RESOLVE TO SAVE LIVES

Vital Strategies

COVID-19

# Weekly Science Review

# June 20-26, 2020

This weekly science review is a snapshot of the new and emerging scientific evidence related to COVID-19 during the period specified. It is a review of important topics and articles, not a guide for policy or program implementation. The findings captured are subject to change as new information is made available. We welcome comments and feedback at **covid19-eiu@vitalstrategies.org**.

IN-DEPTH TOPICS:

## Reopening schools during the COVID-19 pandemic

This week we examine important considerations for deciding how to reopen schools more safely during the Coronavirus Disease 2019 (COVID-19) pandemic. This includes assessing and reducing the risk of COVID-19 for students and adults in schools, the impact of school closures on overall disease spread, experiences opening schools from around the world, and how to reopen schools as safely as possible.

# Susceptibility, severity of illness and transmission of COVID-19 in children

**Main message:** Based on the best evidence currently available, children may be somewhat less likely than adults to get COVID-19, are definitely much less likely to become severely ill if they do get it, and appear to be less likely to spread the virus that causes COVID-19, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), to others than adults are. However, children of all ages have been diagnosed with COVID-19 and, although rare, some have become severely ill and a small number have died. Measures to reduce children's risk include making sure they wash their hands, physically distance themselves from others outside the household, and wear face coverings when appropriate.

To advocate for reopening schools, it is necessary to first establish ways to make students and staff safer within in-person school settings. Though many unknowns remain, it is possible to draw some conclusions from the best science and data currently available about infection dynamics in children.

## Susceptibility of children to COVID-19

Susceptibility refers to how likely children are to get COVID-19. It is distinct from severity of illness, which is how serious the infection can be, although the two may be difficult to separate in some instances. For reasons that are not perfectly understood, **some viruses cause varying rates of infection** for different age groups. One unproven theory is that **recent respiratory infections**, such as colds, that are sometimes more common in children, may provide some "crossover" protection.

There are three main ways to learn which age groups may be more or less susceptible to COVID-19. One way is to analyze the number of cases that occur in different age groups. The second is to look at population studies testing representative samples, which can provide more accurate infection rates. The third is to evaluate contact tracing studies and determine the secondary attack rate after similar exposures to an index case.

### Case incidence is lower in children

Looking at case incidence alone, the infection rate among children is significantly lower than those among both young and older adults. The U.S. CDC reported in a **recent Morbidity and Mortality Weekly Report (MMWR**) that in the U.S., from January 22 to May 30, 2020, only 1.5% of confirmed COVID-19 cases were among those 0-9 years of age, and 3.7% were among those 10-19 years of age. Taking the proportion of people in the U.S. that make up these age groups into account, the overall incidence of COVID-19 cases was 51 per 100,000 population among children 0-9 years old and 118 per 100,000 among those 10-19, compared to 492 per 100,000 among those 30-39 years old and 902 per 100,000 among those over 80 years old. **Another MMWR**, from April 2020, focused specifically on patients under 18 years old and showed that nearly a third of cases under 18 were 15-17 years old, with younger children less likely to be affected. These data show that children make up a much smaller fraction of those being diagnosed with COVID-19. Reports from other countries follow similar patterns. A lower rate of reported COVID-19 among children, however, does not mean a lower rate of infection. Children may be more likely to have asymptomatic or milder disease and therefore may be less likely to be tested for and identified as having COVID-19. In addition, children may have also been shielded from infection after school closures, although **age-dependent modeling data** suggests that this alone does not account for the lower incidence of cases in children.

### Population studies support lower susceptibility

Data from population studies that test for either active infection or antibodies indicating previous infection can be

revealing. There are early data from these types of studies to support the hypothesis that children are less susceptible to COVID-19. In Iceland, which has tested 15% of its total population for active infection, **children were half as likely to be infected as adults** in both targeted and general population testing. In Iceland's general population screening, no children under the age of 10 tested positive, despite nearly 1% of the overall sample testing positive. Looking at seroprevalence studies involving antibody testing, **a study from Switzerland** showed that children 5-9 years old were one third as likely to have a positive antibody test as adults 20-49 years old. The difference in antibody positivity rate between 10-19 year olds did not reach statistical significance when compared to adults 20-49 years old. Other population antibody studies, from **Spain** and the **Netherlands**, have also shown a significantly lower seroprevalence among those younger than 20 years old. Data from some studies, such as this study from the **United Kingdom**, show no difference in positivity rates between adults and children. Nevertheless, most results suggest lower seroprevalence and incidence of active infection among children. A number of population studies are ongoing and will continue to produce additional insight.

