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Invited Review

A multidisciplinary consensus report on approach to adult influenza in primary care: Diagnosis, treatment, prevention of complications and vaccination

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ABSTRACT

Influenza is a major public health concern that can cause infection in all age groups while leading to severe complications, hospitalization, and mortality particularly in the presence of risk factors such as advanced age, chronic comorbidities, immunosuppression and pregnancy. This multidisciplinary consensus report aimed to provide primary care physicians with a practical guidance document on adult influenza in terms of diagnosis, treatment, prevention of complications and vaccination through recommendations based on current scientific evidence for use in daily clinical practice. The report was prepared by a multidisciplinary expert panel involving family medicine, infectious diseases and clinical microbiology, internal medicine, endocrinology and cardiology academicians.

Keywords: adult influenza, diagnosis, complications, referral criteria, high-risk group, anti-viral treatment, chemoprophylaxis, vaccination

Introduction

According to World Health Organization (WHO), seasonal influenza affects around one billion people worldwide every year, causing severe illness in 3-5 million cases and death in 650,000.[1,2] The annual global attack rate for influenza is estimated to be 5% to 10% in adults. In healthy adults, the disease is often self-limited with a full recovery within approximately one week. However, presence of certain risk factors such as advanced age, chronic comorbidities, pregnancy

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and immunosuppression increases the likelihood of a more severe clinical course potentially leading to severe complications, hospitalization and death.[1-3]

Seasonal influenza vaccine is an important public health intervention and the main strategy for prevention of influenza infection, as well as for reducing the risk of developing severe disease, influenza-related complications, hospitalization and mortality.[1,4-6] Vaccination is also associated with lower healthcare resource utilization, reducing the economic burden of influenza.[5-7]

However, public perception of influenza often as a mild and self-limiting disease, vaccine hesitancy and suboptimal real-world utilization of vaccination particularly in high-risk groups are amongst the main obstacles to preventing influenza and related complications.

Primary healthcare plays a pivotal role not only in the diagnosis and treatment of influenza but also in the prevention of disease. Specifically, primary preventive healthcare physicians are responsible for identifying high-risk individuals, evaluating vaccine needs, addressing vaccine hesitancy, and recommending and implementing seasonal influenza vaccination.

This multidisciplinary consensus report aimed to provide primary care physicians with a practical guidance document on adult influenza in terms of diagnosis, treatment, prevention of complications and vaccination, through recommendations based on current scientific evidence for use in daily clinical practice. The report was prepared by a multidisciplinary expert panel involving family medicine, infectious diseases and clinical microbiology, internal medicine, endocrinology and cardiology academicians.

Epidemiological characteristics

Influenza epidemiology is mainly driven by antigenic variation in influenza viruses and shifts in population immunity over time. In temperate climate zones, influenza shows seasonality by causing epidemics mostly in the winter months. In tropical and subtropical climate zones, however, influenza can circulate year-round with one or more peaks in activity.[1,3,8] The seasonality of influenza varies globally in temperate climate zones, with peak periods occurring predominantly between October and April in the Northern Hemisphere, and between April to September in the Southern Hemisphere.[3,5-7]

The timing, duration and severity of the seasonal influenza epidemic vary across years and regions depending on the type of circulating viruses, population immunity level, previous infection or vaccination status, and demographic and environmental factors.[1,2,9] Influenza is an important public health concern increasing the risk of severe complications, hospitalization and mortality particularly, in advanced age and other high-risk groups, as well as the healthcare resource utilization.[3,4,9,10] Besides the increase in health expenditure, it also causes increment in indirect costs resulting from patients' lost productivity and time spent by the caregivers, leading to a considerable economic burden.[11]

Influenza activity is tracked by national surveillance systems in Türkiye. Accordingly, within the context of the sentinel influenza-like illness (ILI) surveillance, clinical and virological data collected from ILI cases in selected provinces and primary care health institutions are analyzed to track influenza trends regarding the type and subtypes of circulating viruses and change in influenza activity over time.[12] Continuous data collection by surveillance, both during and between influenza seasons, enables year-round tracking of virus circulation.

Influenza activity varies with respect to its onset, peak and end. Indeed, in the 2025–2026 season earlier onset of influenza activity compared to previous seasons was reported in some regions of Europe and Northern Hemisphere, along with a predominance of influenza A viruses, A(H3N2) viruses in particular, in circulation.[13-15] This variability indicates that influenza epidemiology should be evaluated based on up-to-date surveillance data rather than fixed calendar intervals.

In Türkiye, influenza activity usually starts to rise in autumn months, reaches its highest peak in winter months and continues till spring. However, given the likelihood of yearly changes in the onset and end of the season and the peak activity period, season-based evaluation of epidemiological status and circulating viruses should be performed as per the national surveillance data.[12,15,16]

Influenza viruses, routes of transmisson and pathogenesis

1. Influenza viruses

Influenza viruses are enveloped, segmented, single-stranded RNA viruses with negative polarity belonging to the Orthomyxoviridae family. They are classified as influenza A, B, C and D viruses.[3]

Influenza A viruses infect a diverse spectrum of hosts including humans alongside animal populations like birds, pigs, horses, and various mammal species. Humans are the primary natural host for the influenza B viruses. Influenza C viruses can infect humans and pigs, while influenza D viruses mainly infect cattle and not considered an established pathogen in humans.[17]

Influenza A and B viruses cause the major burden of seasonal influenza in humans. While influenza A viruses may cause both seasonal epidemics and pandemics, influenza B viruses are responsible for epidemics only. Influenza C virus is often associated with mild and sporadic respiratory infections.[3,18] Both influenza A and B viruses can cause disease in different age groups and severe complications particularly in high-risk individuals (Table 1).

