



PINNACLECARE



Medical Intelligence Report

Date: October 11, 2021

KeyBank, NA, or its affiliates ("Key") is providing these materials for informational purposes. Key has not reviewed the materials for accuracy or completeness, and the studies and research referenced may change as more information becomes available. The material is not intended as medical advice. Please consult your personal health provider if you have any questions or concerns about any symptoms you or a member of your family are experiencing and before starting any treatments discussed in the materials. Pinnacle is not an affiliate of Key. This material should in no way be considered to be a solicitation by Key for business on behalf of Pinnacle, or an endorsement of Pinnacle. Key makes no representations regarding the suitability or otherwise of the products or services provided by the Pinnacle. Any opinions, projections, or recommendations contained herein are subject to change without notice and are not intended as individual investment advice. This material is presented for informational purposes only and should not be construed as individual tax or financial advice. KeyBank does not give legal advice.

Investment products are:

NOT FDIC INSURED • NOT BANK GUARANTEED • MAY LOSE VALUE • NOT A DEPOSIT • NOT INSURED BY ANY FEDERAL OR STATE GOVERNMENT AGENCY



Topic: COVID-19 Research Update



COVID-19 and the Upcoming Flu Season

Researchers and public health officials have been extrapolating how the return to colder weather will affect the rate of transmission of SARS-CoV-2 as well as the other respiratory diseases that are more prevalent in the winter (Branswell, 2021). While there have been large gains in the understanding of transmission and the life cycle of SARS-CoV-2, there are still many unknowns regarding the length of immunity from both vaccination and infection as well as to the ability of the virus to continue to mutate. The timing of availability of a vaccine for children under the age of 12 also affects the predictions for the upcoming months.

The current surge from the spread of the Delta variant has shown signs of lessening. Different experts cite different reasons for the reduction in the number of new cases. The level of vaccination in the United States is relatively high with approximately 56% of the entire population completing vaccination, and approximately 30% of the United States population have had COVID-19 and should be immune to reinfection (Washington Post, 2021 and Sen et al., 2021). There is overlap between the two groups because it is recommended that individuals who have had COVID-19 also get vaccinated, and estimates suggest that the **combined level of immunity from vaccines and infection is around 64% in the United States.**

Cécile Viboud, an infectious diseases epidemiologist at the National Institutes of Health's Fogarty International Center, and her research group have performed nine models of the level of new cases over the next few months.

She predicts that “by the end of November, the Delta wave will have waned and new cases will be down” to levels similar to those in June and July, 2021.

Dr. Viboud stated that the models from her group suggest a lowered rate due to the increasing immunity in the population (Branswell, 2021). The “lowering” in the number of new cases is predicted to be between 7,500 and 15,000 per day in the country, which is still a large number of people getting sick. Dr. Viboud also raised the caveat that this prediction “assumes that no new variant comes in. Because if you get a new variant that either has a higher transmissibility or immune escape potential, then we will see a resurgence.”

Maria Van Kerkhove from the World Health Organization is less optimistic in the predictions for the next few months. She worries that much of the assumptions and details used in modeling

The information provided in this report is not intended to represent a complete compilation of all treatment options available nor is it to be interpreted as medical advice. The information is intended to serve solely as a guide to facilitate a discussion between you and your medical provider(s). Medical decisions should be made only after consultation with and at the direction of your treating physician(s).

Copyright © 2021 PinnacleCare International, LLC. All rights reserved.

No part of this material may be reproduced in any form, or by any means, without the prior written consent of PinnacleCare International, LLC.



programs are based on previous epidemics from influenza, rather than COVID-19. The level of knowledge available about COVID-19 is not sufficient to predict the spread of infections at this time. Therefore, any gaps are filled with information obtained in previous outbreaks of respiratory viruses, and the main respiratory virus present in the world is influenza.

She also hypothesizes that the current reductions in the number of cases in most areas of the world have been driven by changes in human behavior, such as increased mask use or social distancing, rather than an increased level of immunity.

From her interpretation of the available data, there are still too many unprotected individuals in most populations. She does say that while she expects the number of cases to continue to rise and fall due to surges in transmission, the magnitude of the number people affected should begin to decline overall. The infection rates in individuals who are not vaccinated or otherwise protected from infection would continue at the current high levels, however, because the current incredibly infectious strains of the virus would still be in circulation.

The infection fatality rate, defined as the percentage of infected people who die from the disease, has dropped due to the combination of vaccination and post-infection protection.

While the number of people becoming ill may or may not continue at the current high levels, there has been, and should continue to be, a lower rate of severe disease and death from infections.

The possibility of a new variant emerging is also still an unknown. Based on previous research of coronaviruses, researchers expected that SARS-CoV-2 would be slow to mutate. However, this research could not predict how coronaviruses would behave with such widespread transmission.

The Delta variant has outcompeted nearly all other variants of SARS-CoV-2, and sequencing of testing samples indicate that around 88% of cases of COVID-19 are caused by the Delta variant worldwide.

