The coronavirus disease 2019 (COVID-19) pandemic, caused by severe acute coronavirus type 2 (SARS-CoV-2), has significantly affected the lives of many people across North Carolina and the United States. Similar to the rest of the country, the epidemiology of SARS-CoV-2 in the state indicates health disparities among Black and Hispanic/Latino individuals, the presence of hotspots, or counties with high numbers of infected persons, and clusters of transmission among congregate living facilities. There have been many advances in diagnostic methods for SARS-CoV-2 and therapies for hospitalized patients nationwide. Public health strategies have included widespread testing for SARS-CoV-2, optimal management of cases, contact tracing efforts, and a phased reopening of sectors/activities in North Carolina with masks and physical distancing to minimize spread of the virus. In this issue, several authors, researchers, and public health leaders discuss the challenges that North Carolinians have experienced with respect to COVID-19 and several factors that are likely contributing to the health disparities among racial/ethnic minorities who have had the highest number of cases and deaths from SARS-CoV-2. Additional strategies also reported in this issue include the use of strike teams and mobile units to reach populations at high risk for infection and severe illness. Promoting individual and population-level strategies for minimizing transmission of SARS-CoV-2, especially among the most vulnerable, and consistent public health messaging based on science are critical as we face the new year and continued uncertainties around the COVID-19 pandemic.

Introduction

The pandemic caused by severe acute coronavirus type 2 (SARS-CoV-2) has been the most significant pandemic since the 1918 “Spanish Influenza” pandemic. Coronavirus disease 2019 (COVID-19), the illness caused by SARS-CoV-2, has challenged all of us, from the ability of our scientific and medical community to develop and implement widescale diagnostic, therapeutic, and preventive strategies to our public health infrastructure’s efforts to mitigate the impact locally and nationally. The first laboratory-confirmed case was reported in the United States on January 22, 2020. Only nine months later, as of October 21, the country had over 8 million reported cases of SARS-CoV-2 infection and over 200,000 deaths [1]. At that time, North Carolina had over 250,000 reported cases and over 4,000 deaths from COVID-19 [2].

Epidemiology and Health Disparities

Early data from the Centers for Disease Control and Prevention (CDC) identified the most vulnerable groups for COVID-19 as persons with underlying medical conditions (i.e., cardiovascular disease, diabetes, chronic lung disease), and older adults, with a startling death rate of 902/100,000 among persons aged ≥ 80 years [3]. In comparison, the overall US death rate from SARS-CoV-2 infection was 64/100,000 as of October 10, 2020 [1]. The reported death rate in North Carolina was lower than the national rate at 35/100,000; however, 81% of deaths have been among people aged ≥ 65 [2]. Nationwide, persons aged 20–29 years accounted for > 20% of all SARS-CoV-2 infections during June–August 2020 [4]. In North Carolina, persons aged 18–24 represent 16% of all cases, with individuals aged 25–49 representing 40% of cases and 4% of deaths [2].

National surveillance data revealed the health disparities in COVID-19 associated with race/ethnicity of persons affected and area of residence. Compared to non-Hispanic whites, non-Hispanic Blacks had 2.6 times the risk for SARS-CoV-2 infection and 4.7 times the risk of being hospitalized [5]; Hispanic/Latino persons had 2.8 times higher risk for infection and 4.6 times higher risk for hospitalization from COVID-19 [5]. Using cumulative county-level data collected during February–June 2020, the CDC identified US counties that were “hotspots,” based on algorithmic thresholds related to the number of new cases and the changes in incidence [6]. Among all 18 hotspot counties identified in North Carolina, health disparities in COVID-19-associated mortal-
SARS-CoV-2 infection in August, but transmission from pets reported the first dog in the state with laboratory-confirmed SARS-CoV-2 infection [15]. The virus demonstrated to spread from humans to other animals. NCDHHS infected remains unknown. SARS-CoV-2 has been demonstrated to spread from humans to other animals, although the range of other mammals that can become infected remains unknown. SARS-CoV-2 has been demonstrated to spread from humans to other animals. NCDHHS reported the first dog in the state with laboratory-confirmed SARS-CoV-2 infection in August, but transmission from pets or livestock to humans appears rare [15].