Influenza A viruses are classified in subtypes based on the antigenic properties of surface glycoproteins hemagglutinin (HA) and neuraminidase (NA). Influenza B viruses are historically divided into two distinct lineages known as B/Victoria and B/Yamagata. However, as the B/Yamagata lineage has not been confirmed in global surveillance since March 2020, current seasonal influenza vaccines include only the B/Victoria lineage while excluding the B/Yamagata lineage.

2. Antigenic variation: Antigenic drift/antigenic shift

Antigenic drift refers to a gradual accumulation of minor point mutations in HA and NA genes over time. Antigenic shift refers to an abrupt, major change creating a novel influenza A subtype due to gene reassortment when two different strains

Table 1. Comparative characteristics of influenza viruses pathogenic to humans.

	Influenza viruses		
Characteristics	**Influenza A**	**Influenza B**	**Influenza C**
Non-human host	+	–	+
Antigenic drift	+	+	+
Antigenic shift	+	–	–
Epidemics	+	+	+
Pandemics	+	–	–
Severe clinical course	+	–	–

infect the same cell. Global pandemics may occur given the limited population immunity to this novel subtype, in case of sustained and efficient person-to-person transmission. Antigenic shift occurs solely in influenza A but not influenza B viruses (Figure 1).[3,18]

Constant evolution of influenza viruses through antigenic changes altering the surface proteins necessitates the annual updating of the epidemiological characteristics of virus and the seasonal influenza vaccine.[19]

3. Routes of transmission

Immune-suppressed individuals, elderly individuals, and those with chronic comorbidities experience longer viral shedding and infection periods.

Influenza primarily spreads from an infected person to a susceptible person through the inspiration of respiratory droplets (>5μm) and aerosols released during coughs, sneezes, or talks. Contacting surfaces contaminated with respiratory droplets is another route of transmission.[2,20] Incubation period of the disease lasts 1-4 days, while the contagious period extends from the 24 hours preceding the symptom onset to 5 days after. Immune-suppressed individuals, elderly individuals, and those with chronic comorbidities experience longer viral shedding and infection periods (Figure 2).[2,12,20,21]

4. Pathogenesis

The viral surface protein hemagglutinin (HA) binds to sialic acid receptors located on the host respiratory epithelial cells enabling viral attachment to ciliated epithelium, while neuraminidase (NA) is responsible for release of virions from infected cells, and development and progression of disease. Viral replication in ciliated epithelium infects additional epithelial cells as well as alveolar macrophages, which leads to inhibition of cellular protein synthesis and eventual cellular death, through necrosis (epithelial cells) or apoptosis (alveolar macrophages). The ciliary

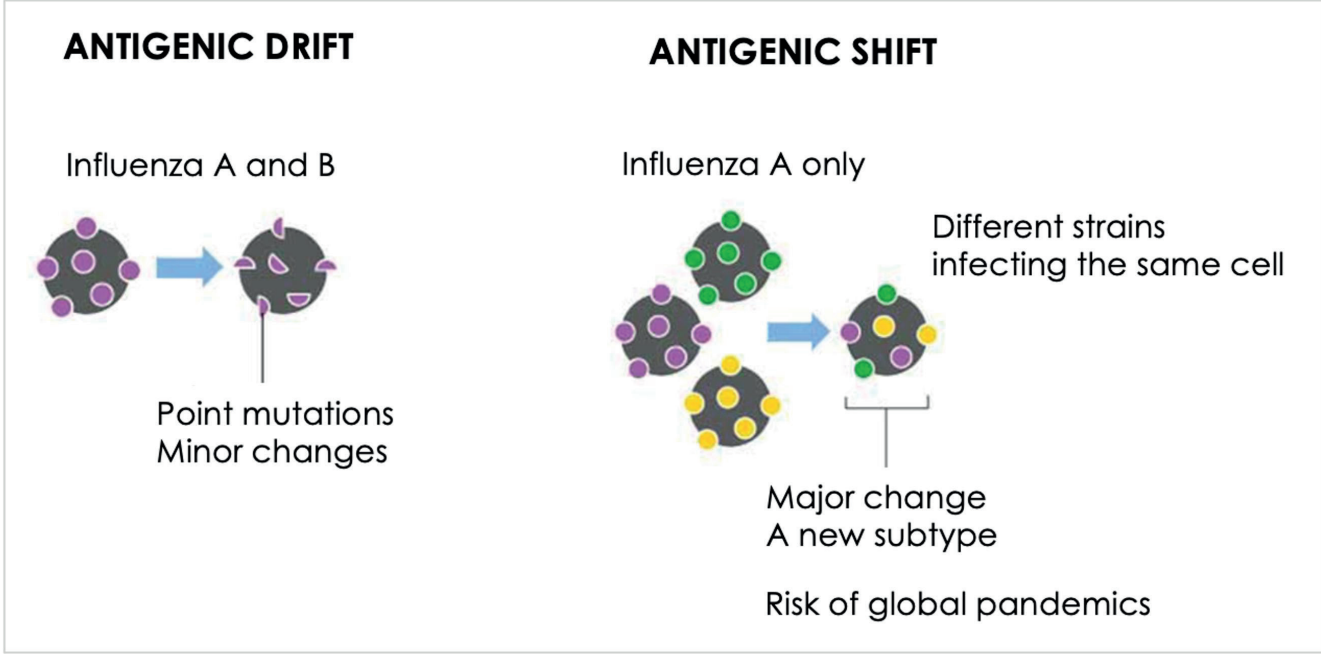


Figure 1. Antigenic variation in influenza viruses.

