Initial reports suggest that COVID-19 is associated with severe disease that requires intensive care in approximately 5% of proven infections. Given how common the disease is becoming, as in prior major severe acute respiratory infection outbreaks—SARS (severe acute respiratory syndrome), MERS (Middle East respiratory syndrome), avian influenza A(H7N9), and influenza A(H1N1)pdm09—critical care will be an integral component of the global response to this emerging infection.

The rapid increase in the number of cases of COVID-19 in Wuhan, China, in late 2019 highlighted how quickly health systems can be challenged to provide adequate care. Case-fatality proportions were 7-fold higher for patients in Hubei Province compared with those outside of the region, 2.9% vs 0.4%, emphasizing the importance of health system capacity in the care of patients who are critically ill with COVID-19. This article discusses issues pertaining to regions where critical care units have the capacity to provide mechanical ventilation, acknowledging that this capacity does not exist in many regions and that capacity could be exceeded in many places. This differential ability to manage the disease will likely have a substantial influence on patient outcomes.

Factors Associated With Requiring Intensive Care

Appreciating typical clinical features and disease course are crucial both to prepare for increasing numbers of patients and to determine how to best treat infected persons. Patients who have required critical care have tended to be older (median age ≈60 years), and 40% have had comorbid conditions, commonly diabetes and cardiac disease. Children generally have been observed to experience a milder illness, although perinatal exposure may be associated with substantial risk. The small numbers of pregnant women infected thus far have had a mild course, but limited cases make predictions about disease course uncertain; however, severe illness in pregnant women was a major concern with influenza A(H1N1)pdm2009. The median duration between onset of symptoms and ICU admission has been 9 to 10 days, suggesting a gradual deterioration in the majority of cases. The most documented reason for requiring intensive care has been respiratory support, of which two-thirds of patients have met criteria for acute respiratory distress syndrome (ARDS).

Differentiating From Other Diseases

Given the presence of a number of circulating respiratory viruses, differentiating COVID-19 from other pathogens, particularly influenza, is important and chiefly done using upper (nasopharyngeal) or lower (induced sputum, endotracheal aspirates, bronchoalveolar lavage) respiratory tract samples for reverse transcriptase–polymerase chain reaction and bacterial cultures. There are suggestive but nonspecific radiographic changes, such as ground-glass opacities on computed tomography. Rapid access to diagnostic testing results is a public health and clinical priority, allowing for efficient patient triage and implementation of infection control practices.

Clinical Management and Outcomes

Management of severe COVID-19 is not different from management of most viral pneumonia causing respiratory failure (Figure). The principal feature of patients with severe disease is the development of ARDS: a syndrome characterized by acute onset of hypoxic respiratory failure with bilateral infiltrates. Evidence-based treatment guidelines for ARDS should be followed, including conservative fluid strategies for patients without shock following initial resuscitation, empirical early antibiotics for suspected bacterial co-infection until a specific diagnosis is made, lung-protective ventilation, prone positioning, and consideration of extracorporeal membrane oxygenation for refractory hypoxemia.

In settings with limited access to invasive ventilation or prior to patients developing severe hypoxic respiratory failure, there may be a role for high-flow nasal oxygen or noninvasive ventilation. However, the high gas flow of these 2 techniques is less contained than in the closed circuitry typical of invasive ventilators, which poses the risk of dispersion of aerosolized virus in the health care environment, such as in the setting of a poorly fitting face mask. Determining the magnitude of this risk, and mitigation strategies, is a crucial knowledge gap.

Septic shock and specific organ dysfunction such as acute kidney injury appear to occur in a significant proportion of patients with COVID-19–related critical illness and are associated with increasing mortality.
with management recommendations following available evidence-based guidelines.7

While no antiviral or immunomodulatory therapies for COVID-19 have yet proven effective, a majority of severely ill patients described to date have received numerous potentially targeted therapies—most commonly neuraminidase inhibitors and corticosteroids—and a minority of patients have been enrolled in clinical trials.

While mortality among all infected patients may be in the range of 0.5% to 4%, among patients who require hospitalization, mortality may be approximately 5% to 15%, and for those who become critically ill, there is currently a wide mortality range, from 22% to 62% in the early Hubei Province case series.2–4 The exact cause of death is unclear at this point, with progressive hypoxia and multi-organ dysfunction being the presumed causes. Case-fatality proportions, both among all COVID-19 patients and among severely ill patients, will likely become more precise and generalizable with increased surveillance to better clarify the number of individuals infected and as greater numbers of infections occur around the globe.

Major Knowledge Gaps
COVID-19 is a novel disease with an incompletely described clinical course, especially for children and vulnerable populations. Risk factors for severe illness remain uncertain (although older age and co-morbidity have emerged as likely important factors), the safety of supportive care strategies such as oxygen by high-flow nasal cannula and noninvasive ventilation are unclear, and the risk of mortality, even among critically ill patients, is uncertain. There are no proven effective specific treatment strategies, and the risk-benefit ratio for commonly used treatments such as corticosteroids is unclear.

It is essential to learn as much as possible through observational studies and clinical trials across a breadth of patient populations and care settings. These should incorporate clear measurements of severity of critical illness so that outcomes can be risk adjusted, and use sufficiently common outcome measures to combine data and validly compare observations across regions.8 Ideally, clinical trials should be structured to promote maximum learning from around the world, such as through the use of master protocols or adaptive platform designs.9,10

Conclusions
In a very short period, health care systems and society have been severely challenged by yet another emerging virus. Preventing transmission and slowing the rate of new infections are the primary goals; however, the concern of COVID-19 causing critical illness and death is at the core of public anxiety. The critical care community has enormous experience in treating severe acute respiratory infections every year, often from uncertain causes. The foundation for care of severely ill patients with COVID-19 must be grounded in this evidence base and, in parallel, ensure that learning from each patient is maximized to help those who will follow.

REFERENCES