**Contact tracing suggests lower susceptibility**

There have been several published and preprint studies on results from contact tracing efforts. The most recent **study from China** showed that those under 20 years old had less than one quarter the odds of contracting COVID-19 from an infected household member compared to older adults. A **preprint systematic review and meta-analysis** analyzed six other studies from China and one each from Australia, Taiwan and Japan. In the meta-analysis, children and young people under 20 years old had about half the odds of contracting COVID-19 compared to adults. Some of the studies showed no difference in infection rates between adults and children after exposure to an infected person, but the overall results point to lower susceptibility in children and young people under 20. There were no studies showing higher susceptibility among children or young people.

The current evidence suggests that children, and especially young children, are less susceptible to COVID-19 than adults.

# Severity of COVID-19 infection in children

Of the three—susceptibility, severity of illness, and transmission—the lower severity of illness among children has the strongest supportive evidence base. Severity of illness can be measured by looking at the number of patients in a given age group requiring hospitalization or intensive care unit (ICU) admission, or who die from COVID-19, as well as looking at the proportion of patients reporting asymptomatic or mild disease.

**Hospitalization, ICU admission and death are less common for children with COVID-19**

Hospitalizations, ICU admissions, and deaths have been consistently less common among children than among adults in the U.S. and elsewhere. The **United States Centers for Disease Control and Prevention (CDC) reports** that rates of hospitalization and ICU admission are lower among children than among adults. Underlying health problems remain a significant contributor to more severe disease among children with COVID-19.

It is conceivable that children presenting to hospitals with COVID-19 may be more likely to be admitted due to a lower threshold to admit and monitor this vulnerable population in the hospital. Accounting for such a bias would likely show even lower severity of illness among infected children. A small minority of cases in children have resulted in death. In the U.S., the pandemic has affected at least 2.5 million and killed more than 125,000 people, yet the number of deaths in those under age 15 **remains very low—less than 30 as of June 20, 2020—** with underlying conditions playing a central role in these relatively isolated poor outcomes.

### Asymptomatic or mild COVID-19 is more common in children

Higher rates of asymptomatic or mild infection among children **have been observed for other respiratory infections**, including **severe acute respiratory syndrome (SARS)**. In most countries, limitations on testing asymptomatic people preclude greater insight into the true proportion of asymptomatic SARS-Cov-2 infections among children and into whether the proportion of asymptomatic cases is higher among children than adults. Nevertheless, data on the small numbers of more severe cases shows that there is a larger proportion of asymptomatic or mild infections among children than adults. **A systematic review and meta-analysis** looking at the best evidence available through mid-April determined that up to 80% of infected children had mild disease, and other individual studies continue to show that children are more likely to experience milder, if any, symptoms. There is general consensus, based on accumulating evidence, that children are less likely to suffer severe illness from COVID-19.

### Multisystem inflammatory syndrome in children (MIS-C)

Health authorities continue to collect information on cases of MIS-C, which has been temporally associated with COVID-19 and is potentially a delayed immune complication of COVID-19 in children and those under 21 years old. Fortunately, cases remain exceedingly rare, affecting two per 100,000 compared to COVID-19 infection which affects 322 per 100,000 for the same age group. Among those who are diagnosed with MIS-C, outcomes remain good despite high severity of illness. The newest information on MIS-C is discussed further in the FAQ section below.

Although children of all ages have contracted COVID-19, the illness is much less likely to be severe in children than in adults.

# COVID-19 transmission by children to others

Higher social contact rates among children have been the basis for school closures to reduce influenza transmission during epidemics. The key to this justification is grounded in the role that children play in transmitting influenza to others. In prior epidemics of respiratory illness, including the flu, whooping cough and others, children have been identified as the main drivers of infection transmission. The same may not hold true for COVID-19, which would remove, during the COVID-19 pandemic, a major rationale that has supported school closures for influenza and other infectious diseases.

**Tracing and testing reports support lower transmissibility from children**

Currently, limited evidence suggests that children may play a smaller role in transmission of COVID-19 than adults. There are several reports to support this assertion, including tracing secondary infections when children are known to be the index case. In an **early study from France** describing a cluster of COVID-19 cases linked to a hotel in the French Alps in February, a 9 year old child who contracted the disease from an adult index case at the hotel subsequently visited three schools and a ski training class. The child accumulated more than 172 contacts while symptomatic, all of whom were contacted. Of the 73 contacts who were tested because they had symptoms or higher-risk exposure, only one tested positive for SARS-CoV-2. **Another tracing and testing report from Australia** showed that an investigation of 735 classmates and 128 school staff did not identify any infected staff members among the 30% tested and identified only two students who may have been infected as a result of school exposure.