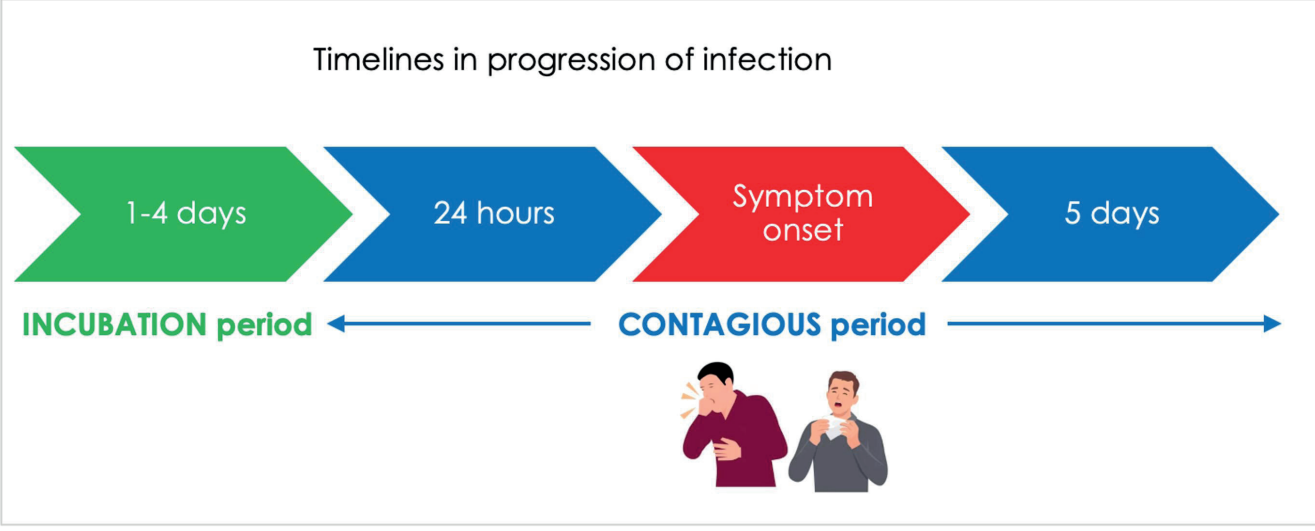


Figure 2. Timelines in progression of infection.

epithelium is shed and replaced by squamous epithelium. Cellular necrosis and/or apoptosis induce an immune response – including cellular immunity within 5 to 7 days and humoral immunity within 10 days – as well as cytokine and chemokine production.[22]

Antibody formation against HA and NA antigens, but not to other viral proteins, offers protection from the disease. Anti-HA antibodies are effective in the prevention of re-infection, while anti-NA antibodies are effective in limiting disease severity and viral contagiousness.[22,23]

Clinical course

Elderly patients can present with more subtle symptoms such as tiredness, decreased appetite, dizziness and weakness, without sore throat or myalgia.

Seasonal influenza manifests a wide-ranging clinical spectrum. Systemic symptoms (i.e., fever, chills, myalgia, tiredness and headache) typically develop suddenly and concurrently with the respiratory symptoms (i.e., dry cough, sore throat and rhinorrhea). Presence of at least one of the systemic symptoms and at least one of the accompanying respiratory symptoms is considered clinically diagnostic. Ocular symptoms (i.e., epiphora, conjunctivitis, photophobia and ophthalmalgia) and rash are rarer symptoms. Elderly patients can present with more subtle symptoms such as tiredness, loss of appetite, dizziness and weakness, without sore throat or myalgia (Table 2).[3,18,20,22]

Sudden onset of symptoms – fever, myalgia, chills, tiredness and cough in particular – differentiate influenza from common cold which presents with gradual stepwise onset of localized symptoms such as rhinorrhea rather than fever/chills.[20]

Complications and risk groups

Age ≥65 years, chronic diseases, immunosupression and pregnancy are risk factors for severe clinical course, complications, hospitalization and mortality.

Influenza is associated with several respiratory and non-respiratory complications (Table 3).[2,3,24]

Table 2. Clinical Manifestations – Symptoms and Signs of Influenza.

	Sudden onset systemic symptoms and signs (at least one)	**Accompanying respiratory symptoms (at least one)**
Young and middle-aged adults	• Fever • Chills • Myalgia • Tiredness • Headache • Rarely ocular symptoms (i.e., epiphora, conjunctivitis, photophobia and ophthalmalgia) and rash	• Dry cough • Sore throat • Rhinorrhea
≥65 age group	• Fever • Tiredness • Loss of appetite • Dizziness • Weakness • NO Myalgia (likely)	• Dry cough • NO Sore throat (likely)

Table 3. Influenza-related complications.

Respiratory complications	**Cardiovascular complications**	**Other complications**
• Primary viral pneumonia • Secondary bacterial pneumonia • Respiratory failure • Acute respiratory distress syndrome	• Temporary ECG alterations • Acute myocardial infarction • Heart failure • Myocarditis • Pericarditis	• Sepsis • Acute renal failure • Multi-organ failure • Lymphopenia and thrombocytopenia • Hemophagocytic syndrome and disseminated intravascular coagulation • Rhabdomyolysis • Premature birth, spontaneous abortion in pregnant women • Neurologic complications (aseptic meningitis, myelitis, encephalopathy, necrotizing encephalitis, Guillain-Barré syndrome, immune-mediated encephalitis or cerebellitis)

Patients who are at increased risk of influenza-related complications, collectively known as the high-risk groups, are listed in Table 4.

