

## EXPERT OPINION

## Vaccination of adults with heart failure and chronic heart conditions: Expert opinion

### Kalp yetersizliği ve kronik kalp hastalıklarında erişkin aşılama: Uzman görüşü

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#### Importance of Vaccination, Vaccine Epidemiology, Risk for Infections, and Current Status in the World and in Turkey

Cardiovascular disease (CVD) is the leading cause of mortality in the world and accounted for 31% of all global deaths in 2015.<sup>[1]</sup> The medical and economic burden associated with CVD is expected to increase in the future with increasing life expectancy. The risk for community-acquired pneumonia (CAP) has been reported to be 3.3 times higher, and invasive pneumococcal disease (IPD) has been reported to be 9.9 times higher in patients suffering from chronic heart conditions, including congestive heart failure, CVD, and valvular heart disease, when compared with individuals who have a sound cardiovascular system.<sup>[2]</sup> CAP (pneumococcal pneumonia, in particular) may require hospital admission, and the reported clinical and economic burden of CAP is significant. The risk for pneumonia-related hospital admission has been shown to be higher in patients who have chronic heart failure (HF) compared with those who do not (Odds ratio: 1.81; 95% confidence interval [CI]: 1.76–1.86).<sup>[3]</sup> CAP-related mortality rates are elevated among the

elderly and in patients with comorbidities.<sup>[4]</sup> *Streptococcus pneumoniae* is the most frequently isolated pathogen in adult patients with CAP. Increasing antimicrobial resistance in pneumococci worldwide further increases the burden of the disease.<sup>[5]</sup> The World Health

Organization (WHO) has recommended investigating and developing new antimicrobials against *S. pneumoniae* as one of the global priority pathogens.<sup>[6]</sup>

The prevalence of concurrent chronic heart conditions in adult patients with CAP varies from 10% to 47% in Europe.<sup>[7]</sup> The prevalence of concurrent chronic heart conditions in CAP has been reported to be 19.9% in Asian countries.<sup>[8]</sup> There are reports indicating that patients with pneumonia may develop cardiac complications during the acute stage of the disease<sup>[9–12]</sup> and that the long-term risk of developing

#### Abbreviations:

CAP	Community-acquired pneumonia
CDC	Centers for Disease Control and Prevention
CI	Confidence interval
COPD	Chronic obstructive pulmonary disease
CVD	Cardiovascular disease
HF	Heart failure
IIV	Inactive influenza vaccines
IPD	Invasive pneumococcal disease
PCV	Pneumococcal conjugate vaccine
PPV	Polysaccharide pneumococcal vaccine
WHO	World Health Organization

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CVD may be increased.<sup>[13,14]</sup> The risk of developing CVD is increased 6-fold in adults during the first year after a hospital admission associated with pneumonia or sepsis (adjusted risk [hazard] ratio: 6.33; 95% CI: 5.65–7.09). Although the risk for CVD gradually declines over time, the risk for CVD remains high even 5 years after such infections (adjusted risk ratio: 1.87; 95% CI: 1.47–2.38).<sup>[15]</sup>

In addition to general measures for health protection (personal hygiene, clean drinking water, waste management, etc.), active and passive immunization is also important in the protection against infections. Active immunization (vaccination) is the most effective and inexpensive method to fight vaccine-preventable infection.<sup>[16]</sup> The main goal of vaccination is to reduce the risks for disease, disability, and death, and to ensure the maintenance of overall health. The incidence of vaccine-preventable disease declined by more than 99% in the 20<sup>th</sup> century as a result of vaccination programs, and certain diseases have even been eradicated.<sup>[17]</sup> Currently, there are many infectious diseases with high mortality and morbidity rates (pneumococcal pneumonia, influenza, measles, varicella, hepatitis A, hepatitis B, rubella, tetanus, etc.) that may occur in adults. The administration of booster doses to adults who received childhood vaccines and the participation of adults who never received childhood vaccines in adult vaccination programs are of paramount importance.<sup>[18]</sup> Regular adult vaccination may help reduce the mortality and morbidity associated with vaccine-preventable diseases, particularly in the elderly.<sup>[19,20]</sup> Vaccination may also help fight antimicrobial resistance. A reduction in the incidence of infectious disease can reduce antimicrobial usage and indirectly lead to a reduction in the prevalence of resistant species.<sup>[21]</sup>

Cardiac events may have a negative impact on short- and long-term mortality rates in patients with pneumonia.<sup>[11,12,22]</sup> Mortality rates in patients with pneumococcal pneumonia and concurrent cardiac events (myocardial infarction, severe arrhythmias, new or worsening congestive HF) have been reported to be higher compared with the mortality rates of patients with pneumonia alone.<sup>[23]</sup> Furthermore, the 10-year survival rate (other than patients who die within the first month) after having pneumococcal pneumonia has been demonstrated to be lower compared with age- and sex-matched individuals.<sup>[24]</sup>

The efficacy of the 13-valent pneumococcal conjugate vaccine (PCV13) in protecting against CAP and IPD in adults has been well established.<sup>[25]</sup> Pneumonia requiring hospital admission is associated with a high mortality rate in the elderly: It has been recorded as 10.7% in those who had received the PCV 13 vaccine previously, 14.1% in patients who had received the 23-valent pneumococcal polysaccharide vaccine, and 16.4% in patients who had never been vaccinated.<sup>[26]</sup>

Before the introduction of PCV13 in our country (from 1996 to 2008), the potential coverage of PCV13 was estimated to be 71.5% of all pneumococcus strains responsible for IPD in adults.<sup>[27]</sup> The combined use of PCV13 and PPV23 according to a vaccination schedule is designed to increase the efficacy and coverage of these vaccines.