Evolutionarily, this means that any further mutations would most likely be based on the Delta variant. There are a finite number of mutations that can occur within a virus and allow the virus to continue to function. Barney Graham, the recently retired deputy director of the NIH's Vaccine Research Center, suggests that if no more advantageous mutations occur and the vaccination of the world population continues, the number of new infections will diminish, which will also lower the chance that a mutation will occur. The rate of transmission of the virus is nearly at the highest rate possible. Changes that could increase other properties of the virus would likely lead to decreases in the transmission, which could help keep the spread of new mutants more contained.

The information provided in this report is not intended to represent a complete compilation of all treatment options available nor is it to be interpreted as medical advice. The information is intended to serve solely as a guide to facilitate a discussion between you and your medical provider(s). Medical decisions should be made only after consultation with and at the direction of your treating physician(s).

Copyright © 2021 PinnacleCare International, LLC. All rights reserved.

No part of this material may be reproduced in any form, or by any means, without the prior written consent of PinnacleCare International, LLC.



Conditions in Highly Vaccinated Areas around the World

Evaluation of areas of the world with high levels of vaccination of the public have allowed for additional insight into how future outbreaks will play out in the United States (McGregor, 2021). In Singapore, **80% of the population has been fully vaccinated**. Even with the high level of the population vaccinated, the city-state has had a surge in new cases of COVID-19 recently with the highest level of new cases being recorded thus far during the pandemic. There has been a rapid increase in rate of new cases, with 180 new cases per week reported on September 1, 2021, approximately 500 per week in the middle of September, and approximately 1,500 per week at the end. Importantly, **there have been very few deaths** or instances of severe disease associated with the surge in cases. The number of people being treated in the intensive care unit has increased from five at the start of the month to 30 people at the end of the month out of a population of 5.7 million people.

During September, 52% of the new cases in Singapore are in vaccinated individuals, but 98% of the total group of people who have been infected in the last 28 days have reported mild or no symptoms of COVID-19.

The Director of Medical Services in Singapore announced that assessment of their data indicated that vaccinated individuals in Singapore are 12-times less likely to die or require hospitalization than those who are unvaccinated.

As of September 28, 2021, government officials announced that they are continuing to relax restrictions in the city, and government briefings are focusing on the number of severe cases of COVID-19 and the number of deaths from COVID-19 rather than the total number of cases. They report that they are “deemphasizing” mild infections to focus on “cases that may require hospitalization.”

Denmark is another country with a very high level of vaccination of its population with **88% of all individuals over 18 years fully vaccinated and 97% of those over the age of 60** (Kupferschmidt, 2021). Because of the high levels of vaccination, the country lifted all of its remaining COVID-19 restrictions on September 10, 2021. Since the restrictions in the country were lifted, the number of cases has been rising, but slower than observed in other areas. For example, the change in the number of cases in Singapore has increased 161% over the last 14 days while the number of cases in Denmark have increased only 31% (New York Times, 2021).

A government public health organization in Denmark published four projections of new cases over the winter. In the first scenario, which is the best-case situation, 90% of the population over the age of 12 years is vaccinated, there is no increase in social activities from the current levels during the winter, and **no surge in cases and hospitalizations occurs**. The worst-case scenario included no further uptake of vaccine by individuals still susceptible to SARS-CoV-2 and an increase in social activity of 10% over the winter, which would be expected to lead to a **large surge in cases and hospitalization similar in size to that from December, 2020 and January, 2021**. The studies did not include the potential complication of waning of protection from vaccines that has been reported in studies from Israel and the United States.

Representatives from the government stated that “If you have a lower coverage in the elderly, you should not try to do what Denmark is trying right now.” For comparisons sake,

The information provided in this report is not intended to represent a complete compilation of all treatment options available nor is it to be interpreted as medical advice. The information is intended to serve solely as a guide to facilitate a discussion between you and your medical provider(s). Medical decisions should be made only after consultation with and at the direction of your treating physician(s).

Copyright © 2021 PinnacleCare International, LLC. All rights reserved.

No part of this material may be reproduced in any form, or by any means, without the prior written consent of PinnacleCare International, LLC.



approximately 90% of individuals over the age of 60 had received two doses of the Pfizer-BioNTech vaccine in Israel at the time that boosters were introduced.

This seemingly small difference in the percentage of individuals over the age of 60 (97% versus 90%) corresponds to a total that is several times as many unvaccinated people between the two countries.

In the United States, 83% of individuals over the age of 65 have been fully vaccinated (New York Times, 2021).

Change from Pandemic to Endemic

The term for an infectious disease that is actively transmitted in a population, but ceases to be an overriding public health threat is **endemic**, as opposed to pandemic. Researchers indicate that even in areas such as Singapore and Denmark with high levels of immunity against SARS-CoV-2 from a highly vaccinated populace, COVID-19 has not reached endemic status. Models of the possible level of disruption from when SARS-CoV-2 becomes truly endemic still have wide variation due to unknowns in the length and strength of the immune response and the long-term potential of new variants of the virus emerging (Kupferschmidt, 2021).