Comorbidity burden – diabetes, chronic obstructive pulmonary disease (COPD), cancer and chronic heart, liver, and kidney diseases – is a critical factor increasing the risk of complications and mortality (particularly in the over-65 age group). Concurrent comorbidities also increase the risk of multiorgan failure and mortality during acute infection. Influenza can also lead to worsening of the underlying disease, in addition to its potentially fatal complications.[3,24,25]

High-risk groups are at increased risk of severe influenza infection (complications and mortality) and worsening of underlying comorbidity.

Table 4. High-risk groups for influenza-related complications.

High-risk Groups
• Elderly individuals (≥65 years of age)
• Asthma, COPD and cystic fibrosis patients
• Multiple sclerosis and Parkinson patients
• Patients with chronic renal, hepatic or hematologic (i.e., sickle cell anemia) diseases
• Patients with metabolic disorders such as diabetes and obesity (body mass index > 40 kg/m^2)
• Patients with cardiac diseases such as congestive heart failure or coronary artery disease
• Immunosuppressive patients (HIV infection, post-transplant patients, patients receiving anti-cancer or biological treatments)
• Pregnant women
• Healthcare professionals
• Individuals living in congregate settings such as prisons and refugee camps
• Caregivers or close contacts of people in need of care

Diagnostic approach

Diagnosis of influenza is primarily clinical.

Diagnosis of influenza is primarily clinical (Table 2), while in selected cases laboratory tests can be used to confirm the diagnosis.[3,26]

These tests include virus isolation in respiratory samples via cell culture, molecular techniques for detection of viral nucleic acid via real-time polymerase chain reaction (RT-PCR)-based nucleic acid amplification test (NAT), detection of antigenic structures via direct fluorescent antibody test (DFA) and detection of specific antibody response via enzyme immunoassay (EIA)-based rapid diagnostic tests.[3,20]

Cell culture and NAT (RT-PCR) are considered the gold-standard tests. NAT (RT-PCR) enables diagnosis of influenza virus in nasopharyngeal samples with 92-95% sensitivity and 98% specificity, besides the influenza A subtyping in isolated samples. While rapid antigen tests can be used for a faster diagnosis, negative test results need careful interpretation given the high probability of false negatives (Table 5).[2,3,20]

Molecular tests (NAT-RT-PCR) are safer than rapid tests.

Timing of influenza tests with respect to clinical symptoms and signs is critical for test sensitivity. Viral shedding peaks within the first 24 to 48 hours of illness onset, then declines rapidly. Viral replication becomes very limited or absent after 5 to 7 days in immunocompetent hosts. Therefore, tests are recommended to be performed within 4 days of symptom onset. However, in case of advanced age, chronic disease, obesity and immunosuppression, viral shedding can last longer than normal (Figure 3).[2,24]

Treatment

In the influenza season, high-risk groups should initiate anti-viral treatment without laboratory testing.

In the influenza season, following the clinical diagnosis of influenza infection and exclusion of a bacterial infection, anti-viral treatment should be promptly started, without laboratory testing, in the high-risk groups (Table 4). In low-risk

Table 5. Laboratory tests used in influenza diagnosis.

	Working principle	Detectable viruses	Turnaround time	Key points
Cell culture	isolation of virus	A and B	3 days	Limited use in routine practice Biosafety risks due to viable infectious virus particles in samples
Molecular technique **"NAT/RT-PCR"**	detection of viral nucleic acid	A/A subtypes and B	1-8 hours	Gold-standard Sensitivity and specificity ↑ Identification of A subtypes Earlier diagnosis with detection of nonviable RNA, compared to cell culture
DFA test	detection of antigenic structures	A and B	2 hours	Lower sensitivity compared to culture and NAT
Rapid tests-EIA	Detection of influenza-specific antibody response	A and B	<30 minutes	Lower sensitivity and specificity culture and NAT High probability of false-negative results

NAT: Nucleic acid amplification test; RT-PCR: Real-time polymerase chain reaction; DFA: Direct fluorescent antibody test; EIA: Enzyme immunoassay