Influenza is one of the leading causes of mortality and morbidity among infectious diseases. Patients with chronic diseases, such as diabetes and CVD, are more likely to develop complications associated with influenza infections. Considering the distribution of chronic diseases in Turkey, the estimated number of people to be included in high-risk groups for influenza varies from 27 to 33 million people.<sup>[28]</sup> A number of cardiovascular complications of influenza infections have been reported.<sup>[29]</sup> Influenza infections have a negative impact on acute/chronic HF. Annual vaccination against influenza has been considered an effective measure for secondary prevention of HF.<sup>[30,31]</sup> The association between an annual vaccination against influenza and lower rates of repeated hospital admissions<sup>[32]</sup> and a reduced risk for all-cause mortality has been demonstrated in patients with chronic HF.<sup>[33–35]</sup>

### Current status in our country and other countries

Various vaccine coverage rates have been reported in regional studies or studies conducted in specific patient groups, but what all of these studies have in common is that the coverage rates are much lower than desired.

Important study sites from our country took part in the international PARADIGM-HF trial (Prospective comparison of ARNI with ACEI to Determine Impact on Global Mortality and morbidity in Heart Failure). Of more than 8000 participants with HF and a reduced ejection fraction, only 21% had received an influenza vaccine within the year before their participation in this study, and 79% had not received an influenza

vaccine in the same period of time. The highest vaccine coverage rate was reported from the Netherlands, with 77.5%, while only 1.6% of participants from our country had received an influenza vaccine.<sup>[35]</sup> The results of this study clearly reflect how low the vaccination rate is in patients with CVD in our country. Although no specific data are available for pneumococcal vaccine coverage among patients with chronic heart conditions, these rates are also expected to be very low. The pneumococcal vaccine coverage rate in patients with chronic obstructive pulmonary disease (COPD) was determined to be 15% and the influenza vaccine coverage rate was found to be 37% in a small-scale study conducted in our country.<sup>[36]</sup> The rate of awareness of influenza and pneumococcal vaccines was 49% and 12%, respectively, and the immunization coverage rate for these vaccines was found to be 40% and 10% among patients with COPD in a study conducted in Izmir in 2008.<sup>[37]</sup> In a study assessing the impact of physician awareness about influenza and pneumococcal vaccines on coverage rates for these vaccines among their patients with diabetes, after being assessed for their knowledge about current vaccination practices, physicians participated in a training program. The results indicated that 87.9% and 83.4% of the patients with diabetes had been recommended to get the influenza vaccine and the pneumococcal vaccine, respectively, over the previous 5 years, and only 27% actually received the influenza vaccine and 9.8% received the pneumococcal vaccine. One year after the training program, the physicians' vaccine recommendation rate increased to 97.6% and 95.1%, respectively, and the vaccine coverage rate increased to 63.3% and 40.7% for the influenza and pneumococcal vaccines, respectively.<sup>[38]</sup>

Therefore, primary and secondary preventive measures for CVD patients should be reviewed more comprehensively. The Center for Population Health and Aging, founded with the support of the Centers for Disease Control and Prevention (CDC), in 2001 announced "10 Key Measures" to healthy aging.<sup>[39]</sup> Regular immunization is among these measures. The vaccines recommended by the CDC for adults include those for influenza, diphtheria, pertussis, tetanus, varicella, human papillomavirus, herpes zoster (shingles), rubella, measles, mumps, pneumococcal disease (PCV13, PPV23), meningococcal disease, hepatitis A, hepatitis B, and *Haemophilus influenzae* type B.<sup>[40]</sup>

Although immunization of adults at risk has been widely neglected, this issue is of paramount importance. The number of those receiving adult immunizations is far from the desired level, in spite of its proven benefits.<sup>[41-43]</sup> Adult vaccination coverage is substantially lower than the global average.

The aim of this consensus report was to raise awareness about the immunization of adults and elderly people with chronic heart conditions who are at risk for infectious diseases with high mortality and morbidity, such as influenza and pneumococcal infections, in the context of the fight against CVD and to provide guidance to health professionals on why and how to vaccinate this population.

### Background Information On Heart Conditions and Vaccination

#### The mechanism of heart failure associated with influenza and pneumococcal infections

Acute respiratory infections such as pneumonia may lead to acute heart conditions. Extension of inflammation induced by respiratory infections may accelerate atherogenesis and disturb the inotropic state. Pro-inflammatory cytokines, such as interleukins, tumor necrosis factor alpha, and C-reactive protein, enhance the expression of cell adhesion molecules on endothelial surfaces. Increased adhesion molecules promote the migration of leukocytes into the intima. This process results in lipoprotein oxidation in the atherogenesis cascade.<sup>[44,45]</sup> In pneumonia, circulating inflammatory mediators (such as cytokines, endotoxins) may lead to left ventricular dysfunction through a direct myocardial depressing effect.<sup>[18]</sup> Increased cytokine expression associated with influenza infections may lead to myocardial remodeling and overproduction of tissue inhibitors of matrix metalloproteinases. These processes may contribute to left ventricular dilatation and the HF phenotype by increasing collagen content in myocardial tissue.<sup>[46]</sup>

#### Susceptibility to pneumonia in adult patients with heart disorders

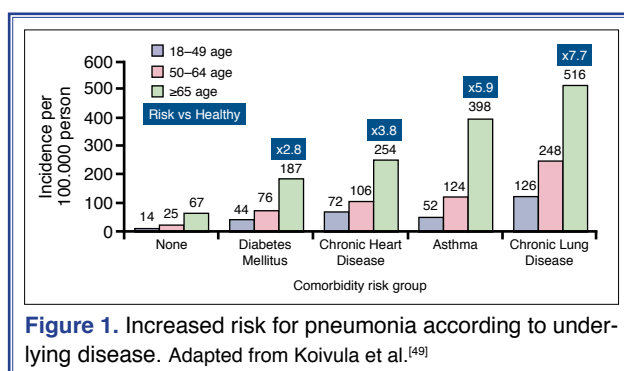
Chronic CVD and lung diseases are among the leading predisposing factors for pneumonia. An epidemiological study demonstrated that heart diseases were the most important risk factors for pneumonia in adult patients over the age of 60 and among heart conditions, chronic compensated HF posed the highest risk for pneumonia.<sup>[47]</sup> Patients with HF are at a substan-

