



## Influenza 2025 Review: Antigenic Trends, Vaccine Impact, and Public Health Challenges

Samira Bashirian<sup>1</sup>, Shahabaddin Sorouri<sup>2</sup>, Mohammad Vahedian-Shahroodi<sup>3</sup>, \*Mohammad Eslamian<sup>4</sup>

<sup>1</sup>MSN, Instructor, Department of Nursing, Faculty of Nursing and Midwifery, Bojnourd Branch, Islamic Azad University, Bojnourd, Iran. <sup>2</sup>Assistant Professor of Pulmonology, Faculty of Medicine, Lung Disease Research Center, Mashhad University of Medical Sciences, Mashhad, Iran. <sup>3</sup>Professor, Department of Health Education and Health Promotion, School of Health, Mashhad University of Medical Sciences, Mashhad, Iran. <sup>4</sup>Department of Neurosurgery, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran.

### Abstract

**Background:** The 2025 influenza season is characterized by antigenic stability in major seasonal strains and the emergence of novel avian influenza variants. This review synthesizes current evidence on the epidemiology, virology, vaccine effectiveness, and public health challenges for both seasonal and avian influenza in 2025.

**Materials and Methods:** A narrative review was conducted using literature from PubMed, Scopus, Web of Science, WHO, CDC, and Google Scholar up to March 2025. Included studies were original research, systematic reviews, surveillance reports, and official guidelines on circulating strains, vaccine effectiveness, emerging variants, and interventions. Two reviewers independently screened and selected studies, extracting data on virus subtypes, vaccine composition, surveillance updates, and public health measures.

**Results:** A/H1N1pdm09 and B-Victoria lineages remained antigenically stable, supporting continued vaccine effectiveness, while A/H3N2 continued to drift, necessitating annual vaccine updates. The B/Yamagata lineage was undetected, prompting a transition to trivalent vaccines for 2025–2026. Emerging avian influenza variants, notably H10N3 and H5N1, highlighted ongoing zoonotic risks, but sustained human-to-human transmission was not observed. For the 2024–2025 season, vaccine effectiveness ranged from 36–54% in adults and reduced pediatric hospitalizations by 63–78%. Enhanced surveillance, including real-time genetic tracking and multidisciplinary analyses, improved outbreak detection, but challenges persisted in vaccine strain selection, production timelines, and equitable distribution.

**Conclusion:** The 2025 influenza season demonstrates the challenge of maintaining vaccine effectiveness amid stable strains and emerging avian variants. Vigilant surveillance, adaptive vaccine strategies, and coordinated public health responses remain essential. The shift to trivalent vaccines and adoption of advanced surveillance tools emphasize the ongoing need for innovation and equity in influenza control.

**Key Words:** Challenges, Emerging variants, Influenza 2025, Seasonal influenza.

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### \*Corresponding Author:

Mohammad Eslamian, MD, Department of Neurosurgery, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran.

Email: [md.eslamian@gmail.com](mailto:md.eslamian@gmail.com)

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## 1- INTRODUCTION

Influenza remains a persistent and evolving threat to global public health, causing annual epidemics that result in significant morbidity, mortality, and economic burden worldwide (1, 2). The 2025 influenza season is unfolding within a landscape shaped by both scientific progress and emerging challenges. On one hand, key seasonal influenza strains such as A/H1N1pdm09 and B-Victoria continue to exhibit antigenic stability, supporting the effectiveness of current vaccines (3, 4).

On the other hand, ongoing antigenic drift in A/H3N2 and the emergence of avian influenza variants—including H10N3 and surging H5N1 subclades—underscore the unpredictable nature of influenza evolution and the need for vigilant surveillance (5-7). Recent advances in vaccine technology, real-time genetic surveillance, and multidisciplinary approaches have enhanced our ability to track and respond to both circulating and emerging strains (8, 9). However, challenges remain, including the complexity of timely vaccine strain selection, the risk of zoonotic spillover, and persistent inequities in vaccine manufacturing and distribution (10, 11).

Additionally, the COVID-19 pandemic has further complicated influenza epidemiology and public health preparedness, highlighting the interconnectedness of respiratory pathogens and the importance of integrated surveillance systems (12, 13).

This review aims to provide a comprehensive synthesis of recent evidence on the epidemiology, virology, vaccine effectiveness, and public health challenges of the 2025 influenza season, with a focus on both seasonal and emerging avian influenza strains.