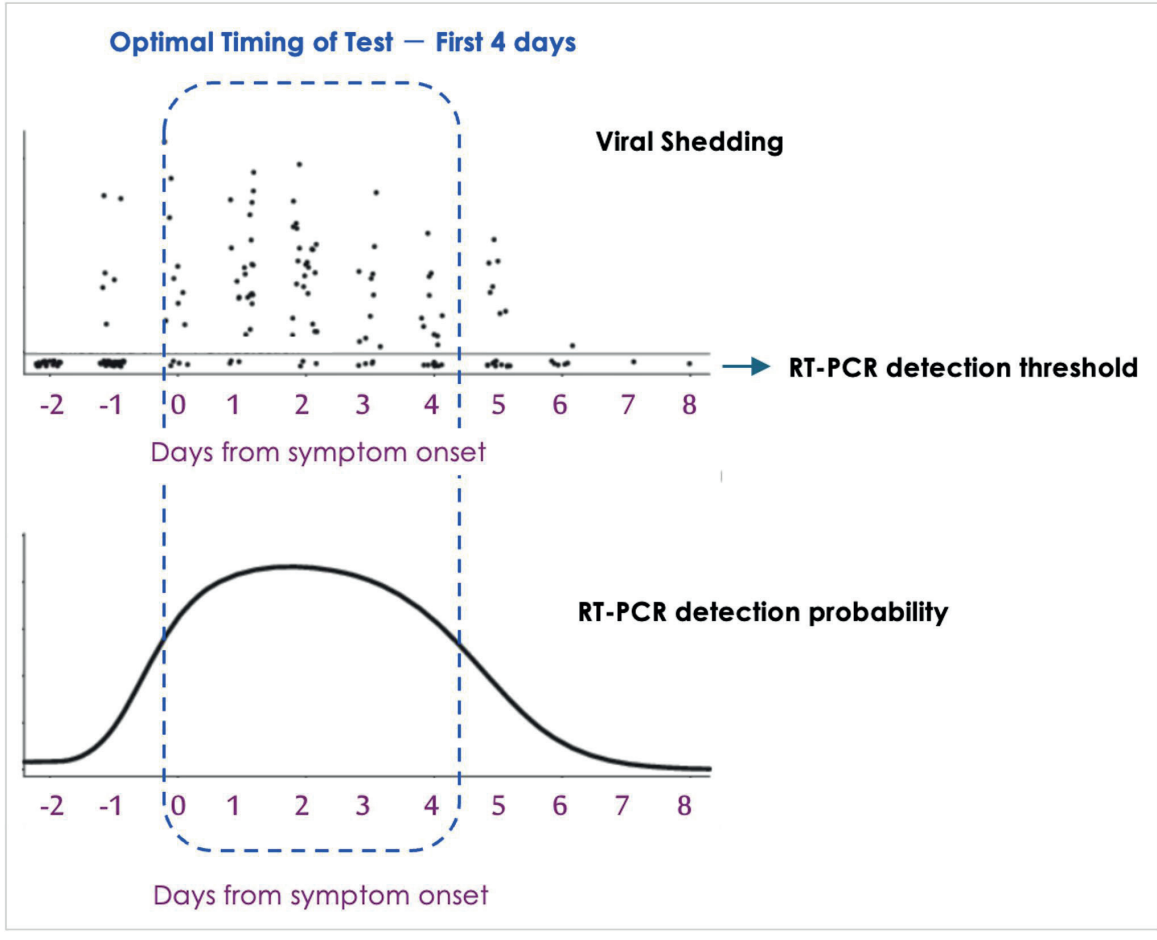


Figure 3. Optimal timing of test.

patients, however, tests should be performed first, if possible, and the decision to initiate anti-viral or symptomatic treatment should be based on test results (Figure 4).[2,3,24]

Outside the influenza season (between May and October), no patient should receive anti-viral treatment without laboratory testing (Figure 4).

Amongst the antiviral agents approved by Food and Drug Administration (FDA) for influenza treatment and/or prophylaxis, oseltamivir and baloxavir are currently available in Türkiye. Oseltamivir is a neuraminidase inhibitor that blocks the viral NA enzyme of influenza A and B viruses, preventing viral particles from releasing from infected host cells. Baloxavir is a cap-dependent endonuclease inhibitor that blocks viral replication by halting mRNA synthesis.[3] Oseltamivir is the most widely prescribed influenza antiviral in the world (Table 6).[3,20]

Symptomatic and supportive therapy is based on bedrest, hydration and use of antipyretic or analgesic (acetaminophen or ibuprofen). Routine use of corticosteroids and use of antibiotics for the purpose of prophylaxis should be avoided. In patients with secondary bacterial pneumonia, empirical antibiotics should be administered as per pneumonia guidelines, while antibiotic treatment is further adjusted according to culture and sensitivity test results if bacterial pathogen is isolated.

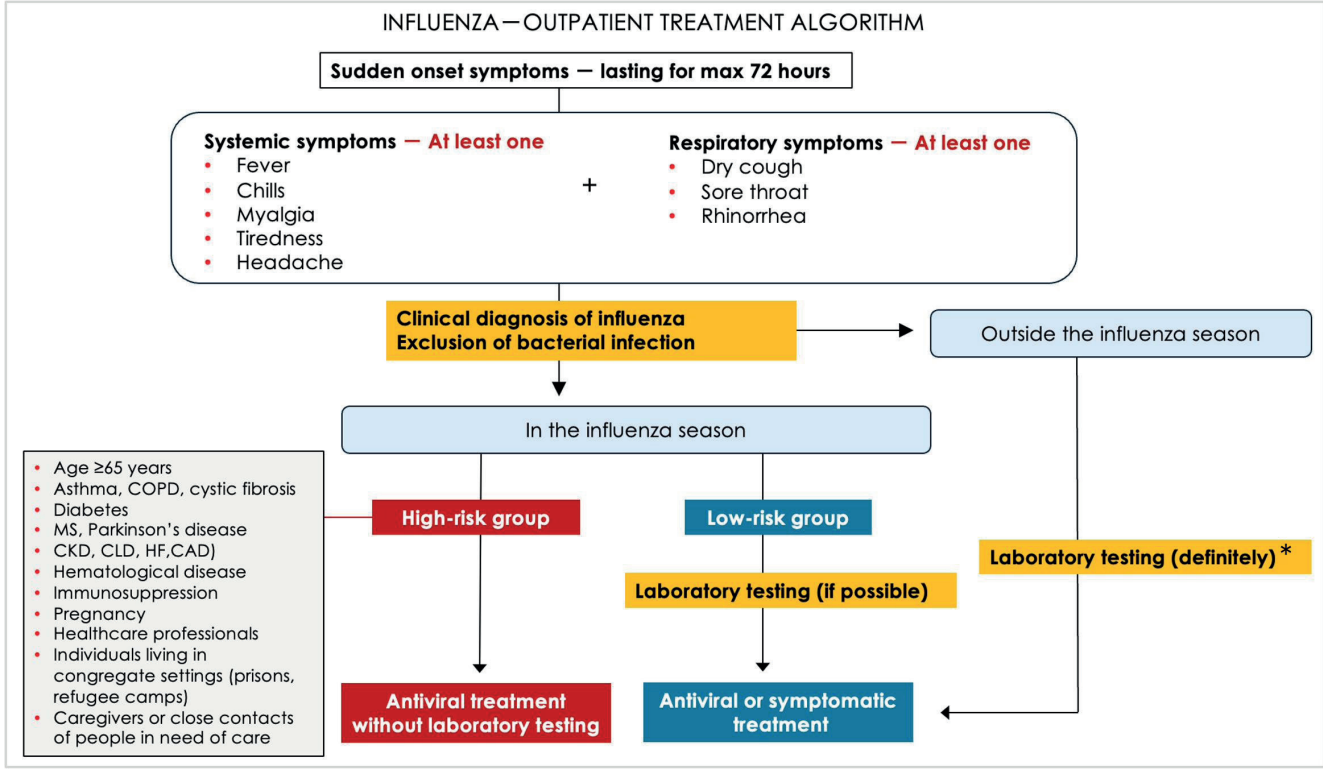


Figure 4. Treatment algorithm in influenza outpatients.