Other studies have indicated that children are more likely infected by their parents or other adults in the household rather than the reverse. In **one study from Germany**, evaluation of transmission chains showed that 81% of children with COVID-19 were most likely infected by a parent. There is also evidence

from the U.S. gathered in **daycare facilities that have remained open throughout the pandemic**. Though not scientific studies, the YMCA and New York City Department of Education, which have served tens of thousands of children and thousands of staff, have not yet reported any clusters or outbreaks.

The data on transmission of COVID-19 from children are limited, and there are reasons to remain cautious: the amount of virus detected in infected children has been shown to be similar to that in adults, and the amount of virus detected in asymptomatic people has been shown to be similar to that in symptomatic patients.

# The role of school closure in controlling COVID-19 transmission

**Main message**: Schools around the globe closed in response to the COVID-19 pandemic. The impact of this measure on reducing transmission was probably smaller than many of the other public health and social measures deployed at the same time. In a growing number of countries, schools are reopening, often with some limitations and largely without, thus far, appearing to have caused increases in new cases. Schools have rarely been the sites of outbreaks or contributed substantially to COVID-19 transmission. Careful preparation and planning for localized closures may be necessary for some time.

Closing schools can reduce transmission of some respiratory infections, and has been considered an effective tool in previous influenza outbreaks and epidemics. There is even a suggestion that **implementing this measure early** in a local influenza epidemic can be more effective. During the **1918 Spanish influenza** pandemic, local decisions about school closure varied; some cities proactively closed schools and

others kept them open as long as possible. In St. Louis, where officials closed schools before the epidemic peaked and kept them closed for 143 days, the mortality rate was only one third of that in Pittsburgh, where leaders reactively closed schools well after the epidemic peak and reopened them just 53 days later. Compiling such experiences and drawing lessons relevant to the COVID-19 situation can be misleading because of differences between transmission and other interventions from setting to setting. In addition, the transmission dynamics of coronaviruses, including the virus that causes COVID-19, are different from seasonal or pandemic influenza. Schools in affected parts of China were not closed until relatively **late into the SARS epidemic in 2003**, and this action did not appear to have affected the epidemic curve. A **systematic review** completed in 2014 concluded that school closing can contribute to reducing transmission of infections to which children are as easily infected as adults and for which the basic reproduction number ($R_0$) is only moderately high ($R_0$<2.0); the basic reproduction number is the average number of people infected by each infected person. These conditions do not appear to hold for COVID-19. **A rapid review** published in April estimated that school closing alone could be expected to reduce COVID-19-related mortality by only 2% to 4%. Other public health and social measures targeting adults more broadly are likely to be much more effective at controlling COVID-19 and should also be in place.

Despite these observations, many schools in the U.S. and around the world have been closed in the context of the COVID-19 pandemic. The United Nations Educational, Science and Cultural Organization **(UNESCO) reported that as of June 26, 144 countries** still had nationwide school closures in place as part of their response to the COVID-19 pandemic. Combined with subnational and local actions, school closure affects more than 67% of students worldwide at this time of this writing. **Sweden stands out** as one country considerably affected by COVID-19 in which day care centers and primary schools remained open for children up to age 15. The move was part of a **controversial strategy** to avoid the strict lockdowns that had been implemented elsewhere. Keeping schools open was justified on the basis of evidence that children are less likely to

be infected, become severely ill, or transmit SARS-CoV-2. Over a period of two months during the epidemic **in Stockholm, very few children** were identified with SARS-CoV-2 infection, and the cumulative incidence of hospitalization for COVID-19 illness in children was only 9 per 100,000, which was 25 times lower than for adults. Similarly, there was no evidence that schools contributed to transmission among students, teachers or the general population. However, the bold strategy designed to avoid the effects of a strict and comprehensive package of public health and social measures **likely contributed to higher case numbers and fatalities in Sweden** compared to neighboring countries.

Over the past two and a half months, schools have reopened to varying degrees in more than 75 countries. Many are resuming on a limited basis and with specific preventive measures in place. **Denmark** and **Finland** were among the first European countries to reopen schools, in mid-April and May, respectively. Media reports and case counts confirm that both countries have continued to control transmission since taking this step. In an increasing number of countries where cases were already trending downward before schools reopened, there is **no evidence of a resurgence** associated with reopening. In several countries, however, reopening was followed by highly publicized closures of individual schools in response to cases or significant risk of exposure among staff or students. In South Korea, many schools reopened in late May. Days later, **251 schools near Bucheon, South Korea, closed again** after an outbreak was detected at an e-commerce distribution site in that community. In South Africa, schools reopened even though case counts were still climbing. Two weeks later, **61 of the 1,509 schools in the Western Cape Province were closed temporarily** to allow for contact tracing and disinfection. These school closures were prompted by individual cases, small clusters, or community-wide outbreaks. Transmission among students or between students and staff has only rarely been documented.