tially higher risk for pneumonia for a number of reasons. Alveolar edema increases the risk for microbial clearance and bacterial infections by blocking the normal physiological mechanisms of the alveolar bed between air and lung tissue.<sup>[48]</sup> It has been reported that 23.7% of patients with pneumonia suffer from HF and that the presence of HF increases the risk of developing pneumonia 1.9-fold.<sup>[49]</sup> Although pneumonia is known to cause acute decompensation of HF, this study concluded that chronic decompensated HF increased the risk for developing pneumonia, pneumonia-related hospital admission, and deaths. These data demonstrate a reciprocal relationship between pneumonia and HF. Another case control study demonstrated that among a variety of heart diseases, only HF was a risk factor for pneumonia (Relative risk: 5.69; 95% CI: 1.69–19.04;  $p=0.0048$ ) and both acute HF and chronic HF increase this risk. Furthermore, a close relationship was found between ventricular dysfunction and the development of pneumonia.<sup>[50]</sup>

In a large, prospective, controlled study of 4988 patients who were diagnosed with CAP without HF, the mean age was 55 years. The patients were followed up for 10 years. The incidence of HF was determined to be 11.9% in the pneumonia group and 7.4% in the control group ( $p<0.001$ ). However, the hospital admission rate for HF within 90 days and 1 year after discharge from the hospital was found to be significantly higher in the pneumonia group than in the control group.<sup>[14]</sup> The risk of developing pneumonia was 3.8 times higher in patients with chronic heart diseases according to a retrospective assessment of data from between 2006 and 2010 obtained from the US-based healthcare database (Fig. 1).<sup>[51]</sup>

### Which heart diseases necessitate adult vaccination?

Heart diseases for which international guidelines



recommend vaccination against influenza and pneumonia and the relevant guidelines are summarized in Table 1. Adult patients with any of the following diseases may benefit from vaccination.

1. Heart failure and cardiomyopathy
2. Atherosclerotic heart diseases
3. Valvular heart diseases
4. Cyanotic congenital heart diseases
5. Pulmonary arterial hypertension

### Commercially Available Vaccines, Side Effects, Contraindications of the Influenza Vaccine

The specific formula of the annual seasonal influenza vaccine is determined by the World Health Organization (WHO). The virus types thought most likely to circulate during the upcoming season are targeted and vaccine manufacturers are informed. Trivalent and quadrivalent vaccines are made available. Trivalent vaccines protect against 2 influenza A species and an influenza B species, while quadrivalent vaccines are also protective against another influenza B species in addition to those included in trivalent vaccines.

Inactive influenza vaccines (IIV): IIV are produced by highly purified and inactivated viruses grown in embryonated eggs. The preservative, ethyl mercury (thiomersal), is only included in inactivated vaccines supplied in multi-dose vials of inactivated vaccines that do not contain aluminum as an adjuvant. Single-dose vaccines (in prefilled syringes) that are available in our country for routine use do not contain thiomersal. Vaccine-induced protection starts from 2 to 4 weeks after vaccination and continues throughout the flu season (6 to 8 months) (CDC).

### Side effects

The side effects associated with influenza vaccines are usually mild and spontaneously resolve within a few days. The most common side effects include pain, erythema and swelling at the injection site, headache, pyrexia, nausea, and myalgia. Fainting may occur, as with any other injection. Although some studies have reported an association between the vaccine and Guillain-Barré syndrome, this association has not been determined in other studies; however, influenza infections may also induce Guillain-Barré syndrome. The prevalence of Guillain-Barré syndrome has been

**Table 1. Vaccines recommended by international guidelines**

Author	Guidelines	Recommendations
European Society of Cardiology	2015 Guidelines for Pulmonary Hypertension <sup>[52]</sup>	Immunization of patients with pulmonary arterial hypertension against influenza and pneumococcal infections is recommended (Class I; Evidence Level C)
	2016 Guidelines on Cardiovascular Disease Prevention in Clinical Practice <sup>[53]</sup>	Annual influenza vaccination of patients with proven cardiovascular disease is recommended (Class IIb; Evidence Level C)
	2016 Guidelines on Diagnosis and Treatment of Acute and Chronic Heart Failure <sup>[54]</sup>	Immunization against influenza and pneumococcal infections may be considered
American Heart Association/ American College of Cardiology	2011 Secondary Prevention and Risk Reduction Therapy in Patients with Coronary and Other Atherosclerotic Vascular Diseases <sup>[55]</sup>	Annual influenza vaccination of patients with cardiovascular disease is recommended (Class I; Evidence Level B)
	2013 Guidelines for the Management of Heart Failure <sup>[56]</sup>	Vaccines against influenza and pneumococcal infections are recommended for secondary prevention
	2014 Guidelines on Valvular Heart Disease <sup>[57]</sup>	Immunization against influenza and pneumococcal infections is recommended for groups of eligible patients with valvular heart disease
Heart Failure Society of America	2010 Clinical Practice Guidelines for Heart Failure <sup>[58]</sup>	Immunization against influenza and pneumococcal infections is recommended for all patients with heart failure, if not contraindicated (Evidence Level B)
Centers for Disease Controls	Advisory Committee on Immunization Practices <sup>[59]</sup>	Annual inactive influenza vaccination of adult patients with chronic pulmonary and cardiovascular diseases is recommended Polysaccharide pneumococcal vaccines are recommended for all adults aged >65 years and younger patients with high-risk immunocompetent diseases, such as chronic cardiovascular diseases (except hypertension)

reported to be 9-fold less in vaccinated populations compared to unvaccinated populations (CDC).

### Contraindications

- People who develop a severe allergic reaction to any component of inactive or recombinant influenza vaccines or people who have had an allergic reaction to any prior influenza vaccination;
- People who have had an anaphylactic-type egg allergy reaction;
- Vaccination should be postponed in people with moderate to severe acute disease (with or without fever) and those who have been diagnosed with Guillain-Barré syndrome in the last 6 weeks.

