Advocating Vaccination of Adults Aged 60 Years and Older in Western Europe:

Statement by the Joint Vaccine Working Group of the European Union Geriatric Medicine Society and the International Association of Gerontology and Geriatrics—European Region


Abstract

Vaccines are an underused public health strategy for healthy aging. Considering the risks of vaccine-preventable diseases and the current low vaccine coverage rates in older European citizens, the two European geriatric and gerontological societies (European Union Geriatric Medicine Society [EUGMS] and International Association of Gerontology and Geriatrics–European Region [IAGG-ER]) convened a Joint Vaccine Working Group to develop a consensus document advocating routine vaccination of aging populations. The mandate of this Working Group was to improve the uptake of routine vaccinations in adults aged 60 years and over. The consensus statement underlines the need to establish, strengthen, and harmonize European policies that continue routine vaccinations to adulthood and that will include older populations. Improved vaccination rates will promote healthy aging by reducing the burden of vaccine-preventable infectious diseases in older populations, a population that is rapidly increasing in Europe.

Introduction

Unlike childhood immunization programs, vaccines are not yet well established as a routine health intervention for the aging population. Low vaccination coverage rates in adults may lead to an increased incidence of diseases such as diphtheria and pertussis in adults in the future. Moreover, infectious diseases in older people remain a significant cause of morbidity and mortality in the increasing population of adults over 65 years and many of these diseases are vaccine preventable. In 2001, lower respiratory infections represented the fourth most frequent cause of death in high-income countries, causing 4.4% of the total deaths, occurring three times more often in adults aged 60 years and older.

Surprisingly, tetanus is still an active disease, with 210 cases in Portugal (1993–2002), 175 cases in England (1984–2000), and 180 cases in Poland (1998–2006) and mainly affecting adults over 50 years of age. In the 1990s, diphtheria epidemics in the newly independent states of the former Soviet Union claimed over 3000 lives, essentially among persons aged 35–50 years. The morbidity from pertussis appears to be substantial in older populations. The annual incidence of herpes zoster in the general population

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is estimated between 3.6 and 14.2 cases per 1000, and the recurrence risk is 8–10 times higher in adults over the age of 60 years.22,23

Without specific vaccine programs for the adult populations aged 60 years and older, these infectious diseases will continue to be a cause of substantial morbidity and mortality ranks in the next decades24,25 whatever diagnostic and therapeutic progresses are made. Furthermore, the worldwide proportion of adults over the age of 60 is expected to increase from 10% in 2002 to 21% in 2050.26 In Europe, in same time period, the increase in size of the 60 years of age population is predicted to reach 160%.26

Because of these data, two European geriatric and gerontological societies—the European Union Geriatric Medicine Society [EUGMS], representing 32 Geriatric National societies of European countries, and the International Association of Gerontology and Geriatrics–European Region [IAGG-ER], representing national societies from 43 European countries—formed a Joint Working Group of experts to formulate vaccination guidelines for use in geriatric medicine (see Table 1) concerning both life-threatening-diseases (influenza, pneumococcal pneumonia, and tetanus/diphtheria) and diseases that mainly impact quality of life (pertussis and herpes zoster).

Longer life expectancies necessitate a careful adaptation of vaccine guidelines based on a better understanding of the reasons for low vaccine coverage in older European citizens and the inability of an aging immune system to produce an appropriate and effective response to vaccination (immunosenescence). The development of new vaccines challenging immunosenescence should not be awaited. The currently available vaccines already have the potential to lower the burden of infectious diseases in both community-dwelling adults aged over 60 years and institutionalized older populations, even if ethical issues are sometimes raised on the age limit for immunization.27 The main focus of this European Joint Working Group is to complement existing information and increase the willingness and acceptance of vaccinating all adults aged 60 and older, their family members, as well as health-care professionals. Special travel-related risks or regional risks and their vaccines (e.g., hepatitis A and B) are not considered within these clinical guidelines.

What Are Current Vaccine Coverage Rates in Older European Citizens?

