

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

Jean-Pierre Michel,¹ Christian Chidiac,² Beatrix Grubeck-Loebenstein,³ Robert W. Johnson,⁴ Paul Henri Lambert,⁵ Stefania Maggi,⁶ Robert Moulias,⁷ Karl Nicholson,⁸ and Hans Werner⁹

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.^{1,2} Low vaccination coverage rates in adults may lead to an increased incidence of diseases such as diphtheria³ and pertussis⁴ in adults in the future.⁵ Moreover, infectious diseases in older people remain a significant cause of morbidity and mortality in the increasing population of adults over 65 years^{6,7} and many of these diseases are vaccine preventable.⁸ In 2001, lower respiratory infections represented the fourth most frequent

cause of death in high-income countries, causing 4.4% of the total deaths,⁹ occurring three times more often in adults aged 60 years and older.¹⁰

Surprisingly, tetanus is still an active disease, with 210 cases in Portugal (1993–2002),¹¹ 175 cases in England (1984–2000),¹² and 180 cases in Poland (1998–2006)^{13–20} 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.³ The morbidity from pertussis appears to be substantial in older populations.²¹ The annual incidence of herpes zoster in the general population

¹Department of Rehabilitation and Geriatrics, Geneva Medical School and University Hospitals, Thonex-Geneve, Switzerland.

²Department of Infectious and Tropical Diseases, Hôpital de La Croix Rousse, Lyon, France.

³Institute for Biomedical Aging Research, Innsbruck, Austria.

⁴University of Bristol, Bristol, United Kingdom.

⁵Geneva Medical School, Geneva, Switzerland.

⁶Center on Aging, Padua, Italy.

⁷Hôpital Charles Foix, Ivry sur Seine, France.

⁸University Hospitals of Leicester NHS Trust, Leicester Royal Infirmary, Leicester, United Kingdom.

⁹Ev. Krankenhaus Elisabethenstift, Darmstadt, Germany.

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 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 2050.²⁵ 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 [IAGGER], 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 re-

gional 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

European Union Geriatric Medicine Society (EUGMS) and International Association of Gerontology and Geriatrics—European Region (IAGGER)

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 IAGGER, 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.

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 benefit^{43–45} 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, 0.55–0.77]) 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-val-

ence pneumococcal vaccine showed an absolute risk reduction of only 2.9%.⁴⁹

A shingles prevention study (vaccinated vs. nonvaccinated subjects aged >60 years) demonstrated an overall reduction in the population incidence of herpes zoster by 51.3% (95% CI, 44.2–57.6%) and the incidence of postherpetic neuralgia (PHN) by 66.5% (95% CI, 47.5–79.2%).⁵⁰ The study found that while the vaccine is less effective at reducing herpes zoster in subjects aged over 70 years than those aged 60–70 years, vaccination was equally effective at reducing the incidence of PHN in the older age group.⁵⁰

Age-related decrease in vaccine-induced antibody responses

A quantitative review of 31 studies (1986–2002) on influenza vaccine antibody responses demonstrated clearly that H1N1, H2N3, and B seroconversion (a four-fold antibody increase) as well as seroprotection (antibody titers >40 units) were both significantly higher in younger adults (17–59 years; $n = 814$) compared to older adults (68–86 years; $n = 3997$). In the two age groups, percentages of seroconversion and seroprotection were, respectively, for H1N1, 60% versus 42% and 83% versus 69% ($p = 0.02$), for H3N2, 62% versus 51% and 84% versus 74% ($p = 0.26$), and for B, 58% versus 35% and 78% versus 67% ($p = 0.03$).³⁵ Moreover, within the older adults, those aged 75 years or less ($n = 1883$) had a significantly higher production of antibodies ($p < 0.001$) compared to those older than 75 years ($n = 2706$).³⁵

A study comparing IgG antibody concentrations before and after pneumococcal vaccination (PPV-23) in 46 old nursing home residents (mean age 85.5 years [range, 63–103]) with 12 healthy younger adults (mean age 37 years [range, 22–46]) showed a significant reduction in postvaccination antibodies in the older group. Geometric mean concentrations of IgG in the nursing home residents for serotypes 6B and 19F (5.1 and 5.8 μ /mL, respectively) were significantly lower than in the young adult group (10.1 and 14.0 μ /mL, respectively) ($p < 0.05$).⁵¹

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.⁵⁶ 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.⁵⁴ However, memory cells appear to be maintained, and restimulation can be used as a basis for building protective recall responses in adults aged over 60.⁵⁵