Nonetheless, schools can be sites of significant transmission. In Israel, s**chools began to reopen** in early May and by May 17, all limitations on class size were lifted. On June 1, a sizable

outbreak was identified, linked to **a single secondary school outside Jerusalem** where 116 students and 14 teachers were infected. The epidemiology of this outbreak has not been published, and it is unclear whether students were significant sources of transmission. In any case, this school-based outbreak contributed to further spread in the surrounding community. These experiences suggest that schools can be reopened cautiously, particularly those that enroll young children. In a **recent preprint article**, investigators conclude that large scale reopening of schools in settings where community transmission is relatively low (such as Norway and Denmark) can be accomplished while controlling or suppressing the epidemic. However, school reopening could contribute to increasing the epidemic growth rate in countries where community transmission is relatively high (such as Germany). Education and public health authorities should carefully consider the risks and potential benefits of schools reopening in their communities. Specific considerations, some of which are described below, might further reduce the relatively low risk of transmission within schools. Above all, **close surveillance** and **planning for how to respond** when cases occur among staff, students and the broader community, including criteria for closing schools on an individual or local basis, should be applied to further minimize the risk.

# Potential impacts of school closures due to COVID-19 and how to reopen schools safely

**Main message**: School closures due to COVID-19 have had major negative effects on students, educators, families and communities. In the United States, there is a national conversation about how schools can reopen safely for the 2020-2021 academic year. Some guidance is available from federal and state public health authorities as well as from expert professional societies within and outside of the U.S. Many countries have reopened their schools to at least some degree,

providing examples of various approaches to educating students while reducing the potential for the spread of COVID-19. There will be significant economic costs associated with the safer reopening of schools which should be balanced against the educational, social and other costs of keeping schools physically closed.

**Potential impacts of school closures due to COVID-19**

Worldwide, it is estimated that at their peak, school closures due to COVID-19 **affected 90% of the world's student population, or 1.6 billion students in 194 countries.** In the U.S., K-12 school closures were mandated in 48 states, the District of Columbia, and all five permanently inhabited U.S. territories. This is estimated to have resulted in the **closure of 124,000 schools, affecting 55.1 million students**. A minority of states have not mandated closure or have already lifted closure orders. In Montana and under the Bureau of Indian Education, school closures are determined at the district level, and in **Idaho**, schools have been allowed to seek district approval to reopen. In the vast majority of states, schools have been ordered closed through the end of the 2019-2020 academic year.

School closures have significant negative impacts on education. Data on changes in scholastic performance due to absenteeism, summer vacation, and weather- or disaster-related school closures inform assessments on the impacts COVID-19-related school closures may have. Some **models suggest that elementary and middle school students could return to school in fall 2020 with a 30% reduction** in learning gains in reading from the prior year compared to a typical school year, and that learning gains in math could be even further reduced. School closures are likely to increase performance gaps between high- and low-achieving students. During summer closures, high-achieving students tend to maintain or even improve their performance while low-achieving students tend to fall further behind. Although such predictions may not be fully borne out if distance learning has allowed students to keep up, a **national survey of 1,720 educators** suggested that more than one fifth of students are

not participating in distance learning, and that truancy rates are highest in the poorest communities, among students who may have the greatest educational needs.

Another **analysis has suggested that learning loss will likely be greatest among low-income, Black and Hispanic students**, with these students falling behind by up to one year of educational time. On a global scale, **experience with other health emergencies** has shown that the impact on education is most devastating in countries with the poorest learning outcomes. During the **ebola epidemic in Sierra Leone, school closures were associated with increased rates of teen pregnancy** which, in turn, reduced the likelihood of girls returning to school after the epidemic. There are other potential **adverse consequences of school closure**, including unintended **strain on the healthcare system due to child care responsibilities of healthcare workers**, mental health effects on students and parents, increased social isolation of students, gaps in child care in homes with working parents, increased child exposure to violence, and lack of access to adequate nutrition for students who rely on school meal programs. Such consequences can have direct negative impacts on scholastic performance and also indirectly augment learning losses; the negative impacts of stress and poor nutrition on learning are well documented.

