NC DEPARTMENT OF HEALTH AND HUMAN SERVICES

ROY COOPER • Governor
KODY H. KINSLEY • Secretary
Mark T. Benton • Deputy Secretary for Health
Susan Kansagra MD, MBA • Assistant Secretary for Public Health
Division of Public Health

To: All North Carolina Clinicians
From: Emma Doran, MD, MPH, Medical Epidemiologist
Subject: 2023-2024 Viral Respiratory Season: **Update for NC Clinicians (8 pages)**
Date: October 18, 2023

This memo provides information and guidance to NC clinicians regarding updates for the 2023-24 respiratory season. As guidance may change during the season, up to date information will be available at flu.nc.gov.

Along with seasonal influenza and RSV viruses, the SARS-CoV-2 virus is now part of the respiratory season. An increased activity of all three viruses at the same time can have a significant impact on the healthcare system. Therefore, preventive measures to reduce the spread of influenza, RSV, COVID-19 and other respiratory viruses are critical.

TESTING

- Diagnostic tests available for detection of viruses in respiratory specimens include molecular assays (including rapid molecular assays, reverse transcription polymerase chain reaction (RT-PCR) and other nucleic acid amplification tests) and antigen detection tests (including rapid influenza diagnostic tests and immunofluorescence assays). Sensitivity and specificity can vary by the pathogen or test type, illness onset to specimen collection, the prevalence of viruses in patient population and other factors. Overall, molecular assays have a higher sensitivity and specificity than rapid antigen tests.

- It is possible for a patient to be infected with two or more viruses at the same time. Co-infections can impact the clinical management of acute respiratory illness. Testing for suspected pathogens should be considered particularly in hospitalized patients with severe respiratory disease. Additional guidance for clinicians when SARS-CoV-2 and influenza viruses are co-circulating can be found here.

- When available, multiplex assays for simultaneous detection of influenza, RSV and SARS-CoV-2 viruses should be used.

- A negative rapid antigen test does NOT rule out infection and should not be used for treatment or infection control decisions during periods when influenza, RSV, and/or SARS-CoV-2 viruses are known to be circulating.

- RSV: Antigen testing is sensitive in children but less sensitive in adults. Healthcare providers should use highly sensitive rRT-PCR assays when testing older children and adults for RSV.

- COVID-19: A negative viral test result does not rule out infection and should be repeated following CDC and FDA recommendations.

- Testing to detect influenza and SARS-CoV-2 is available through a variety of commercial laboratories, health system laboratories, and the North Carolina State Laboratory of Public Health (SLPH). All specimens submitted to SLPH for influenza or SARS-CoV-2 testing from symptomatic patients will be tested for both influenza and SARS-CoV-2. Specific guidance regarding specimen collection and transport is available at SLPH.

- Specimens should be submitted to SLPH for further testing and characterization in the following circumstances:
    - Specimens from confirmed influenza cases with severe illness and a poor prognosis.
    - Specimens from influenza-associated deaths.
    - Patients who die with influenza-like illness but have no laboratory evidence of influenza, SARS-CoV-2, or other respiratory infection on a multiplex panel.
    - Patients who are critically ill with influenza-like illness but have no laboratory evidence of influenza, SARS-CoV-2, or other respiratory infection on a multiplex panel.
    - Patients with influenza-like illness, with or without confirmatory testing for influenza, who have had contact with domestic or wild swine (pigs) or poultry (birds).
    - A sample of patients with influenza-like illness seen at facilities participating in the outpatient Influenza-Like Illness Network (ILINet) or Influenza Hospitalization Surveillance Program (IHSP/RESP-NET).

- Testing at the SLPH should also be considered for other patients in outbreaks in institutional settings or congregate living facilities and clusters of severe or unusual respiratory illness. Testing and management considerations for nursing home residents with acute respiratory illness symptoms when SARS-CoV-2 and Influenza viruses are co-circulating can be found here. Please consult the local health department or Communicable Disease Branch epidemiologist on call (919-733-3419) with questions about whether such testing is appropriate.

CLINICAL MANAGEMENT

- While molecular assays are overall more sensitive and specific than rapid antigen tests, clinicians should consider the pathogen or test type, the time of illness onset to specimen collection and the prevalence of the tested virus in the patient population to interpret test results. If clinically indicated, treatment should not be delayed while awaiting laboratory confirmation. Decisions regarding treatment and clinical management for influenza and COVID-19 should be based on clinical and epidemiologic information and should not wait on test results for patients who are hospitalized, have severe, complicated or progressive illness, or are at high risk for clinical complications.

