancy

7.1 Background

In older people, the ability to defend against infective agents or malignant and autoreactive cells declines with increasing age, whereas susceptibility to disease, cancer, and autoimmune disorders increases. This phenomenon is known as immunosenescence, namely, an age-related decline in immunity that occurs with increasing age [1]. It affects both innate and adaptive immunities, although the latter is compromised to a greater degree. Naïve T cells, T regulatory cells, and B cells all decline in number, as does specific antibody production, whereas the functions of memory cells are relatively preserved. Data suggest that memory B and T cells, once elicited by antigens during youth, are quite resilient to the impact of immunosenescence [2], whereas the ability of B and T cells to interact and respond to new infections, tumors, autoimmune response, or vaccinations becomes limited. The clinical consequence of immunosenescence is therefore an increased susceptibility to infection, along with a greater risk of experiencing severe forms of disease, complications of the disease, and poor outcomes. The reasons for the increased susceptibility to disease in older adults, in addition to the aforementioned waning of immune response, include epidemiological factors, malnutrition, and a large number of other age-associated physiological and anatomical alterations, such as increased risk of invasion by pathogenic organisms due to alterations in the barriers represented by the skin, lungs, and gastrointestinal and urological tract (and other mucosal linings). Research into methods for achieving a higher level of protection over a longer duration, with more persistent immune responses, could improve both vaccine impact and coverage, not only preventing disease but increasing healthy lifespan across the board [3].

The burden of infectious diseases is greatest in young children and elderly adults. It is among older adults that the risk of hospitalization, complications, or aggravation of pre-existing diseases, frailty, increased disability, and death is highest. Seasonal influenza (flu), pneumococcal disease, and herpes zoster (HZ) all have their highest mortality rates in older individuals [4]. However, while vaccination prevention campaigns have achieved high coverage rates in children, vaccine uptake levels remain consistently below target in adults, in both healthy and at-risk populations. A century ago, infectious diseases contributed nearly half of all deaths in developed economies like the USA, but while infectious disease has been greatly reduced, the remaining burden of these diseases is now borne disproportionately by older adults [5].

Pneumonia and influenza are among the top ten causes of death, and the risk of nosocomial infections increases in number and clinical severity in individuals aged 65 and older [6, 7]. Even the clinical presentation of infections in older people is quite often different, with fewer symptoms, low grade fever, delirium, anorexia, or generalized weakness [8], possibly leading to delayed diagnosis or untreated conditions and an increase in related complications and hospitalizations. In the elderly, common infections are more frequent and more severe but older adults with chronic diseases (e.g. diabetes, chronic obstructive pulmonary disease or heart failure) have a greater impairment of immune system and a poorer vaccine response with even more susceptibility [9]. Similarly, residents in senior centers, long-term residential facilities, or other social institutions such as daycare programs have been shown to have a significantly increased risk of infections, with worse outcomes (in terms of morbidity and mortality) compared with non-residents [10].

7.2 Prevention Strategies in Older Adults

There are many strategies to counteract the increased risk of infection in older individuals. In addition to the usual lifestyle recommendations, such as adequate nutrition [11], regular physical exercise, smoking cessation, and stress reduction, routine vaccination is one of the most effective interventions in healthy older adults and a key contributor to healthy aging. Immunization against vaccine-preventable diseases (VPDs) has led to significant reductions in mortality and morbidity from infectious causes. Traditionally, most vaccine policies and initiatives are age-based and focus principally on pediatric vaccination, with less emphasis on vaccine policies for older adults. The benefits of vaccination are most obvious in children because childhood vaccination is well-established as a social norm. By way of comparison, compliance with vaccine recommendations in children exceeds 90% in most high-income countries, but compliance is far lower in adults [5]. In older adults, mortality rates due to VPDs such as influenza and pneumococcal disease have only modestly decreased in recent decades, and these persistently low vaccine uptake rates in adults prevent the full benefits of immunization from being reaped.

Therefore, a shift from the childhood vaccination paradigm to a new life-course approach to vaccination is essential to prevent disability, morbidity, and mortality in older subjects and to promote healthy aging [12, 13].