**Guidance on the safe reopening of schools**

The national conversation on schools in the U.S. has now focused on how they may reopen safely and effectively. Dr. Anthony Fauci, Director of the National Institute of Allergy and Infectious Diseases at the National Institutes of Health and a member of the White House Coronavirus Task Force, has indicated that **school reopening decisions should be based on regional COVID-19 statistics** and that creative modifications to the standard school environment and schedule may be necessary. To guide the safe reopening of schools in the U.S., recommendations have been published at the federal level and by some state departments of public health and/or education. At the federal level, CDC recommends that jurisdictions consider reopening **child care programs** and

**schools** if reopening is consistent with state or local orders, there are mechanisms to protect children and employees at risk of severe illness, and there is capacity to screen all students and employees for symptoms and a history of exposure upon arrival at school. If child care programs or schools reopen, the CDC offers **guidance for administrators on how to plan, prepare and respond to COVID-19**. Recommendations are divided into four scenarios: if a person confirmed to have COVID-19 enters the school, if there is no community transmission, if there is minimal to moderate community transmission, and if there is substantial community transmission. Topics covered include triggers for school dismissal, teaching healthy hygiene habits to students, disinfecting surfaces in the school, monitoring and planning for absenteeism, and strategies for continuing education and other support programs for students in the event of further closures. Many state-issued guides, such as the one from the **California Department of Public Health**, reference CDC guidance and cover similar topics but in greater methodologic depth, with suggestions of specific actions to help achieve a list of goals. In collaboration with medical and public health experts, the **Massachusetts Department of Elementary and Secondary Education** has developed guidelines that are a mix of recommendations and requirements. To avoid interruptions in learning, Massachusetts districts and schools will be required to submit reopening plans that address three possible scenarios: full in-person education with new safety requirements, a hybrid of in-person and remote education, and continuation of remote education. Some states emphasize the practicalities of formulating and executing a school reopening plan at the local level. For example, the **Pennsylvania Department of Education** stipulates that each school create and publicly post a reopening plan that includes specific elements, and secure approval of the plan from the school's governing body before reopening. Other states, such as Texas, have yet to publish guidelines.

Some guidance on how to reopen schools safely is available from expert/professional societies. The **American Academy of Pediatrics** (AAP) has suggested factors that should be considered when schools reopen. Considerations include

issues touched upon in other guidance documents, including the importance of addressing students' mental health issues. Additional suggested considerations include: anticipation of lost educational time and appropriate adjustment of instructional plans so that further stress is not put on students; the creation of an individual educational plan for each child with a disability in order to compensate for lost instructional time and support services; and limited extensions for families to submit required public health-related paperwork (such as vaccination records) given potential delays in accessing routine care during the pandemic. Outside the U.S., German pediatric, infectious disease and public health societies have published **recommendations for the reopening of German schools without "excessive" restrictions**. These recommendations include several departures from U.S. federal guidance. One is the suggestion that if someone with an elevated risk of severe COVID-19 lives in the same household as a school-age child, that an individualized safety plan be developed in consultation with medical experts. Another is the recommendation that an individual confirmed COVID-19 case within a school should not lead to closure of the entire program, but instead to a detailed analysis of the chain of transmission and a balanced approach to infection control. Another is the stipulation that children over the age of 10 wear face masks when out of their assigned classroom seats.

**What schools that have reopened have done**

As schools have reopened in many countries, varying measures have been put in place to reduce the potential for the spread of COVID-19 in and outside schools. Initial reopenings have commonly included only a subset of students. In many countries, the youngest children have gone back to school first. Rationales for this include difficulty engaging young students in distance learning, an effort to unburden caregivers at home, and evidence that the risk of severe COVID-19 illness may be lowest in the youngest school-aged children. **In many European countries, students in "key transition years**," including those in their final years of primary or secondary school, have returned to school as well. In China and South

Korea, students in their final year of secondary school returned to school first.

The **health and safety guidelines introduced in different countries** have been varied. Many countries have implemented temperature checks for staff and students on arrival. Class size has been reduced in some countries but not in others; in some schools, **physical barriers have been set up around desks**. Students are sometimes required to wear masks. Efforts to avoid people congregating include staggered start and end times of the school day, designated doors for entrance and exit, **unidirectional hallways**, teachers rather than students switching classrooms, and meals served in classrooms rather than in cafeterias. There has been fairly uniform implementation of hygiene measures such as frequent hand-washing. Staggered schedules, under which students attend school in-person or online depending on the day, have allowed schools to reduce class sizes while continuing to teach all students. This has been adopted in **Germany and France** and is recommended for consideration in the U.S. The **Department of Education in the United Kingdom** has recommended assigning a small group of students to each other and to one teacher, keeping the group together throughout all learning and play activities, and disallowing mixing between groups. In a number of countries, parents have been **allowed to opt to keep their children home**.