- Certain patients are at increased risk for viral respiratory infection-related complications. These include:
    - Adults 65 years and older.
    - Children younger than 2 years old.
    - People with certain medical conditions including:
        - Difficulty breathing or shortness of breath

        - Asthma
        - Neurologic and neurodevelopment conditions
        - Blood disorders (such as sickle cell disease)
        - Chronic lung disease (such as chronic obstructive pulmonary disease [COPD] and cystic fibrosis)
        - Endocrine disorders (such as diabetes mellitus)
        - Heart disease (such as congenital heart disease, congestive heart failure and coronary artery disease)
        - Kidney diseases
        - Liver disorders
        - Metabolic disorders (such as inherited metabolic disorders and mitochondrial disorders)
    - People who are obese.
    - People younger than 19 years old on long-term aspirin- or salicylate-containing medications.
    - People with a weakened immune system due to disease (such as people living with HIV or AIDS, or some cancers such as leukemia) or medications (such as those receiving chemotherapy or radiation treatment for cancer, or persons with chronic conditions requiring chronic corticosteroids or other drugs that suppress the immune system).
    - Pregnant people and people up to 2 weeks after the end of pregnancy.
    - Tobacco users, current and former.
    - People who live in nursing homes and other long-term care facilities.
    - People from certain racial and ethnic minority groups are at increased risk for hospitalization with influenza, including non-Hispanic Black persons, Hispanic or Latino persons, and American Indian or Alaska Native persons.

- Additionally, certain children are at greater risk for severe RSV illness. They include:
    - Premature infants.
    - Infants up to 12 months, especially those 6 months and younger.
    - Children younger than 2 years with chronic lung disease or congenital heart disease.
    - Children who have neuromuscular disorders, including those who have difficulty swallowing or clearing mucus secretions.

- Patients should seek medical attention for any of the following:
    - Difficulty breathing or shortness of breath.
    - Pain or pressure in the chest or abdomen.
    - Sudden dizziness or confusion.
    - Severe or persistent vomiting.
    - Severe muscle pain.
    - Respiratory symptoms that improve but then return with fever and worse cough.
    - Worsening of medical conditions.
    - In babies, fever above 104° F, bluish gray skin color, lack of responsiveness, or extreme irritation.
    - Any other symptom that is severe or concerning.

- **Influenza:**
    - Clinical judgment is an important factor in treatment decisions. Treatment is recommended as early as possible, including prior to testing, for individuals with suspected or confirmed influenza who have any of the following:
        - Illness requiring hospitalization.

        - Progressive, severe, or complicated illness, regardless of previous health status.
        - Increased risk for severe disease (e.g., persons with certain chronic medical conditions, persons 65 or older, children younger than 2 years, and pregnant women).
    - **Treatment is most effective when started within 48 hours of illness onset. However, treatment of persons with prolonged or severe illness can reduce mortality and duration of hospitalization even when started more than 48 hours after onset of illness.**
    - For hospitalized patients with suspected or confirmed influenza, initiation of antiviral treatment with oral or enterically administered oseltamivir is recommended as soon as possible.
    - For outpatients with complications or progressive disease and suspected or confirmed influenza (e.g., pneumonia, or exacerbation of underlying chronic medical conditions), initiation of antiviral treatment with oral oseltamivir is recommended as soon as possible.
    - For outpatients with suspected or confirmed uncomplicated influenza, oral oseltamivir, inhaled zanamivir, intravenous peramivir, or oral baloxavir may be used for treatment, depending upon approved age groups and contraindications. Additional information on influenza antiviral medications can be found here.

- **RSV:** Antiviral medication is not routinely recommended to fight infection. Most RSV infections go away on their own in a week or two. However, RSV can cause severe illness in some people at high-risk and require hospital supportive care.

- **COVID-19:** There are several FDA-authorized or approved antiviral medications used to treat mild to moderate COVID-19 in people who are more likely to get very sick, if prescribed as soon as possible after diagnosis:
    - Paxlovid (nirmatrelvir co-packaged with ritonavir): for adults and children ages 12 years and older and should be started within 5 days of symptom onset.
    - Lageviro (Molnupiravir): for adults only and should be started within 5 days of symptom onset.
    - Veklury (Remdesivir): for adults and children by intravenous infusions and should be started within 7 days of symptom onset.
    - Additional information on COVID-19 treatment options can be found here.