7.3 Factors Influencing Vaccine Uptake

The low vaccine uptake observed among adults is due to multiple factors. For physicians, barriers to vaccination include a constantly changing landscape with frequent updates to vaccination schedules, lack of knowledge among healthcare providers about the clinical and functional implications of aging, and time and logistic constraints in a busy practice setting. Among patients, obstacles to immunization include social influences, disease-related and vaccine-related factors, general

attitudes toward health and vaccines, habit, awareness and knowledge, practical barriers and motivators, and vaccine hesitancy [14]. Vaccine hesitancy refers to the delay in acceptance or refusal of vaccines despite availability of vaccination services [15], a phenomenon identified by the WHO as one of the ten major threats to global health in 2019.

The reasons behind vaccine hesitancy are complex and may be either individual or general. They generally fit into three categories: lack of confidence (in effectiveness, safety, the system, or policy-makers), complacency (a perceived low risk of acquiring VPD), and lack of convenience (availability, accessibility, and appeal of immunization services, including time, place, language, and cultural contexts) [15, 16]. To shift individual and community attitudes, beliefs, and, consequently, their decision-making toward greater vaccine acceptance, we need to enhance "awareness of the health threat prevented by the vaccine, maintaining availability through trusted channels, ensuring accessibility to all populations, safeguarding affordability through national program, and ultimately, encouraging acceptability by countering specific vaccine hesitancy beliefs" [17].

7.4 The Role of General Practitioners

The family doctor or general practitioner (GP) usually has a long-standing relationship with the patient and good knowledge of the person, their family, and the context in which they live. As a result, the GP can be very influential in achieving objectives in terms of individual and collective vaccine coverage. The GP's role in preventive medicine is especially determinant for older adults. The GP knows the health status of older patients (i.e., whether they are healthy or suffering from chronic diseases) and usually has a good idea of their lifestyle or risk factors. With a long history of regular follow-up comes the likelihood that the GP knows the patient's vaccine history, which can often be difficult to elicit and may be subject to memory bias. This comprehensive knowledge of the patient enables the GP to adopt a targeted approach to immunization with specific action, where warranted, to address vaccine hesitancy. Indeed, despite the public's widespread use of the Internet to search for information on vaccination, the family doctor remains the most trusted source of information. In Italy, research performed in 2017 by CENSIS attributed a critical role to the family doctor as a source of information about influenza (flu) vaccine. In this study, 62.7% of respondents reported that they asked their family doctor about the need for vaccination, as the most reliable and trustworthy source of information [18].

Their privileged position as a trusted source of information on vaccines means that family physicians play a key role in driving vaccine acceptance. The awareness of vaccination in adult populations is very low. In developed countries, the majority of the general population does not see a high incidence of VPDs in their entourage. This leads to a failure to perceive the risk of VPDs in comparison to the rare adverse events associated with vaccination. The perceived susceptibility and severity of influenza among elderly people weakly correlate with vaccination acceptance, but

recommendations from doctors, nurses, or friends/relatives contracting influenza led to a sudden increase in threat perception and subsequent immunization [19].

There are many strategies to enhance vaccine acceptance, most of which come from studies of pediatric immunization. The main features include telling stories, focusing on the benefits of protection, being honest about side effects when asked, not providing only numbers and facts, and building trust with patients [20]. In a study assessing mothers' decision-making regarding vaccination for their children, trust was built when a provider spent time discussing vaccines, did not deride the mother's concerns, was knowledgeable, and provided satisfactory answers, not scientific facts, with tailored information as the main aspects of communication competence [21].

The goal for every family doctor is to seize every opportunity to discuss vaccination with their patients, not only during the flu vaccine campaign but throughout the year, as an integral part of daily practice. With older patients in particular, there are frequent opportunities for medical contact, such as regular check-ups of chronic disease, prescription refills, or during consultations prior to travel, during which it is possible to strengthen the message about vaccination. It is important not only to discuss personal vaccine coverage, but it is also essential to offer the vaccine as soon as possible, preferably in the same session. A study in two major US cities (Houston, Pittsburgh) showed that reducing the number of missed opportunities is associated with a significant increase in coverage rate [22]. Accordingly, vaccine availability and its affordability play a key role in vaccination in older persons. Ease of access, close to home, and at a convenient time, together with affordability of the vaccine are key factors in enhancing the immunization rates and also happen to be the salient characteristics of the local GP practice.