*In patients with severe or progressive illness or those at high risk of influenza-related complications, empiric antiviral treatment should not be delayed while awaiting laboratory confirmation, even outside the typical influenza season, when influenza is clinically suspected.

Table 6. Influenza antivirals available in Türkiye.

	Treatment dose	Prophylaxis dose	Pros	Cons
Oseltamivir (oral suspension/ capsule)	75 mg 2x1 5 days	75 mg 1x1 10 days	• Disease duration↓ • Antibiotics use↓ • LRTI risk↓ • Hospitalization↓ • Bioavailability↑	• Nausea/vomiting • Creatinine clearance ↓[a] • Dose adjustment in dialysis patients [b] • Low effectiveness for Influenza B
Baloxavir (oral suspension/ capsule)	Single dose <80 kg 40 mg ≥80 kg 80 mg	Post-exposure prophylaxis, same as the treatment dose: single dose	• Disease duration↓ • Antibiotics use↓ • Hospitalization↓ • Rapid decline in virus concentration • More effective than oseltamivir in Influenza B	• Similar complication risk with oseltamivir • Not recommended in pregnancy • Not recommended as monotherapy in severe immune deficiency

LRTI: Lower respiratory tract infection
[a] cFor creatinine clearance 31–60 mL/min: 30 mg twice daily for treatment and 30 mg once daily for prophylaxis. For creatinine clearance 11–30 mL/min: 30 mg once daily for treatment and 30 mg every other day for prophylaxis.
[b] in hemodialysis patients: 30 mg (prophylaxis) after every two dialysis sessions and 30 mg (treatment) after each session; in peritoneal dialysis patients: 30 mg (prophylaxis) or 30 mg (treatment) once weekly

Table 7. Referral criteria for adult influenza patients.

Signs of complication development
• Dyspnea, difficulty breathing
• Change in vital signs (hypotension, increased respiratory rate, increased pulse)
• Change in mental status (confusion, agitation, lethargy)
• Signs of severe dehydration or shock
• Development of secondary infection (Bacterial pneumonia, myocarditis, encephalitis)
Non-response to treatment and worsening/prolonged clinical course particularly in the high-risk groups
• Persistent refractory fever (>38°C) lasting for more than 72 hours
• Relapsing fever and severe cough or development of earache after symptom resolution
• Progressive deterioration of general status
• Progressive cough and weakness despite resting and treatment support
• Worsening of underlying chronic disease

Referral criteria

In adult influenza cases, referral criteria for further investigation and treatment include development of severe complications, no improvement in clinical status despite appropriate treatment and follow-up, emergence of hospitalization need and presence of immunosuppression (Table 7).[27,28]

Strategies for prevention and control of adult influenza

1. Antiviral chemoprophylaxis

Chemoprophylaxis should be started within the first 48 hours after exposure.

Oral oseltamivir, single dose baloxavir and inhaled zanamivir are effective in post-exposure chemoprophylaxis for both influenza A and B viruses, each reducing the risk of symptomatic infection by 60-85% (Table 6).[2,23,24]

Post-exposure should be given in recommended doses provided in Table 6.[3] Chemoprophylaxis should be started promptly, within the first 48 hours after exposure, for the maximum benefit.[20]

During an epidemic, pre-exposure chemoprophylaxis can be applied simultaneously with inactive vaccine, in unvaccinated high-risk individuals and healthcare professionals. Alternatively, but rarely, if vaccine is not available or contraindicated, or the patient is immunosuppressed, chemoprophylaxis can be continued during the course of the epidemic. In immunosuppressed hosts, post-exposure prophylaxis should be based on therapeutic doses.[2,3,20] To prevent the development of resistance, the United States Centers for Disease Control and Prevention (CDC) advises against the routine or widespread use of antivirals for chemoprophylaxis.[29]

2. Contact precautions and personal preventive measures

Contact precautions and personal preventive measures involve the disinfection methods for limiting transmission of disease from infected patients or exposed individuals as well as for personal protection (Figure 5).[12,20]