**Educational and economic impacts of reduced class size**

Physical distancing is a primary measure to reduce the spread of COVID-19. If physical distancing is to be practiced within schools, the number of students in each classroom must be limited. Such measures may have educational advantages. A number of studies have **examined the relationship between reduced classroom size and student achievement.** One of the most influential studies, conducted in Tennessee in the 1980s, showed that reducing large class sizes increased student achievement by an equivalent of at least one additional month of schooling. Students whose scholastic performance typically lags behind that of their peers **may benefit the most from reduced class sizes**. There are **significant economic costs**

associated with reduced class sizes. However, these are just some of the staggering costs associated with reopening schools safely and effectively during the COVID-19 pandemic. The costs associated with reducing class sizes may be worth the benefits of keeping students, school employees and communities safe in some epidemiologic scenarios.

# FAQs

## How can individual students reduce their risk of infection once back in school?

To keep everyone safe once back in school, the actions and precautions of individual students and school staff form part of a multipronged approach which also includes action on the part of local governments, school administrations, parents and caregivers. Common sense steps include staying home when feeling ill and promptly asking to go home if symptoms develop while at school. As always, frequent and thorough hand-washing is of utmost importance. Respiratory etiquette is also important, including covering coughs and sneezes in the crease of the elbow or a tissue when possible, followed by hand-washing. Students should also be reminded to avoid touching their faces with their hands. While students may be accustomed to sharing items in school such as books and art supplies, these practices should be discouraged or eliminated. Students should not share personal items such as cups or eating utensils. Students should avoid touching other students, including when on the playground. Individual schools may have additional guidance based on their specific context and situation, including recommendations or requirements on masks and face coverings.

## What more have we learned about multisystem inflammatory syndrome in children (MIS-C)?

In April, reports began to emerge from several countries hard-hit by COVID-19, regarding a **Kawasaki-like inflammatory syndrome** in children that appeared to be related to COVID-19. Public health authorities have continued to monitor MIS-C (also called pediatric inflammatory multi-system syndrome, or PIMS, in some countries), which can present with various symptoms including fever, rash, abdominal pain, diarrhea or fatigue. A **recent article in the *New England Journal of Medicine*** (*NEJM*) reviewed 186 cases of MIS-C admitted to participating hospitals in the U.S. from March 15 to May 20, 2020. Most cases (85%) occurred in children under 15 years old. During hospitalization for MIS-C, the majority of cases (70%) tested positive for either SARS-CoV-2 or antibodies to the virus indicating prior infection. The remainder (30%) had a known link to a contact that was diagnosed with COVID-19 within the month prior to the MIS-C diagnosis. This strengthens the evidence that MIS-C may be related to COVID-19 infection. In 14 of the patients, there was documentation of previous COVID-19 infection occurring 5-51 days before MIS-C diagnosis, with a median of 25 days between COVID-19 diagnosis and MIS-C diagnosis. Most patients (80%) required ICU admission during their hospitalization for support of the heart and lungs, and 4 patients (2%) died. Unlike those at risk for severe illness from COVID-19 alone, most of the patients (73%) hospitalized for MIS-C did not have previous underlying health conditions. Overall outcomes were very good using established treatments for shock and other inflammatory conditions that occur in children such as Kawasaki's Disease. A **second recent article**, also published in the *NEJM* describes similar data from a series of 95 patients in New York State. **This new research** adds to a growing body of evidence that MIS-C is an uncommon but potentially life threatening syndrome in children that has emerged during the COVID-19 pandemic. The new data further support a link to SARS-CoV-2 infection. Further research is being conducted to better understand why some children are affected by MIS-C while others are not. These patients will also need to be monitored after recovery for the possible late complications. The best way to prevent this potential delayed immune complication in children is to take common-sense measures to prevent COVID-19 infection, including the three Ws: wearing masks, washing hands, watching distance.

## Who is at increased risk for severe illness from COVID-19?

This week, the CDC updated its **guidance** for people who need to take extra precautions because they are at increased risk for severe illness from COVID-19. This new guidance says the risk for severe disease steadily increases with age, instead of saying that people ages 65 and over are high risk in comparison with those under 65 years of age. Pregnant women appear to be at higher risk of being hospitalized and needing a ventilator but not of dying, based on a **study** of more than 8,000 pregnant women. The guidance also **clearly outlines** the latest evidence on underlying medical conditions that increase a person's risk of severe disease. The strongest and most consistent evidence shows that these conditions include heart conditions, chronic kidney disease, chronic obstructive pulmonary disease (COPD), obesity (body mass index, or BMI, > 30; previously, 'severe obesity,' or BMI > 40 was listed), sickle cell disease, solid organ transplantation and Type 2 diabetes mellitus. There is mixed or limited evidence that other conditions such as asthma, hypertension and liver disease increase risk for severe disease. A recently published non-peer reviewed publication from South Africa suggested a **modest increase in risk of death from COVID-19** among HIV-infected individuals. The CDC guidance is a living document, and will be updated as understanding of the science around COVID-19 evolves.