For older persons, it is determinant to receive the vaccine in a convenient place that is easy for them to reach, at the right time, with people they know, and this is all the more true when the person suffers from several chronic diseases or cognitive impairment. Moreover, it is very important to take enough time with each person to discuss the issue, provide information about side effects or efficacy of the vaccine or about the scheduled vaccines recommended for their age group, check their understanding regularly, and answer any new questions that may arise. In a study based in Los Angeles County, USA, the researchers found that the major obstacles to vaccine receipt in adults were logistical and structural challenges, especially lack of time for counseling and patient flow, vaccine storage and space, or lack of support personnel, whereas use of electronic tools (adult immunization registry or electronic medical records) was associated with a higher likelihood of administering vaccination [23]. For family doctors who face logistic or time constraints and who are unable to offer vaccination themselves, they should refer patients to partner provider who can administer the vaccine, and they should review the issue with the patient at the next visit to make sure the referral followed through to vaccination.

Communication is a further key issue in influencing vaccination, not only in awareness or acceptance but also in reminder-recall programs during flu season or for other recommended vaccine schedules. There are many studies based on technological tools such as mobile phone-based applications (apps) or e-mail campaigns,

which greatly facilitate outreach, delivering healthcare messages to large numbers with relative ease [24, 25]. There are technological systems that can help doctors to send reminders to patients, or to be proactive (i.e., every time a patient comes to the practice for a prescription or visit, the nurse or doctor receives an alert on the patient's record), or to directly create a list with planned uptake for age group or risk group (chronic diseases, etc.), employer group, or lifestyle group (travelers, etc.). The use of electronic tools for adult immunization registries (at a local or, ideally, national level) can give family doctors the ability to identify gaps in care, track outcomes, and plan recalls for vaccine defaulters.

Creating a national immunization registry for family doctors could achieve more efficient preventive medicine. Immediate availability of up-to-date information on vaccine history, tracking uptake country-wide, in every healthcare context (e.g., emergency room, GP's office, specialist, etc.) would permit more effective and efficient action for older persons. It would help to increase coverage status, reduce possible defaults, and provide the correct schedule to follow, based on age or comorbidity or lifestyle. A vaccine registry can also be used for benchmarking purposes and as an incentive for quality improvement.

In addition to GP practices, the organization of the health system also has a role to play in promoting vaccine acceptance. Smaller practices (1 or 2 doctors) may have more difficulty offering a full array of vaccine products, including maintaining vaccine temperatures and affording rent for space to store vaccines, whereas larger practices (with 11–30 providers or more than 30 providers) and those affiliated with a hospital or large healthcare system are more likely to administer most vaccines [23].

In a recent study in Lazio, Italy, researchers found that flu vaccine uptake was higher in older people assisted by family doctors who got their master's degree more recently, assisted a relatively high proportion of older patients, received influenza vaccination, had a computer assistant, and were associated with other physicians [26]. Working in a team environment allows targeted evidence-based interventions; possibility of facilities (place for storage, cold chain); better knowledge and analysis of vaccine coverage and benchmarks, local and national; reviews and sharing of safety procedures; and reduction of medical errors.

In summary, the role of family physicians in immunization in older people is determinant and includes periodic review of vaccination and counseling about available and recommended vaccines, together with the offer of and administration of the vaccine, as well as control of possible side effects. For GPs who cannot provide vaccination, they should refer patients elsewhere and review the issue at the next visit to check that the vaccine was received. The healthy aging adult needs a proactive approach with integrative interventions for primary prevention (e.g., lifestyle, smoking cessation, etc.), while older individuals or those with comorbidities need more clinical interventions and decisions for immunization.

Almost all countries have established national recommendations for immunization schedules across the lifespan from childhood to older age. Despite some heterogeneity in age thresholds and vaccine recommendations, there are some core vaccines that are widely recommended for older persons and are reviewed below.

7.5 Tetanus, Pertussis, and Diphtheria Vaccine (Tdap)

Administration of the diphtheria-tetanus-acellular pertussis vaccine is routinely recommended in children, with a single booster dose of a vaccine containing tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) in adolescence and a single booster dose of a vaccine containing tetanus toxoid, reduced diphtheria toxoid (Td), or Tdpa every 10 years in adults, according to national recommendations.

Despite these recommendations, immunity to tetanus, diphtheria, and pertussis continues to wane among adults in Europe and the USA [27, 28]. Clinical tetanus, although rare in the USA and Europe, occurs predominantly in unvaccinated or under-immunized older adults, especially older women, who never received the primary series [28, 29].

