115年流感疫苗教育訓練

流感病人之臨床處置

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Case-Based Approach

CASE 1

Outpatient Influenza

Diagnosis · Testing · Antiviral Treatment

CASE 2

Hospitalized Influenza Pneumonia

Initial Management · Severe Disease · Clinical Deterioration

Guideline basis: TSID 2024 · Taiwan CDC 2026 · U.S. CDC 2026 · IDSA 2018

Case 1: Outpatient Influenza

34-year-old woman, previously healthy

Fever 39.0°C · headache · marked myalgia · dry cough

Symptom onset: 30 hours ago

Influenza vaccination received this season

Several coworkers with similar febrile respiratory illness

T 39.0°C · HR 96/min · RR 18/min · SpO_2 98% on room air

No respiratory distress · Lungs clear

> Is influenza testing necessary?

When Should Influenza Enter the Differential?

> “Abrupt onset of fever with cough is most predictive of uncomplicated influenza in adult outpatients, with a sensitivity of >70% during the influenza season.”
>
> IDSA Seasonal Influenza Guideline — Evidence Summary

Clinical Interpretation:

> Abrupt onset

> Fever

> Cough

> Active community influenza circulation

→ Raises the clinical probability of influenza

Important Limitation: Fever and cough are common across respiratory infections. This clinical pattern should trigger suspicion, but does not reliably confirm influenza.

Evidence Note: This statement is derived from the IDSA evidence summary and is not a separately graded recommendation.

Reference: Uyeki TM, et al. Clin Infect Dis. 2019;68:e1–e47. IDSA 2018 Seasonal Influenza Guideline.

Is Laboratory Confirmation Required?

No. Laboratory confirmation is not required for every outpatient with suspected influenza.

CDC 2025 Guidance:

- Clinical diagnosis may be sufficient when influenza is circulating in the community.
- Antiviral treatment decisions do not require laboratory confirmation.

IDSA 2018 Guideline:

In non-high-risk outpatients, influenza testing may be considered when the result is expected to influence clinical management. (C-III)

What may change with the test result?

Antiviral therapy · Antibiotic use · Further diagnostic testing · Management of high-risk contacts

Clinical implication: Test when knowing the result is expected to change what you do next.

Clinical Utility of Influenza Testing

Influenza testing has clinical utility when a positive or negative result would lead to a different next step.

Scenario 1: Antiviral Treatment

In a low-risk outpatient where the treatment decision remains uncertain:

- → **Positive result:** Antiviral treatment favored
- → **Negative result:** Supportive care favored

Scenario 2: Further Evaluation / Antibiotic Use

For febrile respiratory illness with diagnostic uncertainty:

- → **Positive molecular test:** May reduce unnecessary additional testing or antibiotics
- → **Negative result:** Pursue alternative diagnoses when clinically appropriate

Scenario 3: High-Risk Household Contact

When a patient lives with a severely immunocompromised household member:

- → **Confirmed influenza:** May influence post-exposure prophylaxis or early treatment planning for the contact

Guideline Note: IDSA 2018: Influenza testing may be considered in non-high-risk outpatients when the result is expected to influence management. (C-III)

IDSA Seasonal Influenza Guideline, 2018 · CDC Influenza Testing Guidance, 2025

If We Test, Which Test Should We Use?

Guideline recommendation: Rapid molecular assays are preferred over rapid influenza diagnostic tests in outpatients. IDSA 2018 — A-II

Rapid Antigen Test

- Detects viral antigen
- Turnaround: usually **＜15–30 min**
- Traditional RIDT sensitivity:
  - Influenza A: **54.4%**
  - Influenza B: **53.2%**
- Specificity: **＞98%**
- Main limitation: **false-negative** results

Molecular Assay / RT-PCR

- Detects viral RNA
- Rapid molecular assays may provide results within **15–30 min**
- Sensitivity: approximately **92–95%**
- Specificity: **＞98%**
- Preferred when reliable diagnostic confirmation is needed

Key interpretation: The major limitation of rapid antigen testing is **sensitivity**, not specificity.