# Weekly Research Highlights

## Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections

(Nature Medicine, June 18, 2020)

**Main message:** Among COVID-19 patients, those who are asymptomatic have longer durations of viral shedding and less

robust inflammatory responses compared to those who are symptomatic. A high proportion of recovered COVID-19 patients, both symptomatic and asymptomatic, have significantly decreased levels of immunoglobulin G (IgG) and neutralizing antibodies within two months of infection.

- The Wanzhou District Centers for Disease Control and Prevention conducted polymerase chain reaction (PCR) screening among 2,088 quarantined contacts of confirmed COVID-19 cases. Those who tested positive were admitted to a government-designated hospital for centralized isolation. All were monitored for symptoms. Those who were asymptomatic were age-, sex-, and comorbidity-matched with mildly symptomatic COVID-19 patients. Antibodies were measured to characterize the immune response and cytokines were measured to characterize the inflammatory response. Patients were followed through the early convalescent phase, defined as eight weeks after hospital discharge.
- A total of 178 contacts of COVID-19 cases tested positive for SARS-CoV-2 before April 10, 2020. Thirty seven (21%) of those who tested positive had no symptoms during the 14 days prior to testing and did not develop symptoms during hospitalization. The median duration of viral shedding was 19 days in asymptomatic individuals and 14 days in symptomatic individuals, a difference that was significant. Asymptomatic individuals had a reduced inflammatory response compared with symptomatic individuals. Approximately three to four weeks after exposure, 81.1% (30/37) of asymptomatic patients and 83.8% (31/37) of symptomatic patients tested positive for IgG. During the early convalescent phase, among asymptomatic individuals, 93.3% (28/30) and 81.1% (30/37) had reductions in IgG and neutralizing antibody levels, respectively, compared to 96.8% (30/31) and 62.2% (23/37) of symptomatic individuals. The median percentage of decrease in IgG level was 71.1% in the asymptomatic group versus 76.2% in the symptomatic group. In the early convalescent phase, 40.0% (12/30) of asymptomatic

individuals and 12.9% (4/31) of symptomatic individuals became seronegative for IgG.

- The proportion of asymptomatic patients observed may be different from the general population because those identified were at high risk for infection. A longer duration of viral shedding does not necessarily equate with a longer duration of infectiousness or even the presence of viable virus; only PCR testing and not viral culture were performed. Research on the correlates of immunity to SARS-CoV-2 and how to measure immunity continues to evolve.

## Black Lives Matter Protests, Social Distancing, and COVID-19

(National Bureau of Economic Research, June 2020)

**Main message:** In recent weeks, mass protests across the U.S. and around the world prompted concern that these gatherings could increase the transmission of SARS-CoV-2. Data from 315 cities indicate that stay-at-home behavior increased following the onset of the protests. There is no evidence to date that rates of COVID-19 cases increased faster in the three weeks following the start of the protests. The behavior of non-protesters was unanticipated or underestimated in public statements about the potential for the protests to lead to increased COVID-19 cases.

- Researchers evaluated mobile phone tracking data from SafeGraph and local COVID-19 reporting data from May 15 to June 20, 2020, for 315 large urban areas in the U.S. where protests inspired by Black Lives Matter occurred.
- Mobility data showed that a greater proportion of people stayed home after the start of the protests on May 25, compared to before that time. Stay-at-home behavior increased to a greater extent in communities where protests were persistent and accompanied by media reports of violence. The authors conclude that non-protesters increased their stay-at-home behavior. The mobility decline

was more extensive than could be explained by the effect of curfews alone.

- Trends in the daily growth of confirmed cases did not appear to increase following the onset of protests in all but one community. Researchers made appropriate statistical comparisons before and after the protests in each community, as well as between counties where protests began earlier, counties where protests began later and counties with large cities where protests did not occur. However, it is possible that increased transmission related to protests may have occurred but has not yet become apparent.