Although, in Europe, the most severe symptoms of pertussis occur in infants and young children, and most deaths in 2015 occurred in infants too young to be vaccinated, there is nonetheless an increasing incidence of pertussis in adolescents and adults. These age groups are a major source of transmission to infants, especially because mild and asymptomatic cases in adolescents and adults are often not recognized as pertussis [30]. Therefore, in many countries, the National Immunization Advisory Boards suggest immunization with Tdap booster, especially for pregnant women and older individuals [31].

Pockets of diphtheria are reappearing, primarily in resource-limited countries. Approximately 20 to 60 percent of adults become susceptible to diphtheria because of waning vaccine-induced immunity and failure to receive recommended booster immunization. Unvaccinated or inadequately vaccinated travelers to endemic areas are at risk of acquiring this infection [32].

Older adults with and without comorbidities should be reviewed during clinical visits regarding complete primary immunization against tetanus, diphtheria, and pertussis. Those who have not previously been vaccinated against tetanus and diphtheria should receive a series of three vaccines, the first dose and second dose separated by 4 weeks and the third dose given 6–12 months later.

After complete primary immunization, it is recommended to administer a single booster of Td or Tdap every 10 years, according to national recommendations [31, 33, 34]. Studies of the Td vaccine have demonstrated the efficacy and cost-effectiveness of a single booster in producing sustained immunity to both tetanus and diphtheria among older patients (aged 50–70 years) who had received a primary booster series [35].

Older adults should be reviewed every 10 years for the single booster, especially those with grandchildren or living in families with children or pregnant females, in order to receive Tdap for pertussis immunization.

7.6 Influenza Vaccine

The burden of influenza on world health is major, with influenza-related lower respiratory tract infection responsible for an estimated 145,000 deaths among all ages in 2017 according to the Global Burden of Disease study [36]. Influenza

mortality rate was highest among adults older than 70 years [36]. Older people are at high risk of developing serious complications from flu, such as hospitalization (57–70%), increased disability, or death, compared with younger, healthy adults. In the USA, more than 75% of influenza-related deaths occurred among people age 65 and over in the 2018–2019 flu season [37]. Recent studies have investigated influenza infection as a potential trigger for cardiovascular conditions, including acute coronary syndromes and atrial fibrillation [38, 39]. Older adults experience significantly increased morbidity and disability from the flu, especially frail adults older than 65 years or those in long-term care, for whom even relatively mild respiratory illness may lead to a catastrophic chain of events, from taking to bed, disorientation, and respiratory illness to falls, fracture, and worsening clinical conditions of preexistent comorbidities. Vaccination is highly effective in preventing adverse outcomes, as shown by an umbrella review and meta-analysis reporting that in community-dwelling older people, influenza vaccination was associated with a lower risk of hospitalization for heart disease and for flu/pneumonia, with evidence of convincing strength [40].

Most countries recommend flu vaccination for older people, usually from age 60 or 65 years and older. Among the available vaccines, two are specifically designed for people aged 65 years and older, namely, a high-dose flu vaccine (brand name Fluzone High-Dose ®) and the adjuvanted flu vaccine.

The Fluzone High-Dose is a three-component (trivalent) inactivated flu vaccine that contains four times the amount of antigen of standard-dose inactivated influenza vaccines. In the USA, Fluzone High-Dose is licensed only for persons aged 65 years and older [41]. A study published in the New England Journal of Medicine [42] reported that the high-dose vaccine was 24.2% more effective in preventing flu in adults 65 years of age and older relative to a standard-dose vaccine. A separate study [43] reported that Fluzone High-Dose was associated with a lower risk of hospital admissions compared with standard-dose Fluzone for people aged 65 years or older, especially those living in long-term care facilities.

The adjuvanted flu vaccine integrates the MF59 squalene oil-in-water adjuvant, which stimulates a stronger immune response to vaccination. It is licensed for people older than 65 years who often have a lower protective immune response after flu vaccination compared to their younger, healthier counterparts. The adjuvanted flu vaccine was found to be associated with a reduced risk of hospitalization for pneumonia and influenza diagnoses [44] and pneumonia, cerebrovascular, or cardiovascular diagnoses relative to the unadjuvanted vaccine in retrospective studies of medical record data [45].