Evidence:

- Merckx J, et al. Ann Intern Med. 2017;167:394–409.
- IDSA Seasonal Influenza Guideline. Clin Infect Dis. 2019;68:e1–e47.

Back to Case 1

34-year-old woman, previously healthy

Fever · headache · marked myalgia · dry cough

Symptom onset: 30 hours ago

Several coworkers with similar febrile respiratory illness

Rapid influenza antigen test

Negative

Would you still prescribe an antiviral?

Does This Patient Need Antiviral Treatment?

Here are the key guidelines to consider:

CDC 2026 Guidance

Antiviral treatment may be considered for otherwise healthy, non-high-risk outpatients when treatment can be started within 48 hours of illness onset.

No formal evidence grade provided

IDSA 2018 Guideline

Antiviral treatment can be considered in non-high-risk outpatients with documented or suspected influenza when illness onset is ≤2 days.

(C-I)

Clinical Interpretation: In uncomplicated, low-risk influenza, antiviral treatment is reasonable but not mandatory.

Reference: CDC Influenza Antiviral Medications: Summary for Clinicians, 2026 · IDSA Seasonal Influenza Guideline, 2018

What outcome are we trying to improve?

Dobson et al., Lancet 2015 · Individual patient data meta-analysis · 9 randomized trials · 4,328 adults

Symptom duration

97.5 h vs 122.7 h

-25.2 hours

Lower respiratory complications requiring antibiotics

4.9% vs 8.7%

RR 0.56

Hospital admission

0.6% vs 1.7%

RR 0.37

In otherwise healthy adults, the most consistent benefit is approximately 1 day shorter illness.

Nausea: 9.9% vs 6.2% · Vomiting: 8.0% vs 3.3%

Dobson J, et al. Lancet. 2015;385:1729–1737.

Which Antiviral Would You Choose?

Case Context: Otherwise healthy outpatient with uncomplicated suspected influenza. Symptom onset: 30 hours ago.

Given this patient, which antiviral would you choose?

- A. Oseltamivir 75 mg twice daily for 5 days
- B. Baloxavir, single oral dose
- C. Zanamivir, inhaled for 5 days
- D. Peramivir, single IV dose

How Should We Choose an Antiviral?

There is no universal winner for uncomplicated outpatient influenza.

	Oseltamivir	Baloxavir	Zanamivir	Peramivir
Route	Oral	Oral	Inhaled	IV
Course	5 days	Single dose	5 days	Single dose
Major practical advantage	Most clinical experience	Convenience / adherence	Alternative oral-free route	IV administration
Important consideration	Renal dose adjustment	Avoid in pregnancy; interaction with polyvalent cations	Avoid in asthma/COPD or poor inhalation technique	Renal dose adjustment; usually unnecessary for routine outpatient use

Selection should consider: Age · Pregnancy · Renal function · Airway disease · Route · Adherence · Patient preference

Guideline: CDC 2026 and TSID 2024 include oseltamivir, zanamivir, peramivir, and baloxavir as treatment options for appropriate patients with uncomplicated influenza.

CDC Influenza Antiviral Medications: Summary for Clinicians, 2026 · Taiwan Society of Infectious Diseases Anti-Influenza Recommendations, 2024

Baloxavir vs Oseltamivir: Is One Better?

CAPSTONE-1 — Hayden et al., NEJM 2018

Phase 3 randomized, double-blind trial in otherwise healthy adolescents and adults with uncomplicated influenza treated within 48 hours.

Clinical Outcome

Time to symptom alleviation:
Baloxavir: 53.7 h
Oseltamivir: 53.8 h
Placebo: 80.2 h

Clinical symptom relief was similar between baloxavir and oseltamivir.

Virologic Outcome

Baloxavir produced a more rapid decline in viral load and earlier cessation of infectious virus shedding than oseltamivir.

Practical Difference

Baloxavir: single oral dose
Oseltamivir: 75 mg twice daily for 5 days

Important Limitation

Treatment-emergent PA/I38 substitutions with reduced baloxavir susceptibility occurred in ~9.7% of baloxavir recipients.

Bottom Takeaway: Faster virologic response does not necessarily mean faster clinical recovery.