SARS-CoV-2 is primarily transmitted through droplet transmission between persons within a short range (e.g., less than six feet), similar to other respiratory viruses (Table 1). The period of infectivity among most otherwise healthy people without immunosuppression is up to 10 days [16]; among immunocompromised or hospitalized patients, the period of infectivity may be up to 20 days. In addition, an infected person may be infectious starting from 48 hours (or two days) before symptoms or testing positive for COVID-19 [16]. Furthermore, a significant proportion of persons with COVID-19 (estimated 40%-45%) may have subclinical or no symptoms and still transmit the virus [17].

The CDC has acknowledged the potential for airborne transmission of SARS-CoV-2, based on a few well-documented examples that occurred under special circumstances [18]. These circumstances involved enclosed spaces, prolonged exposure to respiratory particles that were generated with expiratory exertion (e.g., shouting, singing, exercising), and inadequate ventilation or air handling. The virus has been shown to remain viable in closed conditions for up to three hours and on certain surfaces for up to 72 hours [19] (Table 1), underscoring the need for frequent disinfection of potentially contaminated surfaces or shared objects with an EPA-approved disinfectant. Like similar enveloped viruses, SARS-CoV-2 is inactivated by 60%-90% alcohol-containing hand antiseptics within 15 seconds [20].

Transmission of SARS-CoV-2 infections is highest among close contacts (defined as individuals who have been within six feet of an infected person for a cumulative total of 15 minutes or more over a 24-hour period) [16]. Among households with a laboratory-confirmed COVID-19 case, the overall secondary attack rate (defined as the probability that an infected individual will transmit the disease to uninfected persons) is estimated to be 18.8% [21 {preprint}], emphasizing the importance of education about home isolation for persons with mild SARS-CoV-2 infections. Persons with COVID-19 can generally discontinue isolation 10 days after symptom onset and after 24 hours with no fever, without the use of fever-reducing medications, and with improvement of other symptoms [22].

Testing and Surveillance

Over 3 million tests for SARS-CoV-2 have been conducted in North Carolina to date, based on patient-level and aggregate data submitted electronically through the NC COVID-19 Surveillance System (NC COVID) and COVID-19 Aggregate Test Reporting (eCATR) [2]. The overall positivity rate was 6.3% as of October 15, 2020 [2].

Local health departments have conducted most of the case investigations in the state after notification of cases in the North Carolina Electronic Disease Surveillance System (NC EDSS), which involves collection of information including symptom onset, source of illness, activities during the case's infectious period, and list of potentially exposed contacts. Surveillance data are updated weekly on the COVID-19 Dashboard [2], which also houses data regarding number of hospitalizations and cases diagnosed at North Carolina hos-
In this issue, Dr. Sickbert-Bennett and Lauren DiBiase describe in detail all the sources of COVID-19 surveillance in North Carolina and provide recommendations for improvements to our current surveillance system [23].

Under the national declaration of a public health emergency due to COVID-19, the United States Food and Drug Administration (FDA) has approved more than 200 diagnostic and antibody tests for SARS-CoV-2 detection under an Emergency Use Authorization (EUA) [24]. Several tests using polymerase chain reaction (PCR) assays that can detect the virus’s genetic material from respiratory specimens collected by either health care professionals or through self-collection in clinics or at home have been authorized for diagnosis of SARS-CoV-2; newer PCR-based tests using saliva as a specimen have also been authorized [24]. Furthermore, SARS-CoV-2 rapid antigen tests that have received EUAs can quickly detect fragments of proteins found on or within the virus by testing swabs collected from the nasal cavity, although antigen tests have substantially lower sensitivity.

Diagnostic testing for SARS-CoV-2 is recommended for persons with symptoms of COVID-19 and for close contacts irrespective of symptoms. Some experts recommend that close contacts wait at least 5 days after last known exposure before testing; however, it is important to note that a negative test following an exposure to a person with COVID-19 does not exclude infection if the contact is still within the 14-day incubation period. Testing is also recommended for individuals with higher risk of exposure or a higher risk of severe disease if they become infected, regardless of symptoms (e.g., health care personnel, first responders, and people in long-term care facilities, homeless shelters, and correctional facilities) [25].