In most European countries, influenza and pneumococcal vaccine recommendations are either age-based (i.e., above a defined age), risk-based (i.e., high-risk population), or exposure-based (health-care professionals). The influenza vaccine recommendations are supported by the World Health Organization (WHO), which set coverage-rate goals for adults aged 60 years and older: 50% by 2006 and 75% by 2010.28 Moreover the European Parliament resolution on the strategy against an influenza pandemic has approved and confirmed WHO’s objectives and goals.29 However, 2007 health risk appraisal studies of older community-dwelling populations living in London, United Kingdom (mean age 74.7 ± 6.7 years), Hamburg, Germany (mean age 71.5 ± 7.6 years), and Solothurn, Switzerland (mean age 74.5 ± 5.8 years) showed that only 71.8%, 59.3%, and 46.1%, respectively, received annual influenza vaccinations.30 Coverage rates for pneumococcal vaccine in 2007 were even lower, with only 12.2% of the English, 10.3% of the German, and 8.7% of the Swiss community-dwelling populations.30 An English national survey conducted in 2006 by general practitioners (GPs) found marked regional variations and an average pneumococcal vaccine uptake reaching 29.8% (range, 22–43.4%) in the 75- to 79-year-old community-dwelling adults and 36.2% (range, 30.8–50.1%) in the over 80-year age group.31 In 2007, in French geriatric units, pneumococcal vaccine coverage was only 21.9% (range, 0–100%).32

In the early 1990s, a survey conducted in Belgium by GPs on tetanus toxoid (TT) vaccine coverage in the community confirmed that the vaccine uptake decreased significantly from 41.7% in men aged 51–60 years to 6.1% in men aged over 80 years.33 A 2002 French National survey found that adults aged over 65 years had significantly lower coverage for tetanus toxoid (60.5%; confidence interval [CI] 95%, 57.3–63.4) and diphtheria (13.3%; 95% CI, 11.4–15.5) vaccines.

**Table 1. Joint Vaccine Working Group Advocating Vaccination of Adults Aged 60 Years and Older in Western Europe**

<table>
<thead>
<tr>
<th>European Union Geriatric Medicine Society (EUGMS) and International Association of Gerontology and Geriatrics–European Region (IAGG-ER)</th>
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<tr>
<td>The two above-mentioned societies concerned with the public health burden of vaccine-preventable diseases, convened this Working Group of experts, chaired by the academic director of the EUGMS (JPM) for the purpose of advocating higher immunization rates among European citizens aged 60 years and older. The main purposes of the Joint Working Group were to (1) conduct an inventory of the current practical guidelines for universally recommended vaccines in adults in European countries, and compare guidelines with the United States, (2) propose an adaptation of current vaccine guidelines designed to support official recommendations, (3) stress the importance of sustain a life course vaccine programme from childhood to adulthood until extreme old age, (4) support the public health, social, and economic value of vaccines to prevent infectious diseases in the whole population, and (5) increase the willingness to vaccinate and the public acceptance of vaccination. The group was composed of geriatricians designated by the two societies (EUGMS, S.M. and J.P.M., and IAGG-ER, R.M. and H.W.) and experts in immunology and vaccines (B-G.L. and P.H.L.), pneumococcal vaccine (C.C.), influenza vaccine (K.N.), and public health (T.K.), who worked on a voluntary basis. Each of the working members was in charge of a specific topic (formulating the bibliography, reporting at each of the 3 meetings and participating in the writing of the paper related to their main expertise). The academic director of the EUGMS assured the coordination of the different chapters and wrote the first draft. All the group participants participated in its improvement and agreed with the content of the final version.</td>
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than the general population, whose coverage rates were, respectively, 71.2% (95% CI, 70.0–72.3) and 33.7% (95% CI, 32.4–35.0) (p < 0.0001).34 To our knowledge, no data exist on pertussis vaccine coverage rates in adults aged 60 years and older.