## 2- MATERIALS AND METHODS

This review was designed to provide a comprehensive and up-to-date synthesis of

the virology, epidemiology, vaccine effectiveness, and public health challenges associated with the 2025 influenza season, with a particular focus on both seasonal and emerging avian influenza strains.

### 2-1. Data Sources and Search Strategy

A literature review was conducted across multiple databases and authoritative sources, including PubMed, Scopus, Web of Science, and the World Health Organization (WHO), the Centers for Disease Control and Prevention (CDC), and Google Scholar. The search covered publications up to March 2025. The following keywords and MeSH terms were used: “influenza 2025,” “seasonal influenza,” “avian influenza,” “antigenic drift,” “vaccine effectiveness,” “influenza surveillance,” “H1N1,” “H3N2,” “H5N1,” “H10N3,” “vaccine strain selection,” and “pandemic preparedness”.

### 2-2. Study Selection and Review Process

The literature search and article selection were performed independently by two reviewers. Titles and abstracts were screened for relevance, and full texts were retrieved for studies meeting the inclusion criteria. Discrepancies or disagreements regarding inclusion or data extraction were resolved through discussion until consensus was reached.

### 2-3. Inclusion and Exclusion Criteria

#### 2-3-1. Inclusion Criteria:

- Types of Publications: Original research articles, systematic reviews, meta-analyses, surveillance reports, and official guidelines.
- Languages: Publications in English or Persian.
- Content Focus: Studies reporting on circulating influenza strains, vaccine composition and effectiveness, emerging zoonotic variants, and public health interventions relevant to the

2024–2025 and 2025–2026 influenza seasons.

### 2-3-2. Exclusion Criteria:

- Studies focused solely on animal models without direct relevance to human health.
- Non-peer-reviewed sources, such as preprints, opinion pieces, or unpublished data.

### 2-4. Data Extraction and Synthesis

Key data extracted from eligible studies included:

- Circulating influenza virus subtypes and genetic lineages
- Vaccine composition and effectiveness
- Reports of emerging avian influenza variants
- Updates and challenges in surveillance systems
- Factors influencing viral evolution and pandemic risk
- Public health response strategies and relevant legal frameworks.

Data were synthesized narratively, and the strengths and limitations of the available evidence were critically appraised to ensure a balanced interpretation of the findings (14).

### 2-5. Ethical Consideration

As this article is a narrative review based solely on previously published data and publicly available reports, no new human or animal subjects were involved, and no ethical approval was required. All sources of information are appropriately cited, and the review adheres to ethical standards for research integrity and transparency in scientific reporting.

## 3- RESULTS

The 2025 influenza season is marked by both the antigenic stability of major seasonal strains and the emergence of

novel avian influenza variants, highlighting the ongoing need for robust global surveillance and adaptive public health strategies (3–7). This dual dynamic means that while current vaccines remain effective for certain established lineages, new zoonotic threats-particularly from avian influenza-continue to pose significant challenges for monitoring, vaccine formulation, and pandemic preparedness (3–7).

### 3-1. Antigenic Stability & Vaccine Updates

A/H1N1pdm09 remains antigenically stable, with circulating viruses closely matching the A/Victoria/4897/2022-like vaccine strain. Although hemagglutinin (HA) mutations such as S91R and S181T have been detected, post-vaccination geometric mean titres (GMTs) against recent variants show no significant reduction in immunity, though gradual immune escape remains a concern (3).

A/H3N2 continues to exhibit antigenic drift, necessitating annual vaccine updates. For 2025–2026:

- Egg-based vaccines: A/Croatia/10136RV/2023-like virus.
- Cell- and recombinant-based vaccines: A/District of Columbia/27/2023-like virus (4, 15).

The B-Victoria lineage remains stable, with the AU21 cluster predominant, supporting continued use of the B/Austria/1359417/2021-like virus in vaccines (3, 4). The B/Yamagata lineage has not circulated since 2020, prompting a shift to trivalent vaccines and necessitating changes in production pipelines and clinical protocols (16).

### 3-2. Emerging Variants of Concern

- **3-2-1. Avian Influenza H10N3:** Four human cases have been reported in China between 2021 and January 2025, all linked to exposure to live poultry.

No sustained human-to-human transmission has been documented, but continued circulation in poultry poses ongoing zoonotic risks and underscores the importance of integrated animal-human surveillance (3, 5, 17).

