It is widely accepted that case-fatality rates for COVID-19 increase with age. Age-specific death rates from China, South Korea, Italy and the United States all confirm the association between age and severity of illness. The charts below depict age-specific death rates by age. Note that the US does not report data using the same age ranges as other countries. This information is used to support guidance for vulnerable groups include people 60 years and older (rest of the world) or 65 and older (USA).
Antivirals for COVID-19

No antivirals have been proven effective for the treatment of COVID-19, despite some small-scale studies and media sources that conclude otherwise. A randomized controlled trial of lopinavir-ritonavir (Kaletra) found no significant difference in time to clinical improvement, 28-day mortality, or viral detectability. Studies of hydroxychloroquine and favipiravir reported improvements in time to negative testing for COVID-19, but these studies are too small and have too many limitations to conclude that these drugs are effective. Also, faster time to viral clearance may or may not correlate with better clinical outcomes and improved survival. More research in the form of large-scale clinical trials is needed to draw any conclusions about the use of antivirals for COVID-19. For more information, please see section “Weekly Research Highlights.”

Pediatric COVID-19

Although no pediatric deaths have been reported from COVID-19, studies suggest that children are as likely to be infected as adults and can experience severe illness. In a study of 366 hospitalized children, COVID-19 was detected in 6 patients; of these 6 patients, one child was admitted to the ICU. Another study of 2,143 pediatric patients with confirmed or suspected COVID-19 found that over 90% of children were asymptomatic, mild, or moderate cases (see Table 2). Children of all ages appear susceptible to COVID-19. No significant gender differences have been reported among children with COVID-19.

Weekly Research highlights

Severe Outcomes Among Patients with Coronavirus Disease 2019 - US, Feb 12-Mar 16, 2020 (CDC MMWR, 18 Mar 2020)

Main message: Severe illness leading to hospitalization, including ICU admission and death, can occur in adults of any age with COVID-19. Those under 19 years old appear to have milder symptoms, with almost no hospitalizations or deaths.
2499 patients in the US - fatality is highest in persons over the age of 85 [10%-27%], followed by people aged 65-84 [3%-11%], persons aged 55-64 years [1%-3%], persons aged 20-54 [<1%], and no fatalities among persons under 20. This analysis aligns with data from China.

Limitations to this data include underestimation of outcomes due to missing data in 9-53% of cases; focus on patients for testing was those with severe diseases, leading to overestimation of prevalence of severe disease; comorbidities were not analyzed; limited testing nationally.

**COVID-19 in a Long-Term Care Facility — King County, Washington, February 27–March 9, 2020 (CDC MMWR, 18 Mar 2020)**

**Main message:** COVID-19 can spread rapidly among long-term care facility residents, staff and visitors, so proactive steps must be taken to prevent the introduction and spread of infection in these settings.

- Case study of long-term residential care facility in Washington state resulted in 129 total cases – 81 residents, 34 staff (of all types), 14 visitors; and 23 deaths.
- The most common chronic underlying conditions among facility residents were hypertension (69.1%), cardiac disease (56.8%), renal disease (43.2%), diabetes (37.0%), obesity (33.3%), and pulmonary disease (32.1%)
- Results also found limitations in effective IPC and staff members working in multiple facilities contributed to intra- and interfacility spread.

**Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1 (NEJM, 17 Mar 2020)**

**Main message:** Fomite transmission of SARS-CoV-2 is plausible, since the virus can remain infectious on surfaces – leading to nosocomial spread and super-spreader events.

- SARS-CoV-2 can last on plastics (72hr), stainless steel (48hr), copper (4hr), and cardboard (24hr).
A Trial of Lopinavir–Ritonavir in Adults Hospitalized with Severe Covid-19 (NEJM, 18 Mar 2020)

Main message: Kaletra, an HIV treatment, did not show benefit in very severe COVID-19 patients

■ Randomized controlled open-label trial of 199 laboratory-confirmed hospitalized COVID-19 patients. 99 in lopinavir-ritonavir (Kaletra) group, 100 in standard care group.

■ No significant difference in time to clinical improvement, 28-day mortality or viral detectability.