**Level of Immunity against Vaccine-Preventable Diseases in Adults Aged over 60**

By retirement age (between 55 and 65 years of age in most western European countries), 60% do not have influenza antibodies resulting from previous vaccinations and/or natural exposures35 and about the same proportion do not have pre-vaccination protective levels of antibodies against the 23 studied Streptococcus pneumoniae serotypes.36

Whereas in 2001, in Spain 60–70% of the over-65 population had an antibody concentration from previous TT vaccination below the protective limit (<0.1 IU/mL).37 A 2007 Belgian study concerning 784 patients (130 were aged over 65 years) admitted in an emergency room found the immunoglobulin G (IgG) antibodies above the minimum protective level (<0.1 IU/mL) in 64.2% (95% CI, 60–67.5) in the whole population and only 35.4% (95% CI, 27.2–43.6) in the over 65 adults.38 A 2004 Dutch survey of around 310 adults over 40 years old confirmed the high percentage of seronegativity for tetanus (24.8% <0.1 IU/mL [95% CI, 20.2–29.9]), diphtheria (29.2% <0.1 IU/mL [95% CI, 24.2–34.5]), and pertussis (from 1.3% with pertussis anti-filamentous hemagglutinin [anti-FHA] to 31.9% pertussis anti-pertussis toxin [anti-PT] [95% CI, 0.3–3.2]).39

Ninety five percent of the population aged over 60 are seropositive for varicella zoster virus.40 This implies only 5% of the aged population has not been exposed to this virus or to varicella vaccine. Due to decreased cell-mediated immunity that occurs with aging, the risk of emergence of herpes zoster increases with advancing age and occurs in 20–25% of the over 60-year-old population.41,42 The widespread low immunological protection against vaccine-preventable diseases in adults aged over 60 requires greater understanding.

**Reasons for Suboptimal Vaccine Responses in Adults Aged over 60**

**Suboptimal clinical responses to vaccination**

Excess mortality studies in cohorts provide conflicting results when considering the preventive effects of influenza vaccination in adults aged 60 years and older. Reports vary from marginal mortality benefit43–45 to reduction of mortality from 23% to 50% of all winter deaths.46,47 However, a recent meta-analysis of 18 randomized control studies in community-dwelling adults (713,872 person-seasons, mean age 74 ± 6 years) within one U.S health maintenance organization (1990–2000) found that influenza vaccination was associated with a 27% reduction in the risk of hospitalization for pneumonia or influenza (adjusted odds ratio [OR], 0.73 [95% CI, 0.55–0.97]) and a 48% reduction in death (adjusted OR 0.52 [95% CI, 0.50–0.55]).48

The effectiveness of pneumococcal vaccine is particularly important in nursing home residents, the majority who are very old and have co-morbidities. Data addressing this issue are very limited. In 1985, a French study, the use of a 14-va-

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**Reduced duration of vaccine-induced antibody responses in older adults**

A 26-year longitudinal analysis of antibody responses after vaccination in adults (mean age 37 years ± 8; range, 23–59) at first observation found that antibody responses were relatively stable, with half-lives ranging from 11 years (range, 10–14) for TT, 19 years (range, 14–33) for diphtheria, and 50 years (range, 30–153) for herpes zoster.52 However, antibody titers were not sustained with aging. Measurements of specific antibody against TT in 734 adults (age 18–93 years, 382 females) proved that age and time since last vaccination shortened significantly the protective antibody titers (p < 0.001).53

**Immunologic basis for the decrease of vaccine response**

The aging process includes numerous immunological changes, collectively called immunosenescence, which is defined as the inability of an aging immune system to produce an appropriate and effective response to a challenge.54,55 The age-related immunological changes affect the T and B lym-
phocyte repertoires, combined with a reduction in the efficiency of antigen-presenting cells, increased number of natural killer cells, and an increased production of autoantibodies. Factors such as thymic involution, signal transduction changes, chronic antigenic stimulation, protein malnutrition, age-related hormonal changes, bed-ridden status, or simply physical inactivity all contribute to immunosenescence and lower immune responses in aging adults. However, memory cells appear to be maintained, and re-stimulation can be used as a basis for building protective recall responses in adults aged over 60.