Hayden FG, et al. N Engl J Med. 2018;379:913–923.

Does Influenza Type Matter?

Study: CAPSTONE-2 — Ison et al., Lancet Infectious Diseases 2020. Phase 3 randomized, double-blind trial in high-risk outpatients with uncomplicated influenza treated within 48 hours.

Overall Clinical Outcome: Median Time to Improvement of Symptoms

- Baloxavir: **73.2 h**
- Oseltamivir: **81.0 h**
- Difference: **7.7 h**

Influenza B Subgroup:

Baloxavir shortened time to symptom improvement by approximately:

27 hours

compared with oseltamivir.

(95% CI: 6.9–42.3 h · p = 0.025)

Clinical Interpretation: Overall efficacy was similar, but baloxavir showed a clinically meaningful advantage in influenza B.

Guideline Context: CDC 2026 specifically notes greater symptom improvement with baloxavir than oseltamivir in influenza B.

Ison MG, et al. Lancet Infect Dis. 2020;20:1204–1214.

CDC Influenza Antiviral Medications: Summary for Clinicians, 2026.

What If She Presents on Day 3?

Same patient.

Same symptoms.

Symptom onset: 72 hours ago

Clinical question: Would you still prescribe an antiviral?

What If She Presents on Day 3?

IDSA 2018

Outpatients who are not at high risk of influenza complications … with illness onset ≤2 days before presentation

Recommendation: Antiviral treatment can be considered — C-I

CDC 2026

Clinical benefit is greatest when antiviral treatment is administered early, especially within 48 hours of illness onset.

- No available data for baloxavir in outpatients treated >2 days after illness onset
- Limited evidence suggests oseltamivir started at 72 hours may still shorten symptoms

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Clinical Takeaway

For this patient, routine benefit is less certain on Day 3.

Treatment may still be individualized, but the strongest evidence supports earlier therapy.

References:

Uyeki TM, et al. Clin Infect Dis. 2019;68:e1–e47.

CDC. Influenza Antiviral Medications: Summary for Clinicians. Updated 2026.

Pregnancy Changes the Treatment Threshold

IDSA 2018

Pregnant women and those within 2 weeks postpartum: start antiviral treatment as soon as possible — **A-III**

CDC 2025–2026 Obstetric Guidance

Pregnancy is a high-risk condition for influenza complications

Do not wait for laboratory confirmation before starting treatment

Treat suspected or confirmed influenza during any trimester

Continue this recommendation through 2 weeks postpartum

Preferred Antiviral

Oseltamivir 75 mg twice daily for 5 days

- Most clinical safety and outcome data in pregnancy
- Preferred treatment during pregnancy

Baloxavir

- Not recommended during pregnancy or breastfeeding because efficacy and safety data are insufficient

References:

Uyeki TM, et al. Clin Infect Dis. 2019;68:e1–e47.

CDC. Antiviral Treatment in Pregnancy and Postpartum. 2025–2026.

Case 1: Key Decisions in Outpatient Influenza

When to suspect influenza: **Acute onset + fever + cough**, interpreted in the context of **current influenza activity** and **epidemiologic exposure**.

Whether to test: Laboratory confirmation is **not required for every outpatient**. Test when the result is **expected to change clinical management**.

Which test to use: When testing is needed, **rapid molecular assays are preferred** over antigen-based RIDTs. A **negative antigen test does not reliably exclude** influenza.

Whether to treat: In otherwise healthy patients with uncomplicated influenza, antiviral treatment **within 48 hours** is **reasonable but not mandatory**.

Which antiviral to choose: Select therapy according to **age, pregnancy, renal function, airway disease, route, adherence, and patient preference**. **No antiviral is universally superior** for all outpatients.

When the threshold changes:

- **>48 hours:** routine benefit is less certain in low-risk uncomplicated disease.
- **Pregnancy / high-risk conditions:** treatment becomes recommended and should not wait for laboratory confirmation.