**Recombinant influenza vaccine:** This vaccine is produced using third-generation production technology, and was approved for use and introduced in 2013 in the US. It is not yet available in our country. This technology does not require an egg-grown vaccine virus. Recombinant influenza vaccine is the only vaccine that is 100% egg-free.

**Live attenuated flu vaccine:** The content (other than live viruses) of the vaccine and the timing of the administration is the same as that of inactive vaccines. As this vaccine is adapted to cold temperatures, it should be stored at  $\leq -15^{\circ}\text{C}$ . The vaccine is given as an intranasal spray and induces both mucosal and systemic immunity. The WHO did not recommend this vaccine for the 2017–2018 season. Live attenuated vaccines are not available in our country.

### Characteristics of pneumococcal vaccines

**PCV13:** PCV13 is a conjugated vaccine that protects against 13 types of *Streptococcus pneumoniae*. Conjugated pneumococcal vaccines are covalently conjugated pneumococcal, antigenic, capsular polysaccharides, and non-toxic proteins (CRM 197, Protein D) of bacteria, such as diphtheria and Haemophilus influenza. The most important characteristic of conjugated vaccines is to induce strong immunogenicity associated with the conjugated protein. These proteins cause a better antibody response through a T-cell-mediated immune response and mucosal immunity (through secretory immunoglobulin A production), as well as immunological memory cell response.<sup>[31]</sup> Therefore, PCV13 may induce long-lasting immunity in both children and adults.

PCV13 is used to provide protection against the inflammation of meninges (meningitis), the fever and chills associated with bacteria that enter the bloodstream (sepsis), and the presence of bacteria or bacterial toxins in the circulating blood (bacteremia), and lung inflammation (pneumonia) caused by *Streptococcus pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F.<sup>[60]</sup> PCV13 is available as a 0.5 mL suspension in a single-use, prefilled syringe for intramuscular injection.

### Side effects

Although no severe effects have been observed with PCV13, it may induce some mild symptoms, such as erythema, swelling, pain or tenderness, pyrexia, decreased appetite, irritability, fatigue, headache, or chills.

### Contraindications

PCV13 should not be administered to individuals with

- A prior history of allergic reactions to PCV13 or PCV7,
- A prior history of allergic reaction to any vaccine that contained diphtheria toxoid,
- Allergic reaction to any component of PCV13.
- Caution should be taken with individuals who have a history of severe allergic reactions or life-threatening allergic reactions. The vaccine can be administered to individuals suffering from a mild common cold; however, administration of the vaccine should be postponed until recovery in those who have a severe health condition.

**PPV23:** PPV23 is a polysaccharide vaccine that provides protection against 23 types of *Streptococcus pneumoniae*. The mechanism of action of polysaccharide vaccines is completely based on the humoral immune response. PPV23 does not stimulate T-cells; therefore, immunological memory does not occur. Antibody response occurs within 2 to 3 weeks, and this response may show individual variations. The serum antibody level is directly related to the level of protection. Serum antibody levels rapidly decline 1 to 2 years after the vaccination in people over the age of 50, and antibodies persist at low levels for up to 10 years.<sup>[8–11]</sup> Revaccination may be required, as persistent immunological memory does not occur. Although revaccination may provide an ongoing antibody re-

sponse in healthy adults and the elderly, vaccines given at short intervals may cause a decline in the antibody level.<sup>[10,12]</sup> Therefore, revaccination should be performed at least 5 years after the initial vaccination.

PPV23 is used to provide protection against inflammation of the meninges (meningitis), fever, and the chills associated with bacteria that enter the bloodstream (sepsis) or the presence of bacteria or bacterial toxins in the circulating blood (bacteremia) and lung inflammation (pneumonia) caused by *Streptococcus pneumoniae* serotypes 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, and 33F.<sup>[60]</sup>

### Side effects

Erythema, pain, fever, and myalgia may occur, which usually resolve spontaneously.

### Contraindications

- PPV23 should not be given to people who have a history of allergic reaction to PPV23 or any component of PPV23;
- Although a mild, common cold does not typically prevent patients from receiving PPV23, the vaccination should be postponed until recovery in those with severe disease;
- Although no adverse effects have been demonstrated in pregnant women or infants born to a mother reporting vaccination during pregnancy, women are recommended to receive the vaccine before becoming pregnant as a precaution.

### Side effects that may occur following any vaccination

Although severe allergic reactions may occur following any vaccination, the risk of developing such a reaction has been reported as 1/1,000,000. These reactions may occur within a few minutes or a few hours after vaccination. While there is a degree of risk, as with any medicinal product, the vaccine-related risk of severe damage or death is very small.

### How to Administer?

#### Turkish Ministry of Health recommendations on vaccinations

In 2016, the Turkish Public Health Institution announced that people should be vaccinated with PCV13 and PPV23. Based on this announcement, those at risk

included patients with heart diseases (cyanotic congestive heart failure and HF, in particular), patients infected with HIV, immunocompromised patients, diseases requiring treatment with immunosuppressive agents, solid organ transplantations, and congenital or acquired immunodeficiency.<sup>[61]</sup>

### Timing of vaccinations

Influenza vaccines should be administered to adults with chronic heart conditions in the autumn (preferably in October, in the northern hemisphere), though they may be administered until February, and should be repeated annually (CDC).

Unlike influenza vaccines, pneumococcal vaccines can be given at any time throughout the year. Both pneumococcal vaccines (PCV13 and PPV23) are recommended for adults.

For individuals who have not previously received a pneumococcal vaccine, first, a single dose of PCV13 should be given, followed by PPV23 at least 1 year later, with a booster dose administered 5 years after the first dose of PPV23. The third dose of PPV23 should be administered to people aged 65 years and older.<sup>[62,63]</sup>

For adults who are not included in the group of patients with HF or chronic heart conditions, the interval between the 2 pneumococcal vaccines (PCV13 and PPV23) should be at least 1 year. However, PPV23 can be administered 8 weeks after the PCV13 administration in adults at high risk who need accelerated vaccination (immunodeficiency, asplenia, cerebrospinal fluid leak, or cochlear implant). If PPV23 was administered first, PCV13 should be given at least 1 year later.<sup>[62,63]</sup>

For patients with active infections and/or who are admitted to hospital for an acute cardiac event (acute coronary syndrome, acute heart failure, acute pulmonary thromboembolism, etc.), pneumococcal vaccines should be administered at discharge from the hospital or during the first follow-up visit after discharge upon recovery from the current illness and once the patient has become hemodynamically stable.