- **3-2-2. Avian Influenza H5N1:** Outbreaks persist in wild birds and domestic poultry, particularly in Cambodia and across Europe and the Americas, with high pathogenicity maintaining pandemic potential. Human cases remain rare and are primarily associated with direct animal exposure. Notably, H5N1 demonstrates high reassortment potential with human H3N2 viruses in vitro, raising concerns about the emergence of novel pandemic strains (2, 3, 6, 7).

### 3-3. Vaccine Effectiveness

For the 2024–2025 season, vaccine effectiveness (VE) varied by age and setting:

- **Adults:** 36–54% outpatient protection, though one study reported negative VE (-26.9%) in working-aged adults (18).
- **Children:** 63–78% reduction in hospitalization risk. European studies aligned with U.S. findings, showing 32–56% VE against influenza A (19, 20).

### 3-4. Surveillance & Preparedness

The expanded WHO Global Influenza Surveillance and Response System (GISRS) now integrates:

- Real-time HA mutation tracking via platforms like Nextstrain (8).
- Multidisciplinary analyses, including genetic sequencing, HA protein modeling, and antigenic cartography (21).
- Enhanced monitoring of SARS-CoV-2 and RSV alongside influenza (9, 22).

Digital tools and artificial intelligence, including centralized platforms like RespiMart, are increasingly used for real-time respiratory virus surveillance, outbreak detection, and prediction, supporting rapid and coordinated responses (23, 24).

### 3-5. Key Challenges

#### 3-5-1. Antigenic Drift and Vaccine Strain Selection:

- **H3N2 Evolution:** Ongoing antigenic drift necessitates frequent vaccine updates. The 2025–2026 vaccines have adopted new strains to address reduced reactivity.
- **H1N1 Stability:** While relatively stable, mutations such as S91R and S181T could gradually enable immune escape (3).

#### 3-5-2. Vaccine Production Timelines & Equity:

- Strain selection must occur 6–8 months before the flu season, creating vulnerabilities to late-emerging variants (11).
- Only 15% of the global population resides in countries with vaccine manufacturing capacity, exacerbating distribution inequities (10).

#### 3-5-3. Transition to Trivalent Vaccines:

- The absence of the B/Yamagata lineage has prompted a shift to trivalent vaccines, requiring reconfiguration of production and clinical protocols (3).

#### 3-5-4. Avian Influenza Reassortment Risks:

- **H5N1:** Demonstrates high reassortment potential with human H3N2 viruses, posing pandemic risks (25).
- **H10N3:** Recent human cases in China highlight zoonotic transmission risks from poultry, though sustained human-

to-human spread remains unobserved (5).

### **3-5-5. Next-Generation Vaccine Development:**

- Universal vaccine strategies targeting conserved HA regions face technical and regulatory hurdles, as well as public acceptance challenges (11, 26).

### **3-5-6. Surveillance & Adaptive Capacity:**

- GISRS now tracks HA mutations in real time but faces challenges integrating data across influenza, SARS-CoV-2, and RSV (9, 22).

### **3-6. Drivers of New Strain Emergence**

- Genetic Diversity & Viral Evolution: Antigenic drift (point mutations) and shift (reassortment) enable rapid adaptation and immune evasion, particularly when avian strains are involved (27-29).
- Environmental & Epidemiological Factors: Seasonal transmission is enhanced by cold, dry conditions, population density, travel, and healthcare infrastructure. The co-circulation of multiple strains increases the risk of reassortment (29, 30).
- Surveillance & Vaccine Challenges: Rapid mutation of HA and NA complicates vaccine strain selection and effectiveness. Limited global manufacturing capacity restricts access, especially in low-resource countries (10, 31).
- Phenotypic Factors: HA stability in different pH environments affects viral infectivity and transmission potential (28).

### **3-7. Public Health Monitoring and Response**

Maintaining effective surveillance systems requires significant infrastructure and trained personnel, which is particularly

challenging in resource-limited settings (5, 7). The COVID-19 pandemic disrupted influenza virus circulation and complicated vaccine effectiveness assessments and planning (15, 32). Public health emergency declarations can accelerate resource mobilization but are often reactive, highlighting the need for proactive planning and coordinated emergency management (33, 34). Transitioning from quadrivalent to trivalent vaccines, due to the disappearance of the B/Yamagata lineage, also requires careful management to avoid disruptions in vaccination efforts (4).