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.⁵⁷ 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.⁵⁷ Meanwhile, highly differentiated effector T cells increase. This accumulation correlates with a failure to produce specific antibodies following influenza vaccination⁵⁸ and is considered a predictor for mortality.^{56,59,60} 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.^{59,60}

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.⁶¹ Second, there is a need to improve the immune responses to vaccines in the immunosenescent population.^{62–65} 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.⁶⁶

Discrepancies 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.⁶⁷ 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).⁶⁷ 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).⁶⁷ 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 2006.⁶⁸

Diphtheria and tetanus toxoid vaccines

In the WHO European region, with the exception of Portugal, the declared target is to maintain $\geq 90\%$ 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.⁶⁹

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.⁷⁰ 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 2005.²¹ Hospitalization rates were highest in infants aged < 6 months (86%) and in adults aged > 85 years (80%).²¹ The morbidity from pertussis in adults can be substantial (7.2% have prolonged cough),⁷¹ 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 and acellular pertussis combined vaccines (TdaP).^{70–74} 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

Toward a New Vaccine Strategy for Adults Aged over 60 Years

In view of the low vaccine coverage rates in adults over 60 and their burden of disease, there is a need to establish and sustain a vaccine program in this population. Such a vaccine program should start in middle age, before the onset of age-related immunological decline. The present consensus statement by the European geriatric and gerontological societies (EUGMS and IAGG-ER) recommends that routine vaccination should be initiated by the sixth decade if not earlier.

Vaccines should be part of a healthy aging strategy, considering that currently the period from retirement age (from 55 to 65 years in most western European countries) to death generally represents two to three decades. Several clinical considerations must be included in it (Table 2):

- Vaccinations: After a complete vaccine history assessment at 60 years of age, recommended vaccines include TdaP,

TABLE 2. PROPOSED VACCINE GUIDELINES FOR ADULTS AGED 60 YEARS AND OLDER IN WESTERN EUROPE

<i>Vaccine program</i>	<i>Recommended vaccines</i>	<i>Clinical considerations</i>
Starting at 60 years (but possibly earlier)	Tetanus-diphtheria-pertussis (TdaP)	Assess the vaccine status - If no evidence of any previous vaccination, start a new complete vaccination series. - If last booster ≥ 10 years before, give a booster dose
	Trivalent influenza vaccine (TIV)	Adapted to the annual strain
	Pneumococcal (PV23)	Assess the vaccine status: if vaccine administered: ≥ 5 years before, give 1 dose
	Herpes zoster	Assess the vaccine status If no evidence of any previous vaccination, give 1 dose
Revaccinations	Influenza (TIV)	Every year
	Pneumococcal (PV23)	Every 5 years
	Tetanus-diphtheria-pertussis (TdaP)	Every 10 years
	Herpes zoster	Not yet determined
Special indications		
1. New injury event	Tetanus-toxoid (TT) or tetanus-diphtheria toxoids (Td) or TdaP	- If no evidence of any previous vaccination, start a new complete vaccination series. - If last booster ≥ 10 years before, give a new booster dose
2. Repeated hospital admissions	Pneumococcal	Ask vaccine history. if vaccine administered ≥ 5 years provide a booster
3. Nursing home admission	Tetanus-diphtheria-pertussis (TdaP)	If no evidence of any previous vaccination, start a new complete vaccination series. - If last booster ≥ 10 years before, give a new booster dose
	Influenza (TIV)	No upper age limit; Herd immunity is important for residents of nursing home as well as for health care professionals
	Pneumococcal	If already vaccinated, a booster is recommended if the initial vaccination was ≥ 5 years
	Herpes zoster	If not already administered, give 1 dose. If already vaccinated, the need for revaccination is not yet known

Contraindications and precautions for every vaccine: Refer to official vaccine recommendations at:

<http://www.ecdc.eu.int>,

<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5510a1.htm>,

<http://www.clinicalanswers.nhs.uk/index.cfm?question=643>.

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.⁷⁵ Choice of Tdap, a tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine follows the ACIP recommendation (see above).⁵

- 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.⁷⁶ 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,^{43,44} as well as (4) the need for country-specific assessment,⁷⁷ 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.^{78–82} 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.⁸³ 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.^{84,85}

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.^{86–88} Improving vaccine uptake in this population requires addressing numerous barriers to adult immunization that involve both consumers' beliefs and health-care professionals' practices.^{89,90}

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 programme for European citizens aged 60 years and older.