INFECTION CONTROL

When influenza, RSV, SARS-CoV-2 and other respiratory viruses are spreading in the community, the risk of spread in healthcare settings increases as well. Clinicians should consult the CDC's infection control actions for respiratory viruses in clinical settings. Long-term care facilities are encouraged to contact their Regional Infection Prevention Support team (RIPS) to ensure they are prepared for respiratory virus season. RIPS teams can help assess infection prevention practices and provide education to staff.

PREVENTION AND CONTROL MEASURES

- **Influenza:**

    - Annual vaccination against influenza is the best way to prevent infection and is recommended for everyone ≥6 months of age who does not have a medical contraindication to vaccination. It's especially important for:
        - People who are at high risk of developing serious complications like pneumonia if they get sick with the flu, and
        - People who live with or care for others who are at high risk of developing serious complications, including healthcare providers.
    - Flu vaccination should begin soon after the vaccine becomes available. Vaccines should continue to be offered throughout the flu season, but ideally, everyone should be vaccinated by the end of October. Evidence from some clinical trials indicate that protection against viruses that are antigenically like those contained in the vaccine extends at least for 6–8 months, particularly in nonelderly populations. Detailed flu vaccine guidance and recommendations can be found here.
    - Post-exposure chemoprophylaxis with either oseltamivir, zanamivir, or baloxavir should also be considered for close contacts of people with influenza who are at high risk for complications of influenza, including pregnant women, if antivirals can be started within 48 hours of the most recent exposure. CDC does not recommend widespread or routine use of antiviral medications for chemoprophylaxis to limit the potential emergence of antiviral resistant viruses. Chemoprophylactic use of antiviral medications is recommended to control outbreaks among high-risk persons in institutional settings. Detailed information regarding influenza antiviral medications can be found here.

- **RSV**: New prevention tools for RSV have become available in 2023:

    - Nirsevimab (Beyfortus) is a monoclonal antibody designed to protect infants and some young children from severe RSV disease. Nirsevimab recommendations are:
        - 1 dose of nirsevimab for all infants younger than 8 months born during or entering their first RSV season.
        - 1 dose of nirsevimab for infants and children 8–19 months old who are at increased risk for severe RSV disease and entering their second RSV season.
    - Adults 60 years of age or older may receive a single dose of RSV vaccine, either GSK (Arexvy) or Pfizer (Abrysvo), using shared clinical decision making.
    - For pregnant women a single dose of the Pfizer (Abrysvo) RSV vaccine during weeks 32 through 36 of pregnancy is recommended immediately before or during RSV season.

- **COVID-19:** As of October 4, 2023, three updated COVID-19 vaccines have become available. Recommendations are as follows:

    - People aged 12 years and older who got COVID-19 vaccines before September 12, 2023, should get one updated Pfizer-BioNTech, Moderna, or Novavax COVID-19 vaccine.
    - People aged 12 years and older who are unvaccinated should get one updated Pfizer-BioNTech, or updated Moderna; or two doses of updated Novavax COVID-19 vaccine.
    - Children aged 5 to 11 years who are not vaccinated or have gotten previous COVID-19 vaccines before September 12, 2023, should get one updated Pfizer-BioNTech or Moderna COVID-19 vaccine.

- Children aged 6 months to 4 years who are not vaccinated should get two doses of updated Moderna (2nd dose 4 to 8 weeks after 1st dose), or three doses of updated Pfizer-BioNTech (2nd dose 3 to 8 weeks after 1st dose and 3rd dose at least 8 weeks after 2nd dose).
- Childre aged 6 months to 4 years who got COVID-19 vaccines before September 12, 2023, should get one or two doses of updated COVID-19 vaccines depending on which vaccine and the number of doses they've previously received. Detailed recommendations can be found here.
- People who are moderately or severely immunocompromised may get additional doses of updated COVID-19 vaccines following this guidance.
- Additional guidance for updated COVD-19 vaccines is available here.

- Flu and RSV vaccines should be deferred for people with suspected or confirmed COVID-19, whether or not they have symptoms, until they have met the criteria to discontinue their isolation as recommended.
- Healthcare providers can co-administer the vaccines for which a patient is eligible in the same visit, including COVID-19 and influenza vaccines. CDC provides no formal guidance about co-administration of RSV vaccines and providers should consider whether the patient is up to date with currently recommended vaccines, the feasibility of their returning for additional vaccine doses, their risk of acquiring vaccine-preventable disease, the vaccine reactogenicity profiles, and patient preferences. More information about RSV co-administration is available here

- Educate patients regarding the importance of basic protective measures including good respiratory hygiene, hand washing, air quality improvements, masks, physical spacing and staying home when sick. These measures help protect against flu, RSV, COVID-19 and other common respiratory viruses. An updated CDC respiratory index provides information on overall respiratory viruses activity nationwide and by state, in addition to detailed information about all 3 viruses including prevention tools. NC dashboards provide detailed NC viral respiratory surveillance data.