**Access to the vaccine**

Figure 2 and Figure 3 show how to access to vaccines in Turkey Health System.

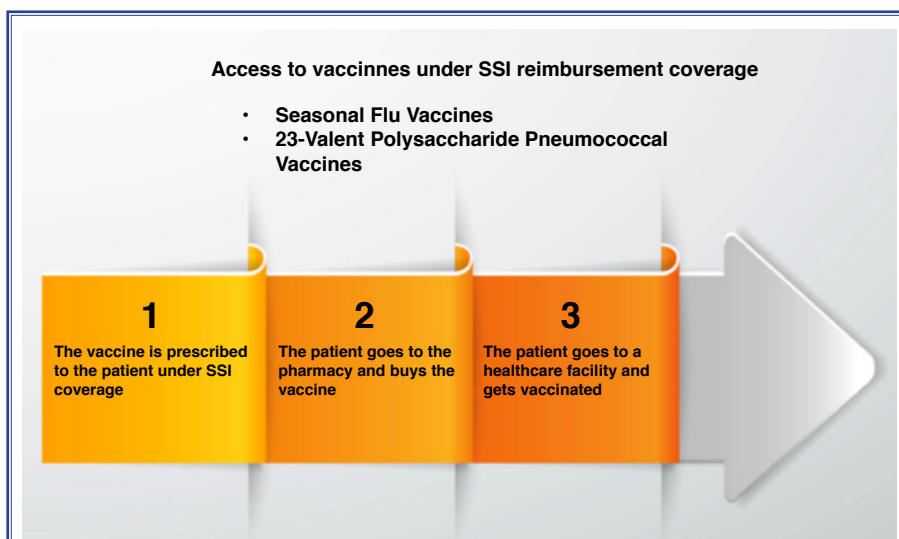
**Use in combination with other vaccines**

- PCV13 and inactive influenza vaccine can be given simultaneously in adults. PCV13 and inactive influenza vaccine are immunogenic and well-tolerated when administered simultaneously.<sup>[64]</sup>

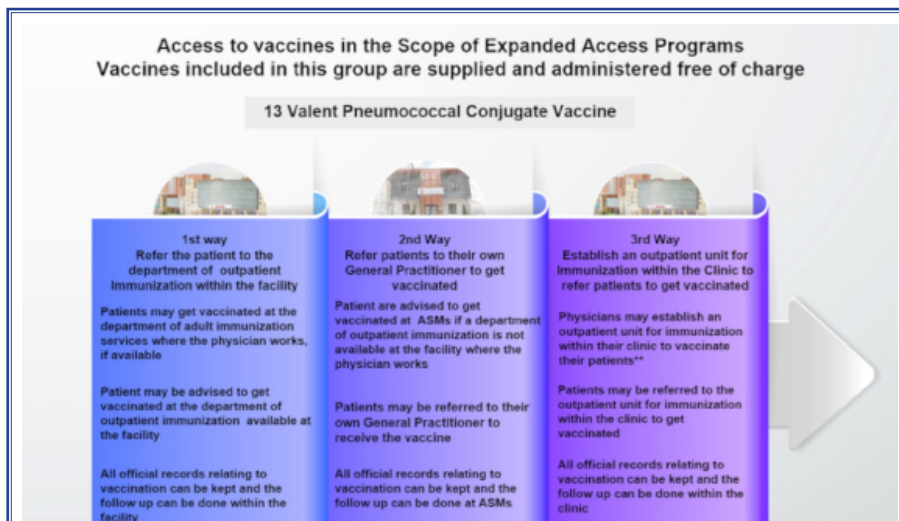
- Simultaneous administration with inactive influenza vaccine may promote patient compliance with vaccines and thereby contribute to improved public health.<sup>[64]</sup>

**Consensus and recommendations**

Although the benefits of vaccines remained unknown, vaccine coverage rates are below the desired level in our country, as in much of the rest of the world. Adults and elderly patients with chronic heart conditions should be vaccinated, as they are at risk for



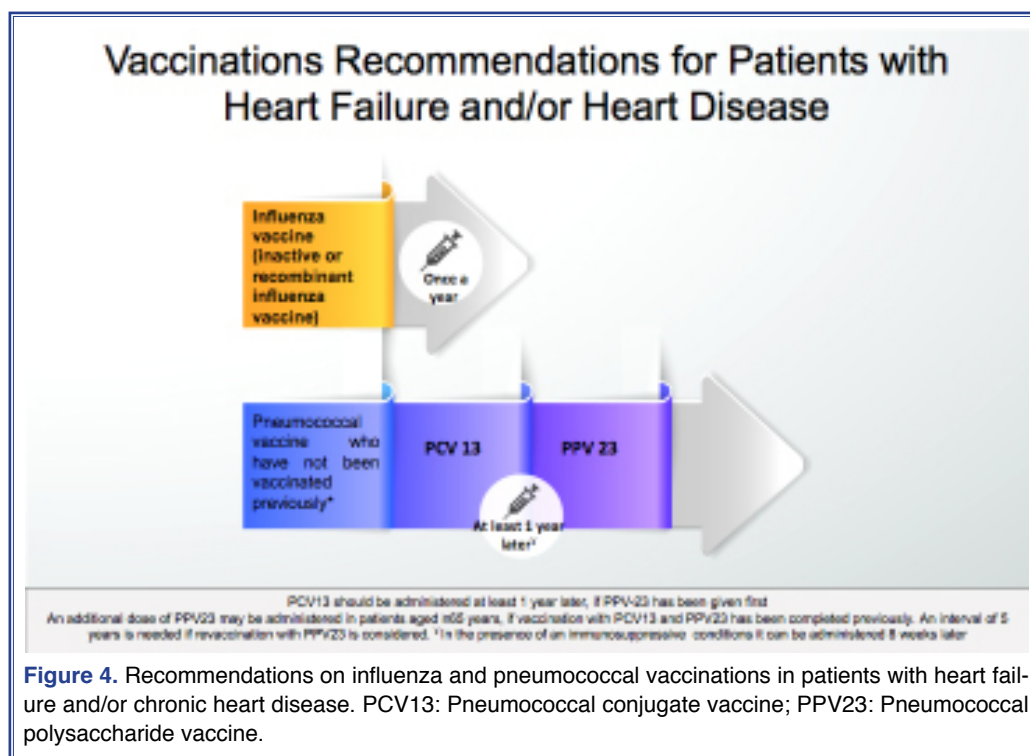
**Figure 2.** The means of access to vaccines reimbursed by the Turkish Social Security Institution. SSI: Turkish Social Security Institution.