Guideline basis:

IDSA Seasonal Influenza Guideline, 2018 · TSID Anti-Influenza Recommendations, 2024 · CDC Influenza Guidance, 2025–2026

Case 2

68-year-old man

Medical history: Type 2 diabetes mellitus · CKD stage 3 · Coronary artery disease

Present illness: Fever, myalgia, and cough for **4 days**. Progressive dyspnea since yesterday.

On arrival to the emergency department:

T 39.1°C · BP 106/64 mmHg · HR 108/min · RR 30/min · SpO_2 **88% on room air**

Chest radiograph: **bilateral interstitial pulmonary infiltrates**

Rapid influenza antigen test performed at a local clinic: **Negative**

Would you start antiviral treatment now?

Day 4 + Negative Rapid Test: Too Late for Oseltamivir?

Answer: Treat now.

IDSA 2018 — Recommendation 18

"Hospitalized with influenza, regardless of illness duration prior to hospitalization"
Start antiviral treatment as soon as possible **— A-II**

CDC 2026

"Antiviral treatment is recommended as soon as possible" for hospitalized patients with suspected or confirmed influenza.

- Do not wait for laboratory confirmation before starting treatment
- Oral or enterically administered oseltamivir is recommended as soon as possible
- Clinical benefit may still occur when treatment is started >48 hours after illness onset

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Taiwan Society of Infectious Diseases 2024

Patients with suspected or confirmed influenza who require hospitalization should receive antiviral treatment immediately

- Once treatment is indicated, antiviral therapy should be given promptly without waiting for laboratory confirmation
- Benefit is greatest within 48 hours, but patients with more severe illness or hospitalization may still benefit when treatment begins after 48 hours

References:

- Uyeki TM, et al. Clin Infect Dis. 2019;68:e1–e47.
- CDC. Influenza Antiviral Medications: Summary for Clinicians. Updated March 2026.
- Taiwan Society of Infectious Diseases. Recommendations for the Use of Anti-Influenza Agents. 2024 revision.

Case 2: Clinical Deterioration

The following day:

Increasing oxygen requirement

HFNC → invasive mechanical ventilation

Nasopharyngeal influenza RT-PCR: Negative

Clinical question:

Can oseltamivir now be discontinued?

A Negative Upper Respiratory PCR Does Not End the Diagnosis

In severe lower respiratory tract disease, obtain a lower respiratory tract specimen.

IDSA 2018 — Recommendation 7

Hospitalized patients with respiratory failure receiving mechanical ventilation should have endotracheal aspirate or bronchoalveolar lavage fluid collected for influenza testing, including patients with negative upper respiratory tract testing.

A-II

CDC 2026

Hospitalized patients with lower respiratory tract disease may have prolonged influenza viral replication in the lower respiratory tract.

- If upper respiratory molecular testing is negative but influenza remains clinically suspected:
- Obtain a lower respiratory tract specimen
- In mechanically ventilated patients, send an endotracheal aspirate for RT-PCR
- Continue antiviral treatment while additional testing is pursued when influenza remains clinically suspected

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Why can this happen?

Upper respiratory viral shedding generally declines after approximately 3–4 days, while viral replication may persist longer in the lower respiratory tract in severe influenza.

In severe influenza pneumonia, specimen site matters.

References:

Uyeki TM, et al. Clin Infect Dis. 2019;68:e1–e47.

CDC. Molecular Assays for Diagnosis of Influenza Virus Infection. Updated 2026.

Which Antiviral Strategies Are Appropriate in Severe Influenza?

A. IV peramivir

B. Standard-dose oseltamivir

C. Double-dose oseltamivir

D. Standard-dose oseltamivir with a prolonged treatment course

E. Baloxavir monotherapy

F. Combination of two neuraminidase inhibitors (Oseltamivir + peramivir)

G. Oseltamivir + baloxavir

Does Critical Illness Require IV Antiviral Therapy?

Not routinely. Enteral oseltamivir remains preferred.

CDC Guidance

> "For hospitalized patients with suspected or confirmed influenza, oral or enterically administered oseltamivir is recommended as soon as possible."

Oseltamivir given orally or through an NG/OG tube is generally well absorbed in critically ill patients.

IV peramivir is not routinely recommended for hospitalized influenza because evidence for clinical benefit is insufficient.