■ In hospitalized adult patients with severe COVID-19, no benefit was observed with lopinavir–ritonavir treatment beyond standard care. Note that these were very severe COVID-19 patients (22% died vs. ~11-14% death rate in other studies).

Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial (IHU – Méditerranée Infection, 18 Mar 2020)

Main message: Hydroxychloroquine, a drug generally used for malaria, should be further investigated for COVID-19. This study is too small and has too many limitations to conclude its effectiveness for COVID-19 treatment.

■ Clinical trial of 42 laboratory-confirmed COVID-19 patients. 26 in hydroxychloroquine group, 16 other patients. 6 patients from hydroxychloroquine group were lost to follow-up. Results are from 36 patients.

■ At day 6 post-study inclusion, 70% of patients in the hydroxychloroquine group tested negative compared to 12.5% of the other patients. When hydroxychloroquine group was separated into hydroxychloroquine only versus hydroxychloroquine and azithromycin, 100% of patients who received hydroxychloroquine and azithromycin tested negative. Faster time to viral clearance may or may not correlate with better clinical outcomes and improved survival.
Japanese flu drug studied in treating coronavirus (The Guardian, 18 Mar 2020; original article unavailable)

Main message: Favipiravir should be further investigated for COVID-19. This study is too small and has too many limitations to conclude that favipiravir is effective in treating COVID-19.

- Clinical trial of 340 patients in Wuhan and Shenzhen
- Patients who were given favipiravir tested negative after a median of four days compared with a median of 11 days for patients who were not treated with the drug
- X-rays confirmed improvements in lung condition in about 91% of the patients who were treated with favipiravir compared to 62% of those who were not treated with the drug
- Japanese health ministry source suggested that the drug was not as effective in people with more severe symptoms
- Faster time to viral clearance may or may not correlate with better clinical outcomes and improved survival.

Questions of the Week

Should COVID-19 patients avoid NSAIDs (such as ibuprofen)?

Although the French Health Minister advised against the use of NSAIDs for treating COVID-19 patients, others noted that there is no clear scientific evidence that COVID-19 patients need to take any extra precautions for NSAIDs. Later WHO clarified that they were not aware of any negative effects of ibuprofen in COVID-19 patients. In general, NSAIDs can be harmful to older populations, those with kidney disease and other comorbidities. Any existing precautions in taking NSAIDs should still hold.

Does smoking increase the risk of infection from COVID-19?

Smokers incur increased risk of pneumococcal lung disease, influenza, and tuberculosis. The data suggest that smokers were
more likely to develop severe COVID-19. Among Chinese patients diagnosed with COVID-19, the odds of disease progression were 14 times higher among people with a history of smoking compared to those who did not smoke. Additionally, another study showed that in China, men are more likely to die from COVID-19 than women. This trend could potentially be explained by the higher smoking rates among men in China. Smoking rates in China during 2018 were estimated at 49.9% in men vs 2.1% in women, according to the WHO. In addition, waterpipes and mouthpieces have been implicated in past outbreaks of other respiratory diseases. The WHO Framework on Tobacco Convention and Control (FCTC) recommends banning the use of waterpipes in all public establishments and avoiding sharing waterpipe mouthpieces at home.

**Should anti-hypertensive medications in the Renin-Angiotensin System inhibition class (angiotensin converting enzymes and angiotensin receptor blockers) be avoided because of the risk of COVID-19?**

Angiotensin Converting Enzyme inhibitors (ACEis) and Angiotensin II Receptor Blockers (ARBs) are standard antihypertensive agents and also recommended treatments for chronic kidney disease, coronary heart disease, or heart failure with reduced ejection fraction. Recently, researchers hypothesized that patients taking ACEis or ARBs may be at risk for more severe COVID-19 illness because of ACE2 upregulation (ACE2 is a likely binding site for the virus that causes COVID-19 disease). A different set of researchers suggested the opposite: that these medications may be protective against COVID-19 and are potential treatments of the infection. Neither hypothesis has any empirical evidence to support it at this time. Randomized controlled trials are currently in development. Hypotheses about ACEi/ARB and COVID-19 risk are a cause for further study, but not for changing treatment of patients who are taking, or who have indications to begin taking these medications.