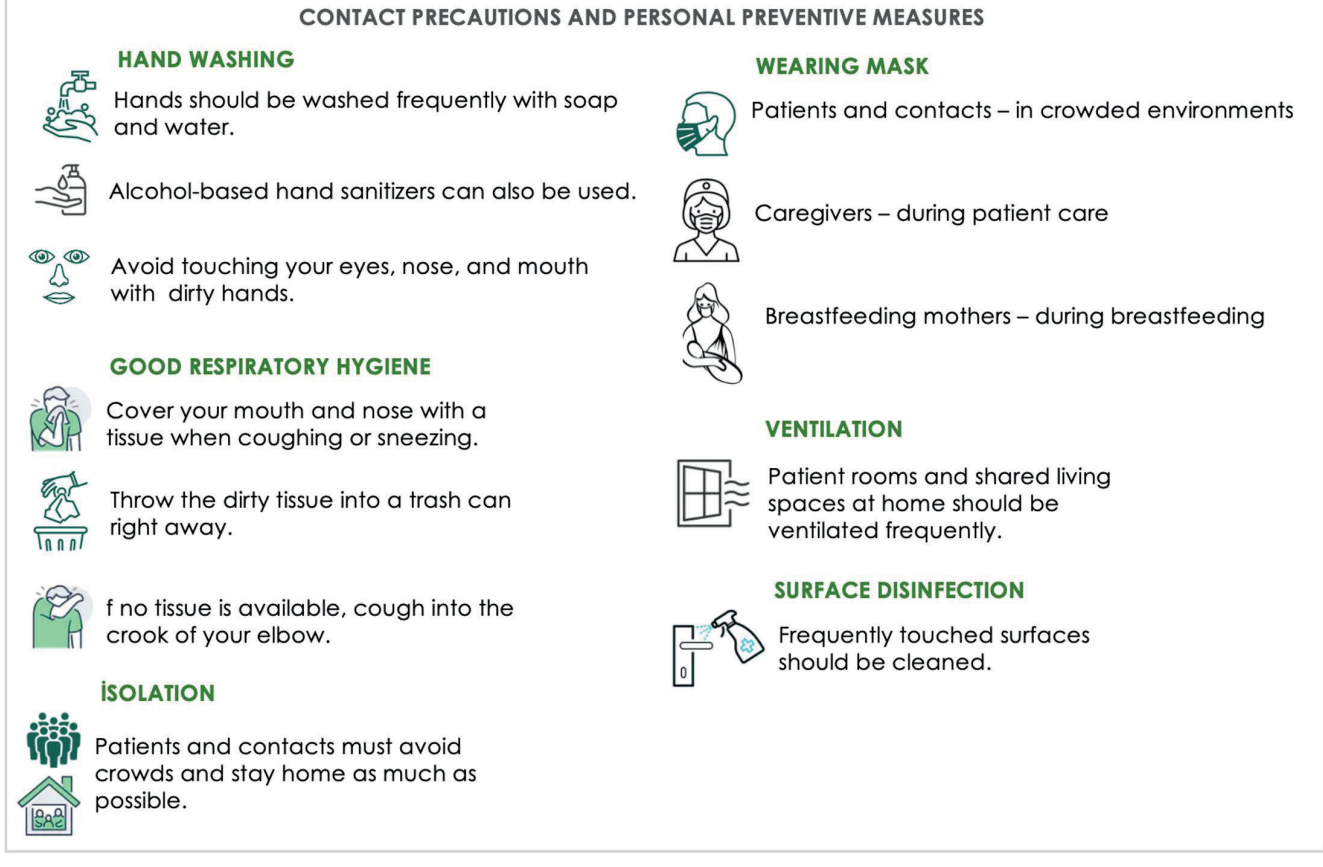


Figure 5. Contact precautions and personal preventive measures.

3. Vaccination

a) Indications and primary target groups

Influenza ranks first among vaccine-preventable diseases as millions of people are affected by seasonal epidemics.[4] Annual vaccination is considered the primary approach for preventing not only the influenza infection but also its severe complications. Therefore, vaccination is particularly important in the high-risk groups. According to the World Health Organization (WHO), key high-risk groups prioritized for seasonal influenza vaccination include pregnant women, older adults, immunocompromised individuals and those with chronic medical conditions, as well as the healthcare professionals.[1,5-7]

While annual influenza vaccination is recommended for almost everyone aged 6 months and older, individuals at high risk of influenza complications are defined as the priority group, enabling implementation of national immunization plans tailored to unique context of each country (Table 4).[1,3,4-7]

b) Optimal timing of vaccination

Vaccination can be performed throughout the influenza season (Early October - Late March).

Timing of vaccination is important for the effectiveness of vaccine and determined by country-specific surveillance data. Türkiye 2025 Surveillance data indicate shift of influenza season to later months with respect to its onset (Late December – Early January) , peak (Late January – Mid-February) and end (Mid-April).[4]

Vaccines administered too early may lose their effectiveness by the time the seasonal flu begins, particularly in elderly people. For this reason, administration of vaccination too early should generally be avoided.[4]

Protective effect of the vaccine begins 1–2 weeks after administration, and protection lasts for 6–8 months or longer in healthy adults. Therefore, vaccination should ideally be offered during autumn months the preceding viral spread, while the vaccination can be performed throughout the influenza season (Early October - Late March).[4,30-32]

c) Recommended vaccine type

Quadrivalent influenza vaccines, implemented since the 2013-2014 season, traditionally contain antigens for two influenza A subtypes (A/H1N1 and A/H3N2) and two influenza B lineages (B/Victoria and B/Yamagata). However, because the B/Yamagata virus strain is no longer circulating in humans since March 2020, many countries and manufacturers have established regulatory frameworks to adopt and manufacture trivalent vaccines, in accordance with the WHO recommendations regarding use of trivalent (A/H3N2, A/H1N1 and B/Victoria) vaccine formulations as of the 2024–2025 influenza season.[31,33] Accordingly, the use of trivalent vaccines is now recognized as the standard of care by the WHO and global health authorities due to their effectiveness, safety, and ability to target current strains.[31,33,34]

Each year, as part of WHO global Influenza Program, viruses from October to April are evaluated in the Northern Hemisphere and those from April and September in the Southern Hemisphere to identify composition of vaccines for the upcoming season, which is announced in February (Northern Hemisphere) and September (Southern Hemisphere).[20,34]

d) Contraindications and side effects

Influenza vaccine is contraindicated for adults with a history of a severe allergic reaction, such as anaphylaxis, to any specific component of that vaccine or a previous dose.