Clinical Trial Evidence

de Jong et al., Clin Infect Dis 2014

- Hospitalized influenza
- IV peramivir 600 mg daily + standard care vs placebo + standard care
- Median time to clinical resolution: 42.5 h vs 49.5 h · **P = 0.97**
- Trial stopped early for futility; no significant clinical benefit demonstrated.

When might IV peramivir be considered?

- Enteral administration is not feasible.
- Gastrointestinal absorption is unreliable.

References:

- CDC. Influenza Antiviral Medications: Summary for Clinicians. 2026.
- de Jong MD, et al. Clin Infect Dis. 2014;59:e172–e185.

Does Severe Influenza Require Double-Dose Oseltamivir?

Routine double dosing is not supported.

CDC 2026

> "Available data suggest that higher dosing may not provide additional clinical benefit."

Standard-dose oral or enterically administered oseltamivir is generally adequately absorbed in critically ill adults.

Randomized Trial — Severe Influenza

South East Asia Infectious Disease Clinical Research Network, BMJ 2013

326 hospitalized patients with severe influenza

More oseltamivir did not produce better virologic or clinical outcomes:

Outcome	Standard Dose (75 mg BID)	Double Dose (150 mg BID)
Day 5 RT-PCR negative	68.2%	72.3% (P = 0.42)
Mortality	5.6%	7.3% (P = 0.54)

No significant differences in ICU stay, oxygen requirement, or mechanical ventilation duration.

References:

- South East Asia Infectious Disease Clinical Research Network. BMJ. 2013;346:f3039.
- CDC. Influenza Antiviral Medications: Summary for Clinicians. 2026.

Should Severe Influenza Be Treated Longer Than 5 Days?

Sometimes. Duration should be individualized in severe or prolonged illness.

CDC 2026

> "The optimal duration and dosing of antiviral treatment are uncertain for severe or complicated influenza."
>
> "Decisions about extended treatment should be guided by clinical judgment in patients whose illness is prolonged."

Additional guidance:

- Longer treatment may be considered in hospitalized patients who remain severely ill after 5 days
- Lower respiratory tract RT-PCR can help guide decisions about extended therapy
- Prolonged lower respiratory viral replication may occur in critically ill patients
- Longer courses may be particularly necessary in immunocompromised patients

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IDSA 2018 — Recommendation 23

Longer antiviral treatment may be considered in:

- Immunocompromised patients
- Hospitalized patients with severe lower respiratory tract disease, especially pneumonia or ARDS

C-III

In severe influenza, duration may change more often than dose.

References:

- CDC. Influenza Antiviral Medications: Summary for Clinicians. 2026.
- Uyeki TM, et al. Clin Infect Dis. 2019;68:e1–e47.

What Is the Clinical Evidence for IV Peramivir in Severe Influenza?

Hospitalized influenza studies used multi-day IV peramivir, but clear clinical superiority has not been established.

Study	Population	Peramivir regimen	Comparator	Key finding
Ison et al., Antiviral Therapy 2014	Hospitalized patients with influenza	**300 mg IV twice daily** or **600 mg IV once daily** for **5–10 days**	Comparison between the two peramivir regimens	Clinical and virologic outcomes were generally similar between the two dosing schedules.
de Jong et al., Clinical Infectious Diseases 2014	Hospitalized influenza	**600 mg IV once daily** for **5 days**	Placebo + standard care	Median time to clinical resolution: 42.5 h vs 49.5 h · P = 0.97 No significant clinical benefit demonstrated.

In hospitalized influenza, published IV peramivir studies:

- Used daily multi-day therapy, not the uncomplicated-outpatient single-dose approach.
- Showed 5-day therapy as the most consistent studied duration.
- Did not establish that intensified peramivir dosing or longer therapy improves survival.

> **Important limitation:** Overall evidence remains limited, and the optimal dose and duration for severe influenza are still uncertain.

References:

Ison MG, et al. Antivir Ther. 2014;19:349–361.

de Jong MD, et al. Clin Infect Dis. 2014;59:e172–e185.

How Do Current Guidelines Position IV Peramivir?