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References

1. Siegrist CA. [Vaccinology update 2005: A new category of recommendations for optimal vaccine protection]. *Rev Med Suisse* 2006;2:67–70.
2. Zimmerman RK, Middleton DB, Burns IT, Clover RD, Kimmel SR. Routine vaccines across the life span, 2007. *J Fam Pract* 2007;56:S18–S37, C1–C3.
3. Vitek CR, Wharton M. Diphtheria in the former Soviet Union: Reemergence of a pandemic disease. *Emerg Infect Dis* 1998;4:539–550.
4. de Greeff SC, Mooi FR, Schellekens JF, de Melker HE. Impact of acellular pertussis preschool booster vaccination on disease burden of pertussis in The Netherlands. *Pediatr Infect Dis J* 2008;27:218–223.
5. Kretsinger K, Broder KR, Cortese MM et al. Preventing tetanus, diphtheria, and pertussis among adults: use of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine recommendations of the Advisory Committee on Immunization Practices (ACIP) and recommendation of ACIP, supported by the Healthcare Infection Control Practices Advisory Committee (HICPAC), for use of Tdap among health-care personnel. *MMWR Recomm Rep* 2006;55:1–37.

6. Htwe TH, Mushtaq A, Robinson SB, Rosher RB, Khardori N. Infection in the elderly. *Infect Dis Clin NAm* 2007;21:711–743.
7. Liang SY, Mackowiak PA. Infections in the elderly. *Clin Geriatr Med* 2007;23:441–456, viii.
8. High K. Immunizations in older adults. *Clin Geriatr Med* 2007;23:669–685, viii–ix.
9. Lopez AD, Mathers CD, Ezzati M, Jamison DT, Murray CJ. Global and regional burden of disease and risk factors, 2001: systematic analysis of population health data. *Lancet* 2006;367:1747–1757.
10. Yoshikawa TT. Perspective: Aging and infectious diseases: past, present, and future. *J Infect Dis* 1997;176:1053–1057.
11. Castro L, Goncalves G, Catarino J. [Reported cases of tetanus in the North of Portugal (1993–2002). Missed opportunities for vaccination]. *Acta Med Port* 2004;17:225–230.
12. Rushdy AA, White JM, Ramsay ME, Crowcroft NS. Tetanus in England and Wales, 1984–2000. *Epidemiol Infect* 2003;130:71–77.
13. Zielinski A. [Tetanus in 1998]. *Przegl Epidemiol* 2000;54:151–156.
14. Zielinski A. [Tetanus in Poland in 1999]. *Przegl Epidemiol* 2001;55:137–140.
15. Zielinski A. [Tetanus in Poland in 2000]. *Przegl Epidemiol* 2002;56:335–338.
16. Zielinski A. [Tetanus in Poland in 2002]. *Przegl Epidemiol* 2004;58:139–142.
17. Zielinski A. [Tetanus in Poland in 2003]. *Przegl Epidemiol* 2005;59:309–312.
18. Zielinski A. [Tetanus in Poland in 2004]. *Przegl Epidemiol* 2006;60:487–489.
19. Zielinski A. [Tetanus in 2005]. *Przegl Epidemiol* 2007;61:287–289.
20. Zielinski A. [Tetanus in Poland in 2006]. *Przegl Epidemiol* 2008;62:333–335.
21. Rendi-Wagner P, Paulke-Korinek M, Stanek G, Khanakah G, Kollaritsch H. Impact of a pertussis booster vaccination program in adolescents and adults on the epidemiology of pertussis in Austria. *Pediatr Infect Dis J* 2007;26:806–810.
22. Gnann JW Jr, Whitley RJ. Clinical practice. Herpes zoster. *N Engl J Med* 2002;347:340–346.
23. Kimberlin DW, Whitley RJ. Varicella-zoster vaccine for the prevention of herpes zoster. *N Engl J Med* 2007;356:1338–1343.
24. Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990–2020: Global Burden of Disease Study. *Lancet* 1997;349:1498–1504.
25. United Nations. World population ageing 1950–2050. In: *Affairs DoEaS*, ed. United Nations, 2002.
26. Michel JP, Gold G. Coping with population aging in the old continent—the need for European academic geriatrics. *J Gerontol A Biol Sci Med Sci* 2001;56:M341–M343.
27. Thiry E, Horzinek MC. Vaccination guidelines: A bridge between official requirements and the daily use of vaccines. *Rev Sci Tech* 2007;26:511–517.
28. World Health Organization. Resolution 56.19; 23 May. World Health Organization, Geneva, 2003.