To date, there have been no randomized, head-to-head comparisons of these two vaccines. No preference is expressed for either vaccine type by the American Advisory Committee on Immunization Practices (ACIP), but it is strongly recommended to administer any available age-appropriate formulation [46]. In Italy, the adjuvanted flu vaccine is recommended [34], but Fluzone High-Dose is not currently available.

The recommendations of the American Centers for Disease Control and Prevention (CDC) and the European Centre for Disease Prevention and Control (ECDC) regarding influenza, pneumococcal, and herpes zoster vaccination in older adults are summarized in Table 7.1.

Table 7.1 Summary of the recommendations from the US Centers for Disease Control and Prevention (CDC) and the European Centre for Disease Prevention and Control (ECDC) for the vaccination of older adults against influenza, pneumococcal disease, and herpes zoster

	Influenza	Pneumococcal disease	Herpes zoster
ECDC	**Inactivated tri- or quadrivalent influenza vaccine** recommended **annually** for:	Vaccination with **PCV13, PPSV23, or a combination of both** is recommended in all European Union countries except Bulgaria, Croatia, Estonia, France, Latvia, Liechtenstein, Lithuania, Portugal, and Romania	Vaccination with the **live attenuated herpes zoster vaccine** is recommended for adults:
	• Adults **≥55 years** in Malta and Poland		• **Aged 50–60 years** in Austria
	• Adults **≥60 years** in Germany, Greece, Hungary, Iceland, Netherlands, Slovakia		• **Aged ≥ 50 years** in the Czech Republic
	• Adults **≥65 years** in Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Ireland, Italy, Latvia, Liechtenstein, Luxembourg, Norway, Portugal, Romania, Slovenia, Spain, and the UK		• **Aged ≥ 60 years** in Greece
	• Specific risk groups only in Lithuania and Sweden		• **Aged ≥ 65 years** in Italy
			• **Aged 65 to 75 years** in France
			• **Aged 70 years** in the UK
			Vaccination with the **inactivated herpes zoster subunit vaccine** is recommended **in Germany** for adults **aged ≥ 60 years**

(continued)

Table 7.1 (continued)

	Influenza	Pneumococcal disease	Herpes zoster
US CDC	**1 dose of influenza vaccine** is recommended **annually** with the inactivated influenza vaccine or the recombinant influenza vaccine for all adults **aged ≥ 65 years**	1 dose of PPSV23 is recommended for all adults **aged ≥ 65 years**. If PPSV23 was administered prior to age 65 years, 1 dose of PPSV23 should be administered at least 5 years after previous dose	For adults **aged ≥ 50 years**, vaccination with the **inactivated herpes zoster subunit vaccine** is recommended (2-dose series, 2–6 months apart, minimum interval 4 weeks), regardless of previous herpes zoster infection or vaccination
		1 dose of PCV13 may be considered in immunocompetent adults based on shared decision-making	For adults **aged ≥ 60 years**, vaccination with the **inactivated herpes zoster subunit vaccine** is recommended (2-dose series, 2–6 months apart, minimum interval 4 weeks) or 1 dose of live attenuated zoster vaccine if not previously vaccinated. The subunit vaccine is preferred over the live attenuated vaccine

PCV13 pneumococcal conjugate vaccine 13-valent, *PPSV23* pneumococcal polysaccharide vaccine 23-valent

7.7 Pneumococcal Vaccine

Pneumococcal disease (PD) can be divided into non-invasive disease, including sinusitis, acute otitis media, and community-acquired pneumonia (CAP), and invasive pneumococcal disease (IPD), characterized by the isolation of *Streptococcus pneumoniae* from otherwise sterile sites and mainly comprising pneumococcal meningitis, bacteremic pneumococcal pneumonia, and pneumococcal bacteremia. The burden of invasive and non-invasive diseases remains high, despite wide access to antibiotic therapies. Furthermore, there is an increasing problem of antibiotic resistance, and susceptibility to macrolide antimicrobials, penicillins, and cephalosporins can no longer be presumed in many countries.

Pneumococcal infections affect people of all ages, but children younger than 2 years of age and adults aged 65 years and older are at higher risk. Invasive pneumococcal disease accounted for over 36,000 cases in the USA in 2011 and 11 to 27 cases per 100,000 in Europe, while incidence rates of non-invasive pneumococcal disease, notably CAP, ranged from 1.6 per 1000 in Spain to 11.6 per 1000 in Finland [47–49]. Both the incidence of pneumococcal disease and the mortality rate increase after age 50 and more sharply after age 65.