**Progressive exhaustion of T cell repertoire and reduced T cell responses with age**

During human aging, one of the most striking changes in the primary lymphoid organs is the progressive involution of the thymus. As a consequence, the production of naïve T cells dramatically declines with age while the proportion of antigen-experienced cells (memory and effectors) increases. There is a significant decrease in the number of naïve T cells that have shortened telomeres as well as a reduced diversity of the T cell receptor repertoire. Meanwhile, highly differentiated effector T cells increase. This accumulation correlates with a failure to produce specific antibodies following influenza vaccination and is considered a predictor for mortality. An interleukin-4 (IL-4)-producing subpopulation of CD8+ T cells that express CD45RO and CD25 is found in 36% of healthy older adults. The loss of naïve T cells may be compensated by IL-4-producing CD8+ T cells, which are more frequently seen in older persons, still raising a humoral immune response than in those failing to produce protective antibodies after vaccination.

Three considerations are made in relation to the issue of immunosenescence. First, there are complex interactions with the combination of frailty, disability, and co-morbidity related with age-related immunological decline. Second, there is a need to improve the immune responses to vaccines in the immunosenescent population. However, this requirement should not delay a campaign to vaccinate aging and aged adults. Many benefits may be gained from beginning such a vaccine campaign for the older populations now. Finally, high coverage rate of immunizations in children can also have a significant impact in lowering the infectious disease burden in the old population through effective herd immunity.

**Disparities in Existing European Vaccine Programs**

**Influenza vaccine**

Influenza vaccine is recommended annually from the age of ≥50 years in Austria; ≥60 years in Germany, Greece, Iceland, and Spain; and ≥65 years in Belgium, Denmark, Finland, France, Ireland, Italy, The Netherlands, Norway, Portugal, Sweden, Switzerland, and the United Kingdom. Moreover financial incentives for vaccination in aged adults vary widely between countries, from full costs paid by the vaccine recipient (Austria), to free provision of both vaccines (France), to public health financing of vaccines but not of clinical services (Switzerland), and to direct financial incentives to GPs to provide vaccines (UK).

**Pneumococcal vaccine**

In 2003, a European survey performed in all of the 15 European Union member states, Switzerland, and Norway plus the 10 accession countries found that the 23 polysaccharide-valent vaccine (PPV-23) was licensed everywhere except in Malta. Moreover, all countries except Portugal have specific recommendations for this vaccine. These clinical recommendations were generally quite consistent, given to adults over the age of 60 or 65 years (one exception is The Netherlands), a history of previous pneumococcal infection, or an increased risk (e.g., anatomic or functional asplenia, immunocompromising condition, or cardiac, liver, pulmonary, or renal chronic diseases, or recipients of organ, bone marrow, or cochlear transplants). For these indications, the vaccine is provided without cost, except in Belgium, Finland, Italy, Lithuania, Luxembourg, and the Slovak Republic. Pneumococcal vaccine recommendations were inconsistent concerning the perceived need for and the schedule of repeated boosters. Revaccination is recommended after the age of 64 years (Italy), or 5 years after the first injection only for those at risk (Finland, Germany, Ireland, Norway, Switzerland, and United Kingdom), or every 6 years (in some Swedish counties). Reimbursement of pneumococcal vaccination is also highly variable. Publicly funded vaccine availability could increase coverage rates, as seen in Australia where this initiative increased pneumococcal vaccination uptake from 39% to 73% in patients aged over 65 years and admitted to a large teaching hospital between 2005 and 2006.

**Diphtheria and tetanus toxoid vaccines**

In the WHO European region, with the exception of Portugal, the declared target is to maintain ≥90% coverage with tetanus-diphtheria toxoid vaccines (Td) and to undertake supplementary immunization for high-risk populations. Booster doses of Td are recommended every 10 years (except in Austria, every 5 years) after completion of the primary series of three doses.