Access to vaccines may be facilitated by giving a signed and stamped document indicating the vaccine requested, the diagnosis of the disease and name of the patient when patients are referred to their own general practitioner. \*\*Necessary procedures and the ways to follow may be learned by contacting the Facility Administration or "Immunization Programs" section of your regional Provincial Health Administration

**Figure 3.** Access to vaccines within the scope of the Expanded Programme on Immunization in Turkey. ASM: Family Health Center.





infectious diseases associated with high morbidity and mortality, such as influenza and pneumococcal infections. Figure 4 illustrates the recommendations on how and when to administer influenza and pneumococcal vaccines to patients with HF and/or heart diseases.

### Recommendations to physicians

- Perform awareness-raising activities to make vaccines a part of the routine practice of physicians and a part of treatment,
- Conduct training sessions, meetings, etc.,
- Add vaccinations to patient record systems, such as discharge reports, discharge protocol and patient files, and follow up on vaccination status,
- Share the consensus report with physicians and appropriate platforms,
- Issue vaccination bulletins.

### Recommendations for patient education and compliance

- Preparation of an immunization record card,
- The use of printed materials, such as posters/brochures, to raise awareness/consciousness

### Recommendations for healthcare facilities and the healthcare system

- Establish a unit for immunization at outpatient clinics,
- Establish special vaccination follow-up systems in cardiology clinics,
- Establish an infrastructure addressing branch centers and city hospitals.

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### REFERENCES

1. Cardiovascular diseases (CVDs). World Health Organization. Fact sheet. May 2017. Available at: <http://www.who.int/mediacentre/factsheets/fs317/en/index.html>. Accessed Oct 31, 2018.
2. Torres A, Blasi F, Dartois N, Akova M. Which individuals are