There are currently two vaccines against pneumococcal infection, namely, the pneumococcal polysaccharide vaccine (PPSV) and pneumococcal conjugate vaccine (PCV). PCV7 vaccination was first approved for children under 2 years of age

in 2000 by the US Food and Drug Administration and in 2001 by the European Union. Additional serotypes were introduced with the update to PCV13 in 2010. Widespread implementation of PCV vaccination in children has profoundly modified the epidemiology of pneumococcal disease in the population [47], with in particular large reductions in IPD in the older population [50]. The randomized CAPITA study investigated the efficacy of PCV13 in preventing IPD and CAP in individuals aged 65 years and older and reported significant efficacy for the prevention of vaccine-type pneumococcal, bacteremic, and non-bacteremic CAP and vaccine-type IPD, but not in preventing all-cause CAP [51].

The pneumococcal polysaccharide vaccine (PPSV23) contains polysaccharide antigen from 23 types of pneumococcal bacteria and has been reported to have a statistically significant effect IPD among healthy individuals aged 65 years of age and older [52, 53]. In a systematic review and meta-analysis of the efficacy of PPSV23 in older adults, pooled efficacy of 73% was reported against IPD caused by any serotype [54].

The US Advisory Committee on Immunization Practices (ACIP) recently revised its recommendations for pneumococcal vaccination in adults, notably removing the recommendation for routine PCV13 use among adults aged ≥65 years on the basis that continued childhood immunization with PCV13 has reduce disease burden among adults to historically low levels via reduced carriage and transmission of vaccine serotypes from vaccinated children (i.e., indirect effects) [55]. In parallel, there has been a substantial decrease in antimicrobial resistance [56].

The ACIP now recommends PPSV23 for all adults 65 years or older and for individuals aged 2–64 years with certain medical conditions or for adults aged 19–64 years who smoke cigarettes. PCV13 vaccination is no longer routinely recommended for all adults aged ≥65 years, but adults aged 65 years or older may discuss and decide, in shared decision-making with their clinician, to receive PCV13 based on the patient's individual risk.

In the European Union, almost all countries recommend either PCV13 or PPSV23, or both, in older adults, but recommendations vary from country to country (https://vaccine-schedule.ecdc.europa.eu/).

7.8 Herpes Zoster Vaccine

Herpes zoster is the clinical manifestation of reactivation of the varicella zoster virus (VZV), which remains latent in the dorsal root or cranial nerve sensory ganglia after primary infection (chickenpox). Herpes zoster affects almost one in three adults during their lifetime. Over 95% of the adult population is seropositive to specific anti-VZV antibodies and therefore is potentially at risk of developing HZ in their lifetime.

In Italy, the estimated incidence is 6.3 cases/1000 person-years; and although hospital admissions are less than 2%, the rate is 69% in patients aged over 65 years [57]. The incidence shows a growing rate of herpes zoster infection with increasing age, reaching over 10 cases per 1000 person-years beyond the age of 80 [58].

Herpes zoster is a considerable cause of morbidity, especially in older, immunosuppressed, or critically ill patients. The illness is associated with significant pain and complications, the most debilitating of which is post-herpetic neuralgia (PHN). PHN is long-lasting pain that persists for some weeks and even months or years after the disappearance of the rash [59], often requiring hospitalization and considerably impairing daily functioning and quality of life. PHN affects one third of all HZ patients [60], and available antiviral and analgesic treatments are relatively unsatisfactory in reducing pain and length of the disease.

Higher relative risks of diagnosis of cardiovascular diseases (tenfold increase), cerebral vasculopathy (fivefold increase) (including acute stroke and transient ischemia), non-arrhythmic myocardiopathy (sevenfold increase), and neuropathy were identified in adults aged 50 years or older with severe herpes zoster requiring hospitalization [61].

There are two available vaccines against herpes zoster: first, a live attenuated unadjuvanted vaccine prepared from the Oka/Merck strain of varicella zoster virus (ZVL) and, second, a recombinant adjuvanted subunit vaccine (HZ/su or RZV).