**Pertussis vaccine**

Routine pertussis vaccination for babies is generally administered at 3, 4, and 5 months of age and in the second year of life. Although regular boosters for all persons aged over 6 years may be desirable, no specific recommendations for boosters exist. Resurgence of pertussis in older populations has been observed in several countries. An Austrian epidemiological survey showed that the mean age of laboratory-reported pertussis cases increased from an average age of 30 years (standard deviation [SD] ± 25.9) in 2000 to approximately 44 years (SD ± 23.7) in 2005. Hospitalization rates were highest in infants aged <6 months (86%) and in adults aged >85 years (80%). The morbidity from pertussis in adults can be substantial (7.2% have prolonged cough), testifying to the high-risk disease transmission between generations. For this reason, it might be advisable to attempt to reduce the burden of pertussis by vaccinating adults aged over 60 with Td andacellular pertussis combined vaccines (TdaP). The U.S. Advisory Committee on Immunization Practices (ACIP) recommends the use of TdaP in: (1) adults aged 19–64 years, replacing Td by TdaP for...
booster immunization if last dose >10 years, (2) adults with last Td <10 years ago if needing protection against pertussis, and (3) adults with or anticipated contact with an infant <12 months of age.5

Herpes zoster vaccine

This vaccine was licensed in 2006 in Europe for preventing herpes zoster and postherpetic neuralgia in immunocompetent individuals aged over 60 years. In January, 2007, the license was modified to include persons aged over 50 years, and vaccine recommendations have been updated in Austria and Switzerland. The Austrian and Swiss authorities recommend herpes zoster from 50 years of age according with European Union vaccine labeling and have authorized concomitant use with influenza vaccine. Herpes zoster vaccine is currently only available in a limited number of countries (Switzerland, Austria, Denmark, Norway, Sweden, and The Netherlands), but should be widely available

<table>
<thead>
<tr>
<th>Vaccine program</th>
<th>Recommended vaccines</th>
<th>Clinical considerations</th>
</tr>
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<tbody>
<tr>
<td>Starting at 60 years (but possibly earlier)</td>
<td>Tetanus-diphtheria-pertussis (TdaP)</td>
<td>Assess the vaccine status</td>
</tr>
<tr>
<td></td>
<td>Trivalent influenza vaccine (TIV)</td>
<td>- If no evidence of any previous vaccination, start a new complete vaccination series.</td>
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<tr>
<td></td>
<td>Pneumococcal (PV23)</td>
<td>- If last booster ≥10 years before, give a booster dose</td>
</tr>
<tr>
<td></td>
<td>Herpes zoster</td>
<td>Adapted to the annual strain</td>
</tr>
<tr>
<td>Revaccinations</td>
<td>Influenza (TIV)</td>
<td>Assess the vaccine status: if vaccine administered:</td>
</tr>
<tr>
<td></td>
<td>Pneumococcal (PV23)</td>
<td>≥5 years before, give 1 dose</td>
</tr>
<tr>
<td></td>
<td>Tetanus-diphtheria-pertussis (TdaP)</td>
<td>Asses the vaccine status</td>
</tr>
<tr>
<td></td>
<td>Herpes zoster</td>
<td>If no evidence of any previous vaccination, give 1 dose</td>
</tr>
<tr>
<td>Special indications</td>
<td></td>
<td>Every year</td>
</tr>
<tr>
<td>1. New injury event</td>
<td>Tetanus-toxoid (TT) or tetanus-diphtheria toxoids (Td) or TdaP</td>
<td>Every 5 years</td>
</tr>
<tr>
<td>2. Repeated hospital admissions</td>
<td>Pneumococcal</td>
<td>Every 10 years</td>
</tr>
<tr>
<td>3. Nursing home admission</td>
<td>Tetanus-diphtheria-pertussis (TdaP)</td>
<td>Not yet determined</td>
</tr>
</tbody>
</table>

All the above-mentioned vaccines can be administered in the event of: Mild to moderate local reactions after a previous vaccination, mild acute illness, current antimicrobial therapy, persons receiving anticoagulant therapy, recent exposure to an infectious disease and, stable neurological disorder.