- Check that patients have appropriate preventive measures to protect against other respiratory illnesses, including pneumococcal vaccine.

SURVEILLANCE AND TRACKING

- **In North Carolina, all influenza-associated deaths (adult and pediatric) are reportable to the local health department. Specimens from patients who die from influenza should be sent to the State Laboratory of Public Health (SLPH) for further characterization.** An influenza-associated death is defined for surveillance purposes as a death resulting from a clinically compatible illness that was confirmed to be influenza (any strain) by an appropriate laboratory or rapid diagnostic test. There should be no period of complete recovery between the illness and death. A death should *not* be reported if:

  - There is no laboratory or rapid test confirmation of influenza virus infection.
  - The influenza illness is followed by full recovery to baseline health status prior to death.
  - After review and consultation, there is an alternative agreed upon cause of death.

- North Carolina Division of Public Health (NC DPH) conducts surveillance for influenza, RSV, COVID-19 and other respiratory viruses using several systems. In addition to reporting of all influenza-

associated deaths, surveillance is conducted for all visits to emergency departments across the state for influenza-like, RSV-like, and COVID-like illnesses, and influenza and COVID-19 hospital admissions for all hospitals are reported weekly. Information on weekly laboratory data is also gathered from the SLPH and from epidemiologists at eight of the state's largest healthcare systems.

- NC DPH conducts wastewater monitoring for COVID-19 and is exploring adding influenza and RSV detection to the state wastewater monitoring program.

- Additionally, NC DPH conducts surveillance and laboratory testing of outpatients seen by clinicians in our Influenza-Like Illness Network (ILINet). 34 practices are participating this year. Please consider joining ILINet if you have not done so.

- Finally, this year in partnership with the CDC, NC DPH will conduct population-based laboratory-confirmed influenza, RSV and COVID-19 associated hospitalization surveillance (RESP-NET) in three large hospital networks. This year, only NC flu hospitalization data will be presented on the RESP-NET interactive dashboard.

- Please contact your local health department to report outbreaks of influenza-like illness (i.e., fever plus cough or sore throat), particularly among young children, and residents of Long-Term Care Facilities or other congregate living facilities. We strongly recommend sending specimen collected from these patients (as well as from any influenza-associated death) to SLPH for further characterization.

NOVEL AND VARIANT INFLUENZA VIRUSES

- Novel influenza is an infection in a person with an influenza A virus that normally circulates in birds. From January 2022 to June 2023, over 800 commercial and backyard H5N1 Highly Pathogenic Avian Influenza (HPAI) outbreaks were reported in 47 states or territories. In North Carolina, H5N1 outbreaks were reported in 9 commercial poultry facilities and 7 backyard flocks. Thirteen sporadic human cases of A(H5N1) were reported from eight countries, including one case in The United States in Colorado.

- Although the current risk to public health remains low, clinicians should consider the possibility of avian flu infection in persons showing signs or symptoms of respiratory illness who have had exposure to wild or domestic birds in the 14 days before symptom onset. Additional avian influenza virus information is available here.

- A variant influenza is an infection in a person with influenza viruses that normally circulate in swine. Swine/variant viruses were detected in 4 people in the United States during the 2022-23 season. No human cases have been detected in North Carolina. Investigations into these cases indicate that the main risk factor for infection is prolonged exposure to pigs, mostly in fair settings, especially for people at high risk of serious flu complications. Early identification and investigation of variant influenza virus infections are important to determine whether the virus is spreading efficiently among people. Please submit specimens from patients with influenza-like illness and recent swine exposure to SLPH for testing regardless of the results of initial influenza testing. Additional information is available here.

A weekly summary of NC respiratory surveillance data is available in our Respiratory Virus Surveillance Dashboard.

Clinicians should contact their local health departments or the Communicable Disease Branch epidemiologist on-call 24/7 number (919-733-3419) for questions about respiratory viruses.

cc: Dr. Erica Wilson, Medical Director, Medical Consultation Unit
Evelyn Foust, Branch Head, Communicable Disease Branch
Dr. Zack Moore, State Epidemiologist