IV peramivir is not the routine preferred inpatient antiviral; it is an alternative when enteral oseltamivir is not feasible or absorption is unreliable.

CDC 2026

Preferred inpatient antiviral

- Oral or enterically administered **oseltamivir remains the recommended** antiviral for hospitalized influenza.
- **IV peramivir may be considered** when oral or enteric oseltamivir cannot be tolerated or absorbed.

Dose and duration

- Hospitalized-patient trials used daily dosing for a minimum of 5 days.
- Longer daily dosing may be considered if the patient remains severely ill after 5 days.

IDSA 2018

- Use a single neuraminidase inhibitor.
- **Do not routinely use higher doses.**
- If IV peramivir is used in hospitalized patients, use a **multiday regimen**.
- Longer duration can be considered in severe lower respiratory tract disease, especially pneumonia or ARDS.

Practical synthesis

When to think of IV peramivir

- No enteral access
- Suspected malabsorption
- Gastric stasis
- Gastrointestinal bleeding

How to use it if chosen

- Think daily therapy, not routine single-dose use.
- Do not escalate dose routinely.
- **Reassess at Day 5**. (Consider extension only if severe illness or ongoing viral replication persists.)

Does Oseltamivir + Peramivir Improve Severe Influenza Outcomes?

Zou et al., International Journal of Infectious Diseases 2020

Multicenter retrospective observational study of adults with influenza A-associated severe pneumonia.

Treatment groups

Antiviral strategy	n	60-day mortality
Oseltamivir	122	40.2%
Peramivir	40	37.5%
Oseltamivir + Peramivir	29	31.0%

Combination vs monotherapy: No significant difference in 60-day mortality · P = 0.658

Interpretation: Oseltamivir + peramivir did not demonstrate clinical superiority over NAI monotherapy.

Important limitations: Retrospective · Nonrandomized · Small combination group (n=29)

Reference: Zou Q, et al. Int J Infect Dis. 2020;92:208–213.

Should Two Neuraminidase Inhibitors Be Combined?

IDSA 2018 — Recommendation 20

> "Clinicians should start antiviral treatment as soon as possible with a single neuraminidase inhibitor … and not use a combination of NAIs." **A-I**

Recommended Approach

Use one neuraminidase inhibitor:

- Oral oseltamivir
- OR inhaled zanamivir
- OR IV peramivir

Do not routinely combine two NAIs

Examples:

- Oseltamivir + peramivir
- Oseltamivir + zanamivir

Reference:

Uyeki TM, et al. Clin Infect Dis. 2019;68:e1–e47. IDSA Seasonal Influenza Guideline.

What Evidence Supports Baloxavir in Hospitalized Influenza?

Study: Shah et al., J Antimicrob Chemother 2020

- Multicenter retrospective cohort
- Adults hospitalized with influenza A
- Baloxavir (n=359) vs. Oseltamivir (n=431)

Clinical Outcomes

Outcome	Baloxavir	Oseltamivir	P value
Hospital length of stay	4 days	5 days	0.45
30-day mortality	3.3%	6.0%	0.079
Time to hypoxia resolution	51.7 h	72.0 h	**<0.001**

Interpretation

Baloxavir was associated with faster resolution of hypoxia, but did not demonstrate a significant reduction in hospital stay or mortality.

Evidence Gap

No adequately powered randomized trial has established baloxavir monotherapy as treatment for hospitalized severe influenza.

Reference:

- Shah S, et al. J Antimicrob Chemother. 2020;75:3015–3022.

Baloxavir + Oseltamivir? Evidence from FLAGSTONE

Trial Design

Kumar D, et al. Lancet Infectious Diseases 2022

Phase 3 · Randomized · Double-blind · Placebo-controlled superiority trial

366 hospitalized patients with severe influenza (NEWS2 ≥4)

- Intervention: Baloxavir + standard-of-care NAI
- Control: Placebo + standard-of-care NAI

Standard-of-care NAI could be oseltamivir, zanamivir, or peramivir.