<table>
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<tr>
<th>Contraindications and precautions for every vaccine: Refer to official vaccine recommendations at:</th>
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</table>

All the above-mentioned vaccines can be administered in the event of: Mild to moderate local reactions after a previous vaccination, mild acute illness, current antimicrobial therapy, persons receiving anticoagulant therapy, recent exposure to an infectious disease and, stable neurological disorder.

Administration: Maintain recommended vaccine storage temperature, and sterile injection technique as well as the injection route and site (for example, persons on anticoagulant therapy can receive subcutaneous instead of intramuscular injections).

A patient vaccination card is strongly recommended.
influenza, pneumococcal, and herpes zoster. The association of influenza and pneumococcal vaccines has potential preventive effects. Choice of Tdap, a tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine follows the ACIP recommendation (see above).• Revaccinations: An annual influenza vaccination is needed, because each year’s vaccine is adapted to the new seasonal strains. Repeated annual influenza immunizations broaden the antigenic protection if the new strains are closely related. Pneumococcal vaccine is recommended every 5 years and Tdap every 10 years. Further studies are needed to determine the duration of the protective effect of a single herpes zoster vaccination and to establish whether a herpes zoster booster is required. Regular booster vaccinations throughout life are important to maintain the ability to respond to recall antigens with aging. • Other special indications for vaccinations should be considered: • In case of trauma or new medical event, a booster (or a complete vaccination) of tetanus toxoid or Tdap may be provided if the previous tetanus vaccination was over 10 years. • In case of repeated hospitalizations, pneumococcal vaccine should be considered if the last immunization dated back to 5 years. • At the time of admission to residential care (approximately 85 years in most of western European countries), a new clinical assessment of vaccine history is recommended to ascertain if any vaccine updates are needed. This assessment needs to consider Tdap, influenza, pneumococcal, and herpes zoster vaccines.

Willingness to Vaccinate and Public Acceptance of Vaccination

These vaccine guidelines for citizens aged 60 years and older proposed by the two European geriatric and gerontological societies would be justified if there is evidence such programs would be cost-effective and safe. Despite existing controversies concerning (1) the estimated influenza-related mortality, (2) the effectiveness of influenza vaccine in older adults, (3) the possible selection biases in cohort studies, as well as (4) the need for country-specific assessment, most of the recent analysis studies of influenza vaccine show a high-impact, cost-effective service for persons aged over 50 years, and even over 70 years. Already, in the mid 1990s, a cost-effectiveness analysis of pneumococcal vaccination for prevention of invasive pneumococcal disease in populations aged over 65 years of 10 western European countries justified a wider use of the vaccine. Most cost-effectiveness analyses of pertussis vaccination in Europe were performed in Germany and based on a Markov model. The results were more sensitive, favoring routine vaccination of adults aged 20–64 years with Tdap, if the incidence of pertussis in this age group was greater than 120 per 100,000 population. More research is needed on the cost effectiveness of all these vaccines in adults aged 60 years and older. Community and patient values for preventing herpes zoster and PHN are currently under investigation to determine the quality-adjusted life years saved. Improving vaccine uptake in this population requires addressing numerous barriers to adult immunization that involve both consumers’ beliefs and health-care professionals’ practices.

Consensus Statement

The EUGMS and IAGG-ER have formed a Joint Working Group to complement existing information, propose vaccine guidelines, and to develop a consensus statement that advocates immunization in adults aged 60 years and older. This consensus statement:

• Demonstrates the need to strengthen and harmonize vaccine strategies at the European level,
• Recognizes the importance of sustaining a life-course vaccine program,
• Promotes healthy aging by increasing vaccine coverage to limit the burden of vaccine-preventable infectious diseases,
• Supports the public health, social, and economic value of vaccination, and indeed, and
• Improves the willingness to vaccinate the most rapidly growing segment of the general population.

Health-care professionals have a critical role to play in the implementation of such consensus vaccine guidelines. Communication and awareness of vaccine-preventable diseases, such as an efficient reminder, recall, and information system, as well as improved access to vaccines, constitute the main pillars for success in establishing a vaccine program for European citizens aged 60 years and older.

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References