- at increased risk of pneumococcal disease and why? Impact of COPD, asthma, smoking, diabetes, and/or chronic heart disease on community-acquired pneumonia and invasive pneumococcal disease. *Thorax* 2015;70:984–9. [CrossRef]
3. Mor A, Thomsen RW, Ulrichsen SP, Sørensen HT. Chronic heart failure and risk of hospitalization with pneumonia: a population-based study. *Eur J Intern Med* 2013;24:349–53.
  4. Welte T, Torres A, Nathwani D. Clinical and economic burden of community-acquired pneumonia among adults in Europe. *Thorax* 2012;67:71–9. [CrossRef]
  5. Lode HM. Managing community-acquired pneumonia: a European perspective. *Respir Med* 2007;101:1864–73. [CrossRef]
  6. Global priority list of antibiotic-resistant bacteria to guide research, discovery, and development of new antibiotics. World Health Organization. Available at: [https://www.who.int/medicines/publications/WHO-PPL-Short\\_Summary\\_25Feb-ET\\_NM\\_WHO.pdf?ua=1](https://www.who.int/medicines/publications/WHO-PPL-Short_Summary_25Feb-ET_NM_WHO.pdf?ua=1). Accessed Oct 31, 2018.
  7. Torres A, Peetermans WE, Viegi G, Blasi F. Risk factors for community-acquired pneumonia in adults in Europe: a literature review. *Thorax* 2013;68:1057–65. [CrossRef]
  8. Song JH, Oh WS, Kang CI, Chung DR, Peck KR, Ko KS, et al; Asian Network for Surveillance of Resistant Pathogens Study Group. Epidemiology and clinical outcomes of community-acquired pneumonia in adult patients in Asian countries: a prospective study by the Asian network for surveillance of resistant pathogens. *Int J Antimicrob Agents* 2008;31:107–14.
  9. Cangemi R, Casciaro M, Rossi E, Calvieri C, Bucci T, Calabrese CM, et al; SIXTUS Study Group. Platelet activation is associated with myocardial infarction in patients with pneumonia. *J Am Coll Cardiol* 2014;64:1917–25. [CrossRef]
  10. Corrales-Medina VF, Suh KN, Rose G, Chirinos JA, Doucette S, Cameron DW, et al. Cardiac complications in patients with community-acquired pneumonia: a systematic review and meta-analysis of observational studies. *PLoS Med* 2011;8:e1001048. [CrossRef]
  11. Corrales-Medina VF, Musher DM, Wells GA, Chirinos JA, Chen L, Fine MJ. Cardiac complications in patients with community-acquired pneumonia: incidence, timing, risk factors, and association with short-term mortality. *Circulation* 2012;125:773–81. [CrossRef]
  12. Corrales-Medina VF, Musher DM, Shachkina S, Chirinos JA. Acute pneumonia and the cardiovascular system. *Lancet* 2013;381:496–505. [CrossRef]
  13. Restrepo MI, Reyes LF. Pneumonia as a cardiovascular disease. *Respirology* 2018;23:250–9. [CrossRef]
  14. Eurich DT, Marrie TJ, Minhas-Sandhu JK, Majumdar SR. Risk of heart failure after community acquired pneumonia: prospective controlled study with 10 years of follow-up. *BMJ* 2017;356:j413. [CrossRef]
  15. Bergh C, Fall K, Udumyan R, Sjöqvist H, Fröbert O, Montgomery S. Severe infections and subsequent delayed cardiovascular disease. *Eur J Prev Cardiol* 2017;24:1958–66. [CrossRef]
  16. Akçakaya N, Camcıoğlu Y, Gür E, Öztürk R. Çocuk ve erişkinlerde aşılama. İÜ Cerrahpaşa Tıp Fak Sürekli Tıp Eğitimi Etkinlikleri. No:71. İstanbul: 2010. Available at: <http://www.ctf.edu.tr/stek/pdfs/71/7101.pdf>. Accessed Oct 31, 2018.
  17. Ünal S. Çalışma hayatında yetişkin aşılamanın yeri ve önemi. Çalışma Hayatında Bulaşıcı Hastalıklar Sempozyumu. Ankara: Feb 2013. Available at: <http://www.hisam.hacettepe.edu.tr/chbhastalik/sunum/SerhatUnalIII.pdf>. Accessed Oct 31, 2018.
  18. Alici DE, Sayiner A, Unal S. Barriers to adult immunization and solutions: Personalized approaches. *Hum Vaccin Immunother* 2017;13:213–5. [CrossRef]
  19. Sessa A, Rossi A, Cricelli I. Adult immunization schedule. The general practitioner's perspective and new tools for a better practice. *J Prev Med Hyg* 2015;56:E9–11.
  20. Şenol E. Erişkin Aşılması. 13. Ulusal Çocuk Enfeksiyon Hastalıkları Sempozyumu. Eskişehir: 2016.
  21. Lipsitch M, Siber GR. How Can Vaccines Contribute to Solving the Antimicrobial Resistance Problem? *MBio* 2016;7. pii: e00428–16. [CrossRef]
  22. Aliberti S, Ramirez JA. Cardiac diseases complicating community-acquired pneumonia. *Curr Opin Infect Dis* 2014;27:295–301. [CrossRef]
  23. Musher DM, Rueda AM, Kaka AS, Mapara SM. The association between pneumococcal pneumonia and acute cardiac events. *Clin Infect Dis* 2007;45:158–65. [CrossRef]
  24. Sandvall B, Rueda AM, Musher DM. Long-term survival following pneumococcal pneumonia. *Clin Infect Dis* 2013;56:1145–6. [CrossRef]
  25. Bonten MJ, Huijts SM, Bolkenbaas M, Webber C, Patterson S, Gault S, et al. Polysaccharide conjugate vaccine against pneumococcal pneumonia in adults. *N Engl J Med* 2015;372:1114–25. [CrossRef]
  26. Baldo V, Cocchio S, Gallo T, Furlan P, Romor P, Bertonecello C, et al. Pneumococcal Conjugated Vaccine Reduces the High Mortality for Community-Acquired Pneumonia in the Elderly: an Italian Regional Experience. *PLoS One* 2016;11:e0166637.
  27. Altun HU, Hascelik G, Gür D, Eser ÖK. Invasive pneumococci before the introduction of pneumococcal conjugate vaccine in Turkey: antimicrobial susceptibility, serotype distribution, and molecular identification of macrolide resistance. *J Chemother* 2015;27:74–9. [CrossRef]
  28. Ciblak MA; Grip Platformu. Influenza vaccination in Turkey: prevalence of risk groups, current vaccination status, factors influencing vaccine uptake and steps taken to increase vaccination rate. *Vaccine* 2013;31:518–23. [CrossRef]
  29. Estabragh ZR, Mamas MA. The cardiovascular manifestations of influenza: a systematic review. *Int J Cardiol* 2013;167:2397–403. [CrossRef]
  30. Kadoglou NPE, Bracke F, Simmers T, Tsiodras S, Parissis J. Influenza infection and heart failure-vaccination may change heart failure prognosis? *Heart Fail Rev* 2017;22:329–36.
  31. Bhatt AS, DeVore AD, Hernandez AF, Mentz RJ. Can Vaccinations Improve Heart Failure Outcomes?: Contemporary Data