The ZVL vaccine is indicated for immunization of individuals aged 50 years or older and is effective and safe in subjects with a positive history of HZ. It is given as a single dose injected under the skin or into the muscle. Clinical studies show a reduction of 51% in the incidence of disease, 61% in disease burden, and 67% in PHN in vaccines [57]. The protection afforded by the ZVL vaccine lasts for 5 years. However, lower vaccine efficacy with increasing age is a feature of existing live attenuated herpes zoster vaccines, falling from 69.8% in those aged 50–59 years to 37.6% in those ≥70 years and 18.3% in those aged ≥80 years [62]. The vaccine is not indicated for the prevention of primary varicella infection (chickenpox) and should not be used in children and adolescents. Contraindications include the following:

- A history of hypersensitivity to any of the excipients or trace residuals (e.g., neomycin).
- Primary and acquired immunodeficiency.
- Immunosuppressive therapy (including high-dose corticosteroids).
- Active untreated tuberculosis.
- Pregnancy.

The recombinant zoster vaccine (RZV) is recommended as the preferred herpes zoster vaccine in the USA, but it is not available everywhere in Europe, despite having received approval from the EMEA. It is given in two doses, administered 2–6 months apart for maximum efficacy. Shingrix has been shown to be highly effective at preventing shingles and post-herpetic neuralgia in adults older than 50 years for at least 4 years after vaccination. The vaccine is also effective at protecting adults older than 18 years who are at increased risk of herpes zoster such as the immunosuppresed patient. Pooled analyses of data from participants aged 70 years and older from the ZOE-50 and ZOE-70 trials (totaling 16,596 participants) reported vaccine efficacy against HZ of 91.3% (95% CI, 86.8 to 94.5; $P < 0.001$) and vaccine

efficacy against PHN of 88.8% (95% CI, 68.7–97.1; $P < 0.001$) [63, 64]. The protection conferred by RZV has been shown to last up to 9 years [65]. Studies examined the safety of Shingrix vaccination five or more years after Zostavax vaccination. Shorter intervals were not studied, but there are no theoretical or data concerns to indicate that Shingrix would be less safe or effective if administered less than five years after a patient received ZVL. Anyway, it is possible to administer RVZ after ZVL at least 8 weeks later [34]. It can also be administered in people who have previously had HZ infection. RZV can be co-administered with non-adjuvanted inactivated seasonal influenza vaccine, 23-valent pneumococcal polysaccharide (PPV23) vaccine, or antigen-reduced diphtheria, tetanus and pertussis (acellular component) (dTpa) vaccine. Vaccines should be administered at different injection sites.

Contraindications to RZV are:

- A history of severe allergic reaction, such as anaphylaxis, to any component of a vaccine or after a previous dose of the RZV.
- Persons known to be seronegative for varicella virus. It is not necessary to screen (either verbally or via laboratory serology) for a history of varicella. However, if a person is known to be varicella-negative via serologic testing, providers should follow guidelines for varicella immunization.
- Ongoing infection with herpes zoster.
- Although not evaluated in pregnant or lactating women, it is advisable to delay administration of RZV in this population.

7.9 Other Vaccines

While flu, pneumococcal disease, Tdap, and herpes zoster are the most commonly recommended vaccines in older adults, primary care providers should be mindful that some patients may require other vaccines. For example, immunization against hepatitis A or B, meningococcal disease, or measles, mumps, and rubella may be indicated in certain patients depending on their health status, their occupational exposures or risks, and their lifestyle behaviors. Older persons undertaking travel to areas with endemic diseases should also be advised to receive appropriate vaccinations prior to departure. All these considerations should be explored on a case-by-case basis with each individual patient, during regular review of immunization status.

7.10 Conclusions

Older persons are at particularly high risk of influenza, pneumococcal disease, and herpes zoster infection. When infected, they are additionally at higher risk of experiencing severe forms of disease, complications, and poor outcomes. In patients with chronic diseases, which is often the case of elderly people, the risk is also augmented. In parallel, advancing age leads to a decline in immunity known as

immunosenescence, whose consequence is an impaired ability to mount and maintain immune response to infection and vaccination. Despite the wide availability, often free-of-charge, of efficacious vaccines against several common infectious diseases, uptake of vaccination is low in older adults and well below recommended target levels, for a variety of patient-, provider- and system-related reasons. Primary care physicians have an influential role in promoting vaccination among older individuals and are key in driving efforts to improve vaccine uptake in this population. No opportunity should be missed to recommend and provide vaccines to older patients, with a view to contributing to healthy aging and preserving functioning and quality of life in older individuals.

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