## **4- DISCUSSION**

The 2025 influenza season demonstrates both encouraging advances and persistent challenges in global influenza control, as revealed by recent surveillance and research (3–7). The antigenic stability of A/H1N1pdm09 and B-Victoria has sustained vaccine effectiveness, with circulating strains closely matching the A/Victoria/4897/2022-like and B/Austria/1359417/2021-like vaccine strains, respectively (3, 4). Despite the detection of HA mutations such as S91R and S181T in A/H1N1pdm09, no significant reduction in immunity has been observed, although ongoing molecular monitoring is warranted (3).

In contrast, A/H3N2 continues to undergo rapid antigenic drift, necessitating frequent vaccine updates, as reflected in the adoption of A/Croatia/10136RV/2023-like and A/District of Columbia/27/2023-like viruses for the 2025–2026 season (4, 15). The disappearance of the B/Yamagata lineage since 2020 has prompted a transition to trivalent vaccines, requiring adjustments in production and clinical protocols (6, 8, 16).

Emerging avian influenza variants, notably H10N3 and H5N1, underscore the ongoing risk of zoonotic spillover. Four human

H10N3 cases have been reported in China, all associated with exposure to live poultry, and continued H5N1 outbreaks in Cambodia and other regions further highlight the necessity of integrated animal-human surveillance and a robust One Health approach (5, 6, 17). While sustained human-to-human transmission has not been observed for either virus, the high reassortment potential of H5N1 with human H3N2 viruses in vitro raises concerns about future pandemic threats (25).

Vaccine effectiveness for the 2024–2025 season ranged from 36–54% in adults and was associated with a 63–78% reduction in pediatric hospitalizations (18–20, 35). However, the emergence of oseltamivir-resistant A/H1N1pdm09 strains (~2.4%) and persistent inequities in vaccine access underscore the need for continued investment in antiviral stewardship and manufacturing capacity (10, 11, 18).

The expansion of the WHO Global Influenza Surveillance and Response System (GISRS), the implementation of real-time HA mutation tracking (e.g., via Nextstrain), and multidisciplinary analyses—including centralized platforms like RespiMart—have enhanced respiratory virus surveillance, outbreak detection, and response capabilities (8, 9, 21, 23). The integration of digital tools and artificial intelligence further supports rapid outbreak identification; however, challenges persist in harmonizing data across influenza, SARS-CoV-2, and RSV, as well as in ensuring timely vaccine strain selection (22, 23, 31).

Looking ahead, strengthening real-time genetic surveillance, investing in next-generation and universal vaccines, and fostering international collaboration are essential (8, 9, 21, 26). Addressing production bottlenecks and ensuring equitable access to vaccines and antivirals will be vital for effective influenza prevention and pandemic preparedness

(10, 11, 31). Future research should prioritize understanding viral evolution, reassortment mechanisms, and vaccine durability, while policymakers must emphasize flexible response systems and global cooperation. Ultimately, sustained innovation, a One Health perspective, and a commitment to global equity are key to mitigating both seasonal and emerging influenza threats (12, 24, 29, 36).

#### **4-1. Study Limitations**

As a narrative review, this article may be subject to selection bias and does not include a formal quantitative meta-analysis. However, every effort was made to include the most current, high-quality, and globally relevant evidence available up to May 2025.

#### **5- CONCLUSION**

The 2025 influenza season underscores the ongoing complexity of influenza control, marked by antigenic stability in A/H1N1pdm09 and B-Victoria, rapid drift in A/H3N2, and persistent zoonotic threats from H10N3 and H5N1 variants. While vaccines demonstrated 36–54% effectiveness in adults and substantial reductions in pediatric hospitalizations, HA mutations, oseltamivir resistance, and frequent strain updates highlight the need for adaptive strategies and robust surveillance. The shift to trivalent formulations and expanded GISRS platforms—including RespiMart for integrated respiratory virus monitoring—exemplify progress amid evolving challenges.

Looking ahead, priorities include next-generation vaccines, enhanced global manufacturing, and advanced surveillance integrating real-time genetic tracking with AI-driven outbreak prediction. Equitable access, One Health integration, and international collaboration remain essential for mitigating seasonal epidemics and potential pandemics. Sustained innovation

and proactive planning will determine our resilience against future influenza threats

**6- CONFLICT OF INTEREST:** None.

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