Primary Outcome

Median time to clinical improvement

97.5 h (Baloxavir + NAI) vs 100.2 h (NAI alone)

Median difference −2.7 h · P = 0.467

No significant clinical superiority

Virologic Effect: Baloxavir combination therapy produced greater antiviral activity and faster viral clearance, but this did not translate into faster clinical improvement.

2025 Post Hoc Analysis — High-Risk Subgroup

Yan M, et al. Open Forum Infect Dis. 2025;12:ofaf439.

- High-risk patients: n = 143
- Overall time to clinical improvement: not significantly different, P = 0.477
- 28-day mortality: 2.17% vs 11.76%, P = 0.02
- H3N2 subgroup: shorter time to clinical improvement with combination therapy

> Interpret cautiously: Exploratory · Post hoc · Small subgroup · Hypothesis-generating

Bottom takeaway: The overall randomized trial was negative; newer subgroup signals are intriguing but not definitive.

What Actually Changes in Severe Influenza Antiviral Therapy?

CDC 2026 — Baloxavir in Hospitalized Influenza

Oral baloxavir is not routinely recommended for hospitalized patients with suspected or confirmed influenza.

Reason: insufficient evidence demonstrating clinical benefit in hospitalized patients.

A randomized trial of baloxavir + neuraminidase inhibitor in hospitalized influenza did not demonstrate superior clinical benefit compared with neuraminidase inhibitor alone.

Severe Influenza: Should We Escalate Antiviral Therapy?

Strategy	Routine escalation?	Guideline-based approach
Route	**NO**	Oral/enteric oseltamivir remains preferred; IV peramivir is not routinely required
Drug	**NO**	Do not routinely switch to baloxavir, peramivir, or zanamivir solely because illness is severe
Dose	**NO**	Higher-dose oseltamivir has not shown additional clinical benefit
Combination	**NO**	Do not routinely combine two NAIs or add baloxavir to an NAI
Duration	**INDIVIDUALIZE**	Longer treatment may be considered in severe or prolonged illness

For prolonged severe disease:

- Lower respiratory tract RT-PCR may help guide decisions about extended antiviral treatment.

References:

- CDC. Influenza Antiviral Medications: Summary for Clinicians. Updated March 10, 2026.
- Uyeki TM, et al. Clin Infect Dis. 2019;68:e1–e47.

Case 2: Pneumonia Continues to Worsen

Case Update

- Influenza A confirmed from a lower respiratory tract specimen
- Appropriate antiviral therapy has been given
- Despite adequate antiviral treatment:
- Progressive bilateral pulmonary infiltrates
- Worsening respiratory failure
- Persistent severe pneumonia

Clinical Question:

Should empiric antibacterial therapy be given?

Influenza Positive ≠ Bacterial Coinfection Excluded

Yes. Severe influenza pneumonia warrants empiric antibacterial therapy while bacterial coinfection is evaluated.

IDSA Influenza Guideline — Recommendation 24

> In patients with suspected or laboratory-confirmed influenza who present with severe disease:
>
> Extensive pneumonia · Respiratory failure · Hypotension · Fever
>
> → Investigate and empirically treat bacterial coinfection, in addition to antiviral therapy. **A-II**
>
> If deterioration occurs after initial improvement:
>
> Investigate and empirically treat bacterial coinfection. **A-III**

ATS 2025 CAP Guideline Update

For hospitalized adults with severe CAP who test positive for a respiratory virus:

Prescribe empiric antibacterial therapy **Conditional recommendation · Very low-quality evidence**

What organisms matter in severe influenza pneumonia?

- *Streptococcus pneumoniae*
- *Staphylococcus aureus*, including MRSA

In critically ill influenza pneumonia, empiric therapy should include MRSA-active coverage when bacterial coinfection is suspected.

Case 2: Influenza-Associated ARDS

Case Update

- Despite appropriate antiviral and antibacterial therapy:
- Progressive bilateral pulmonary infiltrates
- Invasive mechanical ventilation required
- $PaO_2/FiO_2 \approx 110$
- No evidence of cardiogenic pulmonary edema
- The patient now fulfills criteria for moderate-to-severe ARDS.

Should systemic corticosteroids be started for influenza-associated ARDS?