Egg allergy is not a contraindication to influenza vaccination. The Centers for Disease Control and Prevention (CDC) and the Advisory Committee on Immunization Practices (ACIP) state that, beginning with the 2023–2024 influenza season, individuals aged ≥6 months with egg allergy may receive any influenza vaccine (egg-based or non-egg-based) that is appropriate for their age and health status, regardless of the severity of their egg allergy. No additional safety measures are required for individuals with egg allergy beyond the standard precautions recommended for all vaccine recipients.[35]

The side effects of influenza vaccines are mostly mild and temporary, including pain and tenderness at the injection site for less than 2 days as the most common side effect in adults with a prevalence of 10-64%. The rates of vaccination-related fever, headache, myalgia, and weakness are similar to those of the placebo. Serious events like Guillain–Barré syndrome (GBS) are very rare, while influenza itself is associated with a 4 to 7 times greater risk of GBS than the vaccine. Additionally, the trivalent influenza vaccine is inactivated and cannot cause influenza infection.

e) Administering influenza vaccines alongside other vaccines

Influenza vaccines may be co-administered on the same day with all other vaccines, including COVID-19 and pneumococcal vaccines. Influenza vaccines can be administered on the same day as other vaccines, using separate anatomical injection sites.

Importance of vaccination in high-risk groups

Annual influenza vaccination is essential in all high-risk group individuals to avoid morbidity and mortality.[3]

1. Effects of annual influenza vaccination in high-risk groups

Vaccination in high-risk groups:
↓ development of influenza infection
↓ complications, hospitalization and mortality
↓ worsening of underlying comorbidity

Rationale and clinical outcomes of annual influenza vaccination in high-risk groups (advanced age, diabetes, COPD, cardiovascular disease, chronic kidney disease, pregnancy) are summarized in Table 8.[7,20,21,25,30,36-49]

In acute myocardial infarction patients, early-season influenza vaccination was reported to be more advantageous than late-season vaccination in terms of all-cause mortality reduction, while two modalities had similar effectiveness in terms of myocardial infarction and stent thrombosis.[50] In heart failure patients, repeated vaccination and vaccination earlier in the year were reported to be more effective in reducing mortality risk when compared to intermittent and late-season vaccination.[51]

Dual influenza and pneumococcal vaccination is considered more effective in cardiovascular risk (stroke, congestive heart failure, ischemic heart disease and myocardial infarction) reduction.[44]

2. Guideline recommendations

Current national and international guidelines recommend annual influenza vaccine in high-risk groups.[7,32,45,49,52-59]

Table 8. Rationale and clinical outcomes of annual influenza vaccination in high-risk groups.[7,20,21,25, 30,36-49]

	Annual Influenza Vaccination	
	Rationale	**Clinical outcomes**
Age ≥ 65 years	• Co-occurrence of multiple risk factors • Comorbidity burden • Immunosenescence • Functional losses [36,37]	• Infection risk↓ • Influenza-related hospitalization and mortality risk↓ • Cardiovascular complication risk↓ • Functional deterioration↓ [7,38]
Diabetes	• Chronic hyperglycemia-related immune dysfunction • Association of glycemic variation and suboptimal glycemic control with hospitalization and mortality [25,39]	• Infection risk↓ • Risk of hospitalization for influenza and diabetes↓ • All-cause mortality↓ • Risk of cardiovascular event and mortality↓ [40,41]
COPD	• Influenza virus as a major driver of COPD exacerbations [42]	• Infection risk↓ • Frequency and severity of exacerbations↓ • Secondary pneumonia↓ • Hospitalization risk↓ • Mortality risk↓ [7,42]
CVD	Influenza infection causes • Plaque destabilization (direct vascular effect) • Myocardial inflammation (indirect effect) • Activation of local/systemic proinflammatory and prothrombotic pathways [21,43]	• Infection risk↓ • Cardiovascular complication risk↓ • Cardiovascular event risk↓ (particularly at age ≥ 65 years) • MACE↓ • Myocardial infarction risk↓ • Ischemic heart disease risk↓ • Stroke risk↓ • Improved prognosis and reduced hospitalization and mortality in HF patients [30,43-45]
CKD	• Pre-existing immune dysfunction • Ongoing immunosuppressive treatment [46]	• Infection risk↓ • Secondary bacterial pneumonia↓ • Hospitalization risk↓ • Cardiovascular event risk↓ • Mortality↓ [20,46,47]
Pregnancy	• Susceptibility to infection/complication due to adaptive changes in immune, respiratory and circulatory systems • Viral pathogen response↓ • Lung capacity↓ [20,48-49]	• Complication risk↓ • Mortality risk↓ [7]

CKD: Chronic kidney disease; COPD: Chronic obstructive lung disease; CVD Cardiovascular disease; HF: Heart failure; MACE: Major adverse cardiac events.

Conclusion

Influenza is a disease that can lead to severe illness, complications and death in high-risk adult groups. Annual vaccination, as a highly cost-effective public health tool, represents the most effective approach for preventing disease and related complications. Annual influenza vaccination is essential to avoid hospitalization and mortality in all high-risk individuals. This multidisciplinary consensus report seems to provide primary care physicians with a practical guidance document in this regard.

Ethical approval

This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

Author contribution

The authors declare contribution to the paper as follows: Study conception and design: GZÖ, MT, MA, HA, TT; data collection: GZÖ, MT, MA, HA, TT; analysis and interpretation of results: GZÖ, MT, MA, HA, TT; draft manuscript preparation: GZÖ, MT, MA, HA, TT. All authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest to disclose.

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