29. European Parliament. [P6 - TA (2005) 0406] 26 October. Brussels: European Community, 2005.
30. Stuck AE, Kharicha K, Dapp U et al. Development, feasibility and performance of a health risk appraisal questionnaire for older persons. *BMC Med Res Methodol* 2007;7:1.
31. Noakes K, Pebody RG, Gungabissoon U, Stowe J, Miller E. Pneumococcal polysaccharide vaccine uptake in England, 1989–2003, prior to the introduction of a vaccination programme for older adults. *J Public Health (Oxf)* 2006;28:242–247.
32. Gavazzi G, Wazieres B, Lejeune B, Rothan-Tondeur M. Influenza and pneumococcal vaccine coverages in geriatric health care settings in France. *Gerontology* 2007;53:144–149.
33. Montrieux C, Collette G, Limme C, Seidel L, Albert A, Giet D. [Evaluation of tetanus vaccine coverage in rural society]. *Rev Med Liege* 2002;57:97–103.
34. Guthmann JP FL, Antona D et Lévy-Bruhl D. [Couverture vaccinale diphtérie, tétanos, poliomyélite chez l'adulte en France: résultats de l'enquête santé et Protection Sociale, 2002]. *Bull Epidemiol Hebdomadaire* 2007;51–52, 441–445.
35. Goodwin K, Viboud C, Simonsen L. Antibody response to influenza vaccination in the elderly: a quantitative review. *Vaccine* 2006;24:1159–1169.
36. Rubins JB, Alter M, Loch J, Janoff EN. Determination of antibody responses of elderly adults to all 23 capsular polysaccharides after pneumococcal vaccination. *Infect Immun* 1999;67:5979–5984.
37. Bayas JM, Vilella A, Bertran MJ et al. Immunogenicity and reactogenicity of the adult tetanus-diphtheria vaccine. How many doses are necessary? *Epidemiol Infect* 2001;127:451–460.
38. Stubbe M, Swinnen R, Crusiaux A, Mascart F, Lheureux PE. Seroprotection against tetanus in patients attending an emergency department in Belgium and evaluation of a bedside immunotest. *Eur J Emerg Med* 2007;14:14–24.
39. Van Damme P, Burgess M. Immunogenicity of a combined diphtheria-tetanus-acellular pertussis vaccine in adults. *Vaccine* 2004;22:305–308.
40. Wutzler P, Farber I, Wagenpfeil S, Bisanz H, Tischer A. Seroprevalence of varicella-zoster virus in the German population. *Vaccine* 2001;20:121–124.
41. Yawn BP, Saddier P, Wollan PC, St Sauver JL, Kurland MJ, Sy LS. A population-based study of the incidence and complication rates of herpes zoster before zoster vaccine introduction. *Mayo Clin Proc* 2007;82:1341–1349.
42. Gnann JW, Jr. Vaccination to prevent herpes zoster in older adults. *J Pain* 2008;9:S31–S36.
43. Simonsen L, Reichert TA, Viboud C, Blackwelder WC, Taylor RJ, Miller MA. Impact of influenza vaccination on seasonal mortality in the US elderly population. *Arch Intern Med* 2005;165:265–272.
44. Simonsen L, Taylor RJ, Viboud C, Miller MA, Jackson LA. Mortality benefits of influenza vaccination in elderly people: an ongoing controversy. *Lancet Infect Dis* 2007;7:658–666.
45. Mangtani P, Cumberland P, Hodgson CR, Roberts JA, Cutts FT, Hall AJ. A cohort study of the effectiveness of influenza vaccine in older people, performed using the United Kingdom general practice research database. *J Infect Dis* 2004;190:1–10.
46. Vila-Corcoles A, Rodriguez T, de Diego C et al. Effect of influenza vaccine status on winter mortality in Spanish community-dwelling elderly people during 2002–2005 influenza periods. *Vaccine* 2007;25:6699–6707.
47. Vu T, Farish S, Jenkins M, Kelly H. A meta-analysis of effectiveness of influenza vaccine in persons aged 65 years and over living in the community. *Vaccine* 2002;20:1831–1836.
48. Nichol KL, Nordin JD, Nelson DB, Mullooly JP, Hak E. Effectiveness of influenza vaccine in the community-dwelling elderly. *N Engl J Med* 2007;357:1373–1381.
49. Gaillat J, Zmirou D, Mallaret MR et al. [Clinical trial of an antipneumococcal vaccine in elderly subjects living in institutions]. *Rev Epidemiol Sante Publique* 1985;33:437–444.