What Does the Influenza-Specific Evidence Show?

Ni et al., Critical Care 2019

Systematic review and meta-analysis of 10 studies (6,548 adults with influenza pneumonia) comparing corticosteroid exposure vs. no corticosteroid exposure.

Outcome	Finding
Mortality	**RR 1.75** (95% CI 1.30–2.36) – Higher with corticosteroids
Secondary infection	**RR 1.98** (95% CI 1.04–3.78) – Higher with corticosteroids
ICU length of stay	+2.14 days (95% CI 1.17–3.10)
Mechanical ventilation duration	No significant difference

Clinical Interpretation

A consistent signal of harm exists, but causality cannot be established from these data. Corticosteroid exposure is **associated with**, not proven to cause, increased mortality and secondary infection risk.

Reference: Ni YN, et al. Crit Care. 2019;23:99.

Corticosteroids in Influenza-Associated ARDS: Guideline Position

Do not use corticosteroids solely to treat influenza pneumonia or influenza-associated ARDS.

WHO 2024

> In patients with suspected or confirmed influenza with or at risk of severe illness:
>
> Suggest **NOT** administering corticosteroids
>
> Conditional recommendation · Very low-certainty evidence

IDSA 2018 — Recommendation 30

> Do not administer corticosteroid adjunctive therapy for:
>
> Influenza · Influenza-associated pneumonia · Respiratory failure · ARDS
>
> unless clinically indicated for another reason.
>
> **A-III**

ATS 2025 Severe CAP Guideline

Systemic corticosteroids are suggested for severe CAP in general.

However, this recommendation **explicitly excludes** severe CAP caused by influenza pneumonia. Influenza is listed as a factor that **weakens** the recommendation for corticosteroids.

Steroids may still be appropriate for another indication

- Refractory septic shock
- Asthma/COPD exacerbation
- Adrenal insufficiency

If the Patient Continues to Deteriorate…

Consider complications beyond progressive viral pneumonia.

Bacterial superinfection

S. aureus / MRSA, *S. pneumoniae*, *S. pyogenes*

Influenza-associated pulmonary aspergillosis (IAPA)

Often opportunistic in critically ill

Myocarditis / cardiomyopathy

Direct viral injury or immune-mediated

Encephalopathy / encephalitis

Neurologic manifestations of severe influenza

Myositis / rhabdomyolysis

Muscle damage from severe infection

Thromboembolic complications

Increased risk in severe illness

Organizing pneumonia / other inflammatory lung injury

Post-viral pulmonary complications

台灣感染症醫學會-抗流感病毒藥物使用建議

台灣感染症醫學會 The Infectious Diseases Society of Taiwan

抗流感藥物使用對象、劑量與療程

藥物	Oseltamivir Capsule		Oseltamivir Oral Suspension		Zanamivir		Peramivir		Baloxavir Marboxil	
使用方式	吞服/無法吞服者（如需使用鼻胃管者）則打開膠囊泡水或糖漿服用 懷孕哺乳首選		經調配後服用		經口吸入 懷孕哺乳: 利>弊投予		單次點滴靜脈注射15 分鐘以上 懷孕哺乳: 利>弊投予		單次口服 可以磨粉 懷孕哺乳不建議	
適用年齡	成人及兒童 (含一個月大新生兒)		成人及兒童 (含一個月大新生兒)		5 歲(含)以上		小兒(早產兒及新生兒除外)及成人		成人及兒童 (5 歲以上)	
標準治療劑量	輕症	重症	輕症	重症	輕症	重症	輕症	重症	輕症	重症
	13歲以下依體重調整劑量； 13歲(含)以上或體重40kg以上者75mg BID		40kg以下兒童依體重調整劑量； 40kg以上兒童或成年人及青少年為75mg BID		10mg BID	不建議使用	成人 300mg; 小兒 10-12 mg/kg	成人 600mg QD	<20kg單次服用20mg ≧20 至 <80kg 單次服用 40mg ≧80kg 單次服用 80mg	現無臨床數據
標準療程	5天	5天	5天	現無臨床數據	5天		單次	可依症狀連續多日反覆投予	單次	