increased risk of infections (10). In adults >65 years of age, waning innate and acquired immunity associated with decreased function of memory cluster of differentiation (CD)-8+ T cells results in increased susceptibility to viral infections and severe disease (18, 19). Early in the COVID-19 pandemic, older age was identified as a significant risk for increased mortality and hospitalization due to SARS-CoV-2 (20).

Rapid microbiological diagnosis of acute respiratory infections has both therapeutic and prognostic implications. Knowledge of the virus epidemiology and a complete history and physical examination may assist in determining the most likely responsible pathogen (21). While healthy, immunocompetent hosts usually recover from acute respiratory infections without the need for laboratory diagnosis or treatment, specific diagnosis in immunosuppressed patients and those with underlying conditions is necessary for implementing appropriate, targeted therapy when available.

Laboratory testing is necessary because the accuracy of clinical diagnosis alone is limited. In one study, clinical diagnosis of pneumonia based only on clinical findings such as fever, cough, sputum production, abnormal chest auscultation, and dyspnea had limited value in differentiating infectious vs noninfectious pneumonia, and bacterial vs viral pneumonia (22). Imaging studies, specifically chest X-rays and computer-tomography (CT) scans are necessary to diagnose pneumonia. However, imaging studies are not specific enough to definitively distinguish between viral and bacterial infections (23). The addition of procalcitonin and C-reactive protein significantly increased the sensitivity of clinical diagnosis from an area under the curve (AUC) of 0.79 (95% CI, 0.75–0.83) when all clinical findings were combined to an AUC of 0.92 (95% CI, 0.89–0.94); $P < 0.001$ (24). While these biomarkers improve the accuracy of clinical assessment for pneumonia, the specific etiology remains unknown. This limitation of clinical diagnosis alone or in combination with imaging and other biomarkers underscores the need and the importance of viral diagnostics for the rapid detection of respiratory viruses.

WHAT TESTS SHOULD BE USED TO DETECT RESPIRATORY VIRUSES?

Several testing methodologies are available for the detection of respiratory viruses. They differ on several counts including the viral target (e.g., protein, DNA, RNA), performance characteristics, sample type used, level of complexity, and regulatory classification (Table 2). Respiratory viral testing can be performed in centralized laboratories, at the point of care, or outside of a healthcare setting. The different settings dictate the type of tests that can be utilized and are based on the complexity of the selected test as determined by the FDA during the premarket approval process. Examples of commercially available in vitro diagnostic (IVD) tests are listed in Table 3.

Sample Types for Respiratory Virus Testing

Nasopharyngeal swabs (NPSs) have been the gold standard specimen for detection of respiratory viruses. NPSs must be collected by a trained healthcare provider, limiting who can collect and where the test must be collected such as provider vs self-collection. Collection of NPSs is often associated with resistance from patients due to discomfort and may result in suboptimal specimen quality (25). Collecting swabs from multiple sources is an option for increasing the sensitivity of respiratory virus detection if NPS collection is not feasible (26). However, sensitivities do vary by study and there is currently no clear consensus on what specimen types are routinely acceptable for each virus detection (27). Due to the SARS-CoV-2 pandemic and subsequent strain on reagents, supplies, staffing, and testing, the impact of different swab types on assay accuracy and sensitivity of testing has been more extensively