50. Oxman MN, Levin MJ, Johnson GR et al. A vaccine to prevent herpes zoster and postherpetic neuralgia in older adults. *N Engl J Med* 2005;352:2271–2284.
51. Romero-Steiner S, Musher DM, Cetron MS et al. Reduction in functional antibody activity against *Streptococcus pneumoniae* in vaccinated elderly individuals highly correlates with decreased IgG antibody avidity. *Clin Infect Dis* 1999; 29:281–288.
52. Amanna IJ, Carlson NE, Slifka MK. Duration of humoral immunity to common viral and vaccine antigens. *N Engl J Med* 2007;357:1903–1915.
53. Kovaïou RD, Herndler-Brandstetter D, Grubeck-Loebenstein B. Age-related changes in immunity: implications for vaccination in the elderly. *Expert Rev Mol Med* 2007;9:1–17.
54. Targonski PV, Jacobson RM, Poland GA. Immunosenescence: role and measurement in influenza vaccine response among the elderly. *Vaccine* 2007;25:3066–3069.
55. Pawelec G, Akbar A, Caruso C, Solana R, Grubeck-Loebenstein B, Wikby A. Human immunosenescence: Is it infectious? *Immunol Rev* 2005;205:257–268.
56. Fulop T, Larbi A, Wikby A, Mocchegiani E, Hirokawa K, Pawelec G. Dysregulation of T-cell function in the elderly: Scientific basis and clinical implications. *Drugs Aging* 2005;22:589–603.
57. Pfister G, Weiskopf D, Lazuardi L et al. Naive T cells in the elderly: Are they still there? *Ann N Y Acad Sci* 2006;1067: 152–157.
58. Saurwein-Teissl M, Lung TL, Marx F et al. Lack of antibody production following immunization in old age: association with CD8(+)CD28(-) T cell clonal expansions and an imbalance in the production of Th1 and Th2 cytokines. *J Immunol* 2002;168:5893–5899.
59. Chiu WK, Fann M, Weng NP. Generation and growth of CD28nullCD8+ memory T cells mediated by IL-15 and its induced cytokines. *J Immunol* 2006;177:7802–7810.
60. Schwaiger S, Wolf AM, Robatscher P, Jenewein B, Grubeck-Loebenstein B. IL-4-producing CD8+ T cells with a CD62L++(bright) phenotype accumulate in a subgroup of older adults and are associated with the maintenance of intact humoral immunity in old age. *J Immunol* 2003;170: 613–619.
61. Fried LP, Ferrucci L, Darer J, Williamson JD, Anderson G. Untangling the concepts of disability, frailty, and comorbidity: implications for improved targeting and care. *J Gerontol A Biol Sci Med Sci* 2004;59:255–263.
62. Bright RA, Carter DM, Daniluk S et al. Influenza virus-like particles elicit broader immune responses than whole virion inactivated influenza virus or recombinant hemagglutinin. *Vaccine* 2007;25:3871–3878.
63. Guebre-Xabier M, Hammond SA, Ellingsworth LR, Glenn GM. Immunostimulant patch enhances immune responses to influenza virus vaccine in aged mice. *J Virol* 2004;78: 7610–7618.
64. Frech SA, Kenney RT, Spyr CA et al. Improved immune responses to influenza vaccination in the elderly using an immunostimulant patch. *Vaccine* 2005;23:946–950.
65. Glenn GM, Kenney RT. Mass vaccination: Solutions in the skin. *Curr Top Microbiol Immunol* 2006;304:247–268.
66. Weycker D, Edelsberg J, Halloran ME et al. Population-wide benefits of routine vaccination of children against influenza. *Vaccine* 2005;23:1284–1293.
67. Pebody RG, Leino T, Nohynek H, Hellenbrand W, Salmaso S, Ruutu P. Pneumococcal vaccination policy in Europe. *Euro Surveill* 2005;10:174–178.
68. Ridda I, MacIntyre RC, Lindley RI et al. Predictors of pneumococcal vaccination uptake in hospitalized patients aged 65 years and over shortly following the commencement of a publicly funded national pneumococcal vaccination program in Australia. *Hum Vaccin* 2007;3:83–86.
69. Lobanov A. Immunization programme in the European region: Progress and challenges. WHO: <http://www.worldbank.org/eca/presentations/ecshd/2006/>, 2006.