Other tests using blood samples have received EUAs for the qualitative detection of antibodies to SARS-CoV-2. Antibodies are generally detectable 1-3 weeks after symptom onset, indicating the development of an adaptive immune response [26]. It is still unknown whether and to what degree an antibody response indicates immunity to future infection, and reinfection with SARS-CoV-2 has been reported in a small number of persons [27]. A study conducted in North Carolina that enrolled outpatients and inpatients across a health system representing 267 different zip codes identified a low prevalence of 0.8% for SARS-CoV-2 based on antibody testing during late April through June [28]. A nationwide study reported that fewer than 10% of the adult population developed antibodies against SARS-CoV-2 during the first wave of the pandemic [29].

### Table 1

**Characteristics of SARS-CoV-2, Therapeutic Options, and Infection Prevention**

| Pathogen | Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) |
|----------|--------------------------------------------------------|
| **Characteristics**a | |
| Incubation period | 2-14 days (median 4-5 days) |
| Period of infectivity | 2 days before symptom onset (or testing positive) to day 10 (immunocompetent); Up to 20 days (hospitalized and/or immunocompromised) |
| Transmission | Respiratory droplets; direct contact and fomite; possibly airborne in special circumstances; rare vertical transmissionb |
| Duration in environment | Up to 3 hours from aerosols; up to 72 hours on various surfacesc |
| Reproductive number (RO)d | ~2 -3 secondary cases (1.66 among high-density counties)g |
| Household secondary attack rate | -18.8%h |
| **Therapeutic options** | |
| Pre-exposure prophylaxis | None |
| Post-exposure prophylaxis | None |
| Treatment for hospitalized patients | Remdesivir, dexamethasone, prone ventilation |
| **Infection prevention**i | |
| Preventive measures | Masks, physical distancing, hand-washing or alcohol-based hand sanitizers, disinfection of potentially contaminated surfaces and shared objects outside the home |
| Isolation period (ambulatory persons) | 10 days from symptom onset and resolution of fever for at least 24 hours, without the use of fever-reducing medications, and with improvement of other symptoms |
| Quarantine period | 14 days since last exposure |
| Disinfection | List N products approved by the EPA; bleach solution containing 5.25%-8.25% sodium hypochlorite |

EPA= Environmental Protection Agency

aInformation from the Centers for Disease Control and Prevention for COVID-19, unless otherwise noted.
bReference 18; cMeyerowitz EA, Richterman A, Gandhi RT, Sax PE. Transmission of SARS-CoV-2: a review of viral, host, and environmental factors. Ann Intern Med. 2020; M20-5008. doi: 10.7326/M20-5008; dReference 19; 

eThe reproductive number means the average number of infected contacts per infected individual. 
fSy KTL, White LF, Nichols B. Population density and basic reproductive number of COVID-19 across United States counties. medRxiv. 2020. doi: 10.1101/2020.06.12.20130021 (pre-print); gReference 21 (pre-print); hReference 30; ihttps://www.epa.gov/pesticide-registration/list-n-disinfectants-coronavirus-covid-19
Clinical Management

The National Institutes of Health (NIH) created clinical criteria for defining the severity of illness from COVID-19, which have been useful in identifying appropriate therapies for individual patients (Table 2) [30]. Mild to moderate pulmonary disease occurs in the majority (81%) of persons with symptomatic COVID-19. However, persons with severe to critical illness from SARS-CoV-2 can develop cardiac, hepatic, renal, hematological, neurological, and other complications (e.g., thromboembolic events). In North Carolina, an estimated 51.1% of adults are at higher risk for severe COVID-19 illness based on age ≥ 65 years, having at least one underlying health condition, or both [2]. Multisystem inflammatory syndrome in children (MIS-C) and adults (MIS-A) can also result in multiorgan involvement [31]; as of October 10, 2020, there have been 43 cases of MIS-C reported in North Carolina [2]. In this issue, Dr. Rolfe and coauthors describe the frequency and numerous long-term sequelae of SARS-CoV-2 infection observed among patients [32]. Importantly, persistent symptoms are common and may occur even among asymptomatic patients who were never hospitalized.