## Effect of Dexamethasone in Hospitalized Patients with COVID-19 – Preliminary Report

(MedRxIV, Preprint, June 22)

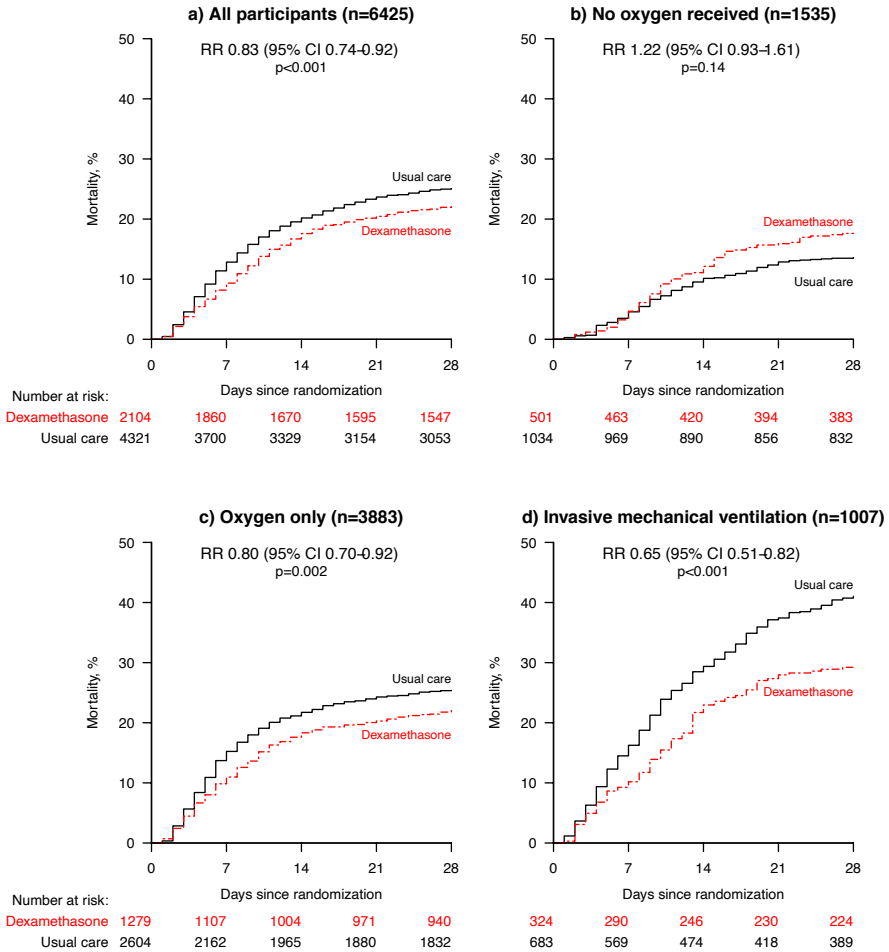
**Main message:** Dexamethasone, a corticosteroid medication, reduced death from COVID-19 in patients needing a ventilator by one third and in patients requiring other oxygen support by one fifth. Dexamethasone did not reduce the risk of death in those not needing a ventilator or other oxygen therapy. The preliminary data in this paper show that by using dexamethasone, one death may be prevented for every eight patients with COVID-19 on a ventilator and every 25 patients receiving other oxygen therapy.

- This ongoing randomized controlled trial, called the RECOVERY trial, is evaluating dexamethasone as well as other potential therapies for suspected or confirmed COVID-19 cases. Researchers are looking at the effect of dexamethasone compared to usual care in patients hospitalized with varying levels of oxygen support. In this preliminary report, there were 6,425 participants: 1,007 receiving oxygen support through a ventilator, 3,883 receiving other oxygen support, and 1,535 not requiring oxygen support. Through 2:1 randomization, 4,321 patients

were allocated to the usual care group and 2,104 patients were allocated to the dexamethasone group.

- For patients on a ventilator, the relative risk for 28-day mortality was 0.65 among those receiving dexamethasone compared to those receiving usual care. For patients receiving other oxygen support, the relative risk for 28-day mortality was 0.80. There was a greater benefit seen in patients recruited after one week of illness, which is thought to be the start of the inflammatory phase of illness. There was no benefit from dexamethasone in patients not receiving oxygen therapy, and the data suggested potential harm in this group, although results were not statistically significant. Among patients requiring mechanical ventilation or supplemental oxygen, subgroup analysis was not reported to indicate whether the timing of dexamethasone later in the course of illness was associated with improved outcomes.
- This study did not analyze laboratory inflammatory parameters or viral load markers to potentially correlate the measured benefit to these values. The study is ongoing, and the results in this preprint article were preliminary and have not yet been subject to peer review. It is possible that the major benefit of dexamethasone treatment may be later in the course of illness, when inflammatory responses may worsen patient illness; the optimal time course of administration of dexamethasone is not known.

## 28 day mortality in all patients (panel a) and seperately according to level of respiratory support received at randomization (panels b-d)

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