70. Cortese MM, Baughman AL, Brown K, Srivastava P. A “new age” in pertussis prevention new opportunities through adult vaccination. *Am J Prev Med* 2007;32:177–185.
71. Hu JJ, Lu CY, Chang LY et al. Survey of pertussis in patients with prolonged cough. *J Microbiol Immunol Infect* 2006; 39:54–58.
72. Huang Y, Rohani P. Age-structured effects and disease interference in childhood infections. *Proc Biol Sci* 2006;273: 1229–1237.
73. Wendelboe AM, Van Rie A, Salmaso S, Englund JA. Duration of immunity against pertussis after natural infection or vaccination. *Pediatr Infect Dis J* 2005;24:S58–S61.
74. Forsyth KD, Wirsing von Konig CH, Tan T, Caro J, Plotkin S. Prevention of pertussis: Recommendations derived from the second Global Pertussis Initiative roundtable meeting. *Vaccine* 2007;25:2634–2642.
75. Christenson B, Hedlund J, Lundbergh P, Ortqvist A. Additive preventive effect of influenza and pneumococcal vaccines in elderly persons. *Eur Respir J* 2004;23:363–368.
76. Smith DJ, Forrest S, Ackley DH, Perelson AS. Variable efficacy of repeated annual influenza vaccination. *Proc Natl Acad Sci USA* 1999;96:14001–14006.
77. Nicholson KG. Socioeconomics of influenza and influenza vaccination in Europe. *Pharmacoeconomics* 1996;9(Suppl 3):75–78.
78. Patel MS, Davis MM. Could a federal program to promote influenza vaccination among elders be cost-effective? *Prev Med* 2006;42:240–246.
79. Nichol KL, Nordin J, Mullooly J. Influence of clinical outcome and outcome period definitions on estimates of absolute clinical and economic benefits of influenza vaccination in community dwelling elderly persons. *Vaccine* 2006;24:1562–1568.
80. Maciosek MV, Coffield AB, Edwards NM, Flottesmesch TJ, Goodman MJ, Solberg LI. Priorities among effective clinical preventive services: Results of a systematic review and analysis. *Am J Prev Med* 2006;31:52–61.
81. Turner DA, Wailoo AJ, Cooper NJ, Sutton AJ, Abrams KR, Nicholson KG. The cost-effectiveness of influenza vaccination of healthy adults 50–64 years of age. *Vaccine* 2006; 24:1035–1043.
82. Prosser LA, O'Brien MA, Molinari NA, et al. Non-traditional settings for influenza vaccination of adults: Costs and cost effectiveness. *Pharmacoeconomics* 2008;26:163–178.
83. Evers SM, Ament AJ, Colombo GL et al. Cost-effectiveness of pneumococcal vaccination for prevention of invasive pneumococcal disease in the elderly: An update for 10 Western European countries. *Eur J Clin Microbiol Infect Dis* 2007;26:531–540.
84. Lee GM, Murphy TV, Lett S et al. Cost effectiveness of pertussis vaccination in adults. *Am J Prev Med* 2007;32:186–193.
85. Lee GM, Riffelmann M, Wirsing von Konig CH. Cost-effectiveness of adult pertussis vaccination in Germany. *Vaccine* 2008;26:3673–3679.
86. Brisson M, Pellissier JM, Levin MJ. Cost-effectiveness of herpes zoster vaccine: flawed assumptions regarding efficacy

- against postherpetic neuralgia. *Clin Infect Dis* 2007;45:1527–1529.
87. Rothberg MB, Virapongse A, Smith KJ. Cost-effectiveness of a vaccine to prevent herpes zoster and postherpetic neuralgia in older adults. *Clin Infect Dis* 2007;44:1280–1308.
 88. Lieu TA, Ortega-Sanchez I, Ray GT et al. Community and patient values for preventing herpes zoster. *Pharmacoeconomics* 2008;26:235–249.
 89. Johnson DR, Nichol KL, Lipczynski K. Barriers to adult immunization. *Am J Med* 2008;121:S28–S35.
 90. Kotchen TA. Why the slow diffusion of treatment guidelines into clinical practice? *Arch Intern Med* 2007;167:2394–2395.

Address reprint requests to:

Jean-Pierre Michel

*Department: Rehabilitation and Geriatrics
Geneva Medical School and University Hospitals
3 chemin du Pont Bochet
Thonex-Geneve, Switzerland 1226*

E-mail: jean-pierre.michel@hcuge.ch

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