The NIH has also issued COVID-19 treatment guidelines for patients depending on the severity of illness, based on scientific data and review from an expert panel that includes members from North Carolina academic institutions [28]. For mild to moderate illness from COVID-19, there are no specific therapies for persons managed at home that have been formally recommended at this time. For hospitalized patients, the FDA recently approved remdesivir, an intravenous antiviral agent with activity against SARS-CoV-2, for use in adult and pediatric patients aged 12 and older and weighing at least 40 kilograms (about 88 pounds); younger children may be provided remdesivir under an EUA [33]. The NIH COVID-19 treatment guidelines also recommend the use of dexamethasone as an anti-inflammatory agent for hospitalized patients requiring supplemental oxygen and those with severe or critical illness [30]. Other therapies for SARS-CoV-2 infections, including convalescent plasma and monoclonal antibodies (specific proteins that are made to decrease the virus’s ability to make more copies), are being investigated through clinical trials in North Carolina and across the country. It should be noted that there is no recommended pre- or post-exposure therapy for SARS-CoV-2.

Contact Tracing

Contact tracing is an important public health strategy for COVID-19 in order to identify people who have recently been in close contact with someone who is infected, allow rapid notification for testing, and provide support for necessary resources if the contact becomes symptomatic [16]. The CDC has supported and led a nationwide, coordinated training effort to build a public health COVID-19 contact-tracing workforce, and has responded to requests for assistance from hotspot counties in the United States. In June 2020, the CDC and the US Public Health Service (USPHS) deployed multidisciplinary teams to North Carolina to assist with case investigation, contact tracing, and data management; the CDC Foundation also provided additional contact tracers to support local health departments in the state to manage these hotspots [34].

In addition to traditional contact tracing procedures, digital contact tracing tools like SlowCOVIDNC are now being utilized by public health to enhance efforts during this pandemic. SlowCOVIDNC uses Bluetooth technology to let users anonymously share a positive COVID-19 test result through an app, which can notify other users who may be close contacts [2]. NCDHHS is also using a COVID-19 Community Team Outreach (CCTO) Tool, which provides a platform to manage cases and contacts, perform digital outreach, and store data in a central repository. CCTO provides local health departments access to contact-tracing data collected by other organizations during outbreak or cluster investigations [2].

Impact on our Communities

Since March 2020, numerous outbreaks or clusters of SARS-CoV-2 have been reported in North Carolina in congregate living facilities, such as long-term residential care and

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**TABLE 2. National Institutes of Health Criteria for SARS-CoV-2 Infections Based on Severity of Illness**

| Severity of Illness       | Clinical Criteria                                                                                     |
|---------------------------|--------------------------------------------------------------------------------------------------------|
| Asymptomatic or presymptomatic | Individuals positive for SARS-CoV-2 using a virologic test (i.e., a nucleic acid amplification test or antigen test), but without symptoms consistent with COVID-19 |
| Mild                      | Individuals with any sign and symptom of COVID-19 (e.g., fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell) but without shortness of breath, dyspnea, or abnormal chest imaging |
| Moderate                  | Individuals with evidence of lower respiratory disease during clinical assessment or imaging and saturation of oxygen (SpO₂) ≥94% on room air at sea level |
| Severe                    | Individuals with SpO₂ <94% on room air at sea level, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO₂/FiO₂) <300 mmHg, respiratory frequency >30 breaths per minute, or lung infiltrates >50% |
| Critical                  | Individuals with respiratory failure, septic shock, and/or multiple organ dysfunction                  |

*National Institutes of Health. COVID-19 Treatment Guidelines: What’s New in the Guidelines. NIH website. https://www.covid19treatmentguidelines.nih.gov/whats-new. Updated October 9, 2020. Accessed October 16, 2020.*
The COVID-19 pandemic continues to take a large toll in North Carolina and across the United States. As we face the uncertainties of a new year with COVID-19, our medical and public health community will need to remain steadfast in our messaging to the public, especially as vaccines become widely available for SARS-CoV-2. In this issue, Dr. Sturgill emphasizes the importance of consistent and accurate public health messaging and patient education, based on scientific and evidence-based resources [41].

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