- and Future Directions. *JACC Heart Fail* 2017;5:194–203.
32. Kaya H, Beton O, Acar G, Temizhan A, Cavusoğlu Y, Guray U, et al; TREAT-HF Investigators. Influence of influenza vaccination on recurrent hospitalization in patients with heart failure. *Herz* 2017;42:307–15. [CrossRef]
  33. de Diego C, Vila-Córcoles A, Ochoa O, Rodriguez-Blanco T, Salsench E, Hospital I, et al; EPIVAC Study Group. Effects of annual influenza vaccination on winter mortality in elderly people with chronic heart disease. *Eur Heart J* 2009;30:209–16. [CrossRef]
  34. Blaya-Nováková V, Prado-Galbarro FJ, Sarría-Santamera A. Effects of annual influenza vaccination on mortality in patients with heart failure. *Eur J Public Health* 2016;26:890–2.
  35. Vardeny O, Claggett B, Udell JA, Packer M, Zile M, Rouleau J, et al; PARADIGM-HF Investigators. Influenza Vaccination in Patients With Chronic Heart Failure: The PARADIGM-HF Trial. *JACC Heart Fail* 2016;4:152–8. [CrossRef]
  36. Özsü S, Uçar E, Arslan Y, Maden E, Bilgiç H. The Frequency of Influenza and Pneumococcal Vaccination in COPD. *Solum* 2011;13:21–5. [CrossRef]
  37. Erer OF, Karadeniz G, Gazibaba D, Ürpek G, Yalnız E, Aktoğu SÖ. Immunization in the chronic obstructive pulmonary disease: can we have really done it? *İzmir Göğüs Hastanesi Dergisi* 2013;27:31–40.
  38. Satman I, Akalin S, Cakir B, Altinel S; diaVAX Study Group. The effect of physicians' awareness on influenza and pneumococcal vaccination rates and correlates of vaccination in patients with diabetes in Turkey: an epidemiological Study "diaVAX". *Hum Vaccin Immunother* 2013;9:2618–26. [CrossRef]
  39. "10 Keys™ to Healthy Aging Work book and the Instructor Manual. Mar 3, 2018. Available at: [http://www12.edc.gsp.hitt.edu/CHA\\_OAEP/Documents/ParticipantWorkbook2016.pdf](http://www12.edc.gsp.hitt.edu/CHA_OAEP/Documents/ParticipantWorkbook2016.pdf). Accessed Apr 2018.
  40. Recommended Immunization Schedule for Adults Aged 19 Years or Older, United States, 2018. Feb 6, 2018. Centers for Disease Control and Prevention. Available at: <https://www.cdc.gov/vaccines/schedules/hcp/imz/adult-compliant.html>. Accessed Nov 1, 2018.
  41. Cafiero-Fonseca ET, Stawasz A, Johnson ST, Sato R, Bloom DE. The full benefits of adult pneumococcal vaccination: A systematic review. *PLoS One* 2017;12:e0186903. [CrossRef]
  42. Tan LLJ. A review of the key factors to improve adult immunization coverage rates: What can the clinician do? *Vaccine* 2018;36:5373–8. [CrossRef]
  43. Ünal S. Erişkin Aşılama Programları, Oranlar? 6. Ulusal Aşı Sempozyumu. Ankara: 2015.
  44. Libby P, Theroux P. Pathophysiology of coronary artery disease. *Circulation* 2005;111:3481–8. [CrossRef]
  45. Berliner JA, Subbanagounder G, Leitinger N, Watson AD, Vora D. Evidence for a role of phospholipid oxidation products in atherogenesis. *Trends Cardiovasc Med* 2001;11:142–7.
  46. Mann DL. Inflammatory mediators and the failing heart: past, present, and the foreseeable future. *Circ Res* 2002;91:988–98.
  47. Thomsen RW, Kasatpibal N, Riis A, Nørgaard M, Sørensen HT. The impact of pre-existing heart failure on pneumonia prognosis: population-based cohort study. *J Gen Intern Med* 2008;23:1407–13. [CrossRef]
  48. Ware LB, Matthay MA. Clinical practice. Acute pulmonary edema. *N Engl J Med* 2005;353:2788–96. [CrossRef]
  49. Koivula I, Sten M, Mäkelä PH. Risk factors for pneumonia in the elderly. *Am J Med* 1994;96:313–20. [CrossRef]
  50. Klare B, Kubini R, Ewig S. Risk factors for pneumonia in patients with cardiovascular diseases. [Article in German]. *Pneumologie* 2002;56:781–8. [CrossRef]
  51. Shea KM, Edelsberg J, Weycker D, Farkouh RA, Strutton DR, Pelton SI. Rates of pneumococcal disease in adults with chronic medical conditions. *Open Forum Infect Dis* 2014;1:ofu024. [CrossRef]
  52. Galiè N, Humbert M, Vachiery JL, Gibbs S, Lang I, Torbicki A, et al; ESC Scientific Document Group. 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension: The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS): Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT). *Eur Heart J* 2016;37:67–119. [CrossRef]
  53. Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, Capapano AL, et al; ESC Scientific Document Group. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts) Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). *Eur Heart J* 2016;37:2315–81. [CrossRef]
  54. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JG, Coats AJ, et al; Authors/Task Force Members; Document Reviewers. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur J Heart Fail* 2016;18:891–975. [CrossRef]
  55. Smith SC Jr, Benjamin EJ, Bonow RO, Braun LT, Creager MA, Franklin BA, et al. AHA/ACCF secondary prevention and risk reduction therapy for patients with coronary and other atherosclerotic vascular disease: 2011 update: a guideline from the American Heart Association and American College of Cardiology Foundation endorsed by the World Heart Federation and the Preventive Cardiovascular Nurses Association. *J Am Coll Cardiol* 2011;58:2432–46. [CrossRef]
  56. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE Jr, Drazner MH, et al. 2013 ACCF/AHA guideline for the man-

- agement of heart failure: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. *Circulation* 2013;128:1810–52. [CrossRef]
57. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP 3rd, Guyton RA, et al; ACC/AHA Task Force Members. 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation* 2014;129:e521–643. [CrossRef]
58. Lindenfeld J, Albert NM, Boehmer JP, Collins SP, Ezekowitz JA, Givertz MM, et al; Heart Failure Society of America. HFSA 2010 Comprehensive Heart Failure Practice Guideline. *J Card Fail* 2010;16:e1–194. [CrossRef]
59. Kim DK, Riley LE, Hunter P; Advisory Committee on Immunization Practices. Recommended Immunization Schedule for Adults Aged 19 Years or Older, United States, 2018. *Ann Intern Med* 2018;168:210–20. [CrossRef]
60. Taylan M. Pnömonokok Aşılıarı. *Güncel Göğüs Hastalıkları Serisi* 2014;2:98–105.
61. Risk Grubu Aşılamaaları. Sağlık Bakanlığı, Türkiye Halk Sağlığı Kurumu. Mayıs 27,2016. Sayı: 21001706/131.99.
62. EKMUD. Erişkin Bağışıklama Rehberi. Türkiye Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Uzmanlık Derneği, Erişkin Bağışıklama Rehberi Çalışma Grubu. 2. Güncelleme, Mayıs 2016. Available at: <http://ekmud.org.tr/calisma-grubu/4-bagisiklama-calisma-grubu>. Accessed Nov 1, 2018.
63. Şenol E, Azap A, Erbay A, Alp Çavuş S, Karakuş R, Acar A. Pneumococcal Vaccine as One of the Immunization Coverage Targets for Adulthood Vaccines: A Consensus Report of the Study Group for Adult Immunization of the Turkish Society of Clinical Microbiology and Infectious Diseases. *Klinik Dergisi* 2018;31:2–18. [CrossRef]
64. Frenck RW Jr, Gurtman A, Rubino J, Smith W, van Cleeff M, Jayawardene D, et al. Randomized, controlled trial of a 13-valent pneumococcal conjugate vaccine administered concomitantly with an influenza vaccine in healthy adults. *Clin Vaccine Immunol* 2012;19:1296–303. [CrossRef]

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