The **best-case scenario** would be if SARS-CoV-2 follows the cycle of other coronaviruses. Endemic versions of coronaviruses cause a first infection early in childhood for most people, leading to an immune response that decreases over time. As the immune response drops, there is less protection from infection, but protection from severe disease remains. Mild infections lead to symptoms associated with the common cold over the years, but the viruses rarely change enough to escape detection by the immune system.

If the immune response against SARS-CoV-2 **decreases over time to a level where there is no longer protection from severe disease**, there could be subsequent outbreaks, more similar to those prevalent now, emerging after periods of low transmission. During a period of low transmission, the immunity against infection and severe disease would decline due to a lack of exposure to SARS-CoV-2 through mild infections. Populations that have high numbers of people with low levels of immunity would then be susceptible to outbreaks where vulnerable individuals would have a high rate of severe disease. In this type of situation, it is better for the population if there is a constant, high-level of mild disease so that individuals become infected while their immunity is still high. The subsequent infections then reactivate the immune response to keep the cycle going.

Scenarios where SARS-CoV-2 behaves more like influenza virus, however, are worrying for public health officials. In this situation, **the virus mutates rapidly so that new strains are observed every year that vary to a sufficient degree that protection from previous exposure is limited**. Reinfections would be more severe than those observed from the currently endemic coronaviruses. It is difficult to predict how stable SARS-CoV-2 will eventually become, but during this first world-wide outbreak it has shown that it can change faster than some of the types of influenza currently circulating in humans. Trevor Bedford of the Fred Hutchinson Cancer Research Center has suggested that it is a reasonable expectation that

The information provided in this report is not intended to represent a complete compilation of all treatment options available nor is it to be interpreted as medical advice. The information is intended to serve solely as a guide to facilitate a discussion between you and your medical provider(s). Medical decisions should be made only after consultation with and at the direction of your treating physician(s).

Copyright © 2021 PinnacleCare International, LLC. All rights reserved.

No part of this material may be reproduced in any form, or by any means, without the prior written consent of PinnacleCare International, LLC.



SARS-CoV-2 could infect one-third of the United States population every year, causing 50,000 to 100,000 deaths after the pandemic.

Transmission of Other Respiratory Viruses

The use of public health measures to prevent transmission of SARS-CoV-2 has also led to a reduction in the transmission of other respiratory viruses. Because of the lack of circulation of these illnesses, many people are expected to have a reduced immune response to the viruses. An example of the effect this might have on public health was observed in Hong Kong in the fall of 2020. Because of the low level of COVID-19 at the time, Hong Kong schools were able to resume in-person teaching. Soon after the start of the school year, there were large outbreaks of rhinovirus, one of the viruses that leads to symptoms of the common cold. Some children became so ill they required hospitalization for rhinovirus infection.

There have also been increases in serious infections with respiratory syncytial virus (or RSV) in the United States (CDC, 2021). RSV is normally most prevalent in the winter months, but due to lifting of public health measures to reduce transmission of SARS-CoV-2, there was an abnormally large number of cases during the summer of 2021 in the Southern regions of the United States. The CDC released a Health Advisory through the Health Alert Network warning that “older infants and toddlers might now be at increased risk of severe RSV-associated illness since they have likely not had typical levels of exposure to RSV during the past 15 months.” Additionally, young infants under the age of six months were more likely to require treatment in the hospital if they are infected with RSV.

There were 2,000 confirmed cases of RSV in the United States during the week of July 10, 2021, compared to less than twelve during the week of July 25, 2020.

An article published in the journal *Pediatrics* described the differences observed during the pandemic compared to the flu seasons in 2016 to 2019 at the Maimonides Children’s Hospital in Brooklyn, New York (Agha, 2021). **There were no cases of RSV treated at the hospital between September, 2020 and January, 2021.** The first infant with RSV was admitted to the hospital in March, 2021. Between March and May, 2021, 66% of the children who tested positive for RSV were admitted to the hospital, and the median age of those admitted to the hospital was six months. A large number of those (81%) who were treated in the hospital required care in the pediatric intensive care unit. During the 2019–2020 season, the median age of admitted patients was 17 months, and only 45% required treatment in the pediatric intensive care unit.

The rise of these other respiratory viruses also complicates the control of COVID-19 because the symptoms are the same. The only way to identify the virus responsible for even mild symptoms is a diagnostic test (Branswell, 2021). The increased prevalence and difficulty diagnosing the illness is expected to stress the health care system, as well as school systems and child care operations.

Influenza has also been all but absent throughout the pandemic. In the timeframe assessed in the above article describing RSV at Maimonides Children’s Hospital. There were **only five cases of flu** in the 2020-2021 flu season (Agha, 2021). Depending on the respiratory virus, co-

The information provided in this report is not intended to represent a complete compilation of all treatment options available nor is it to be interpreted as medical advice. The information is intended to serve solely as a guide to facilitate a discussion between you and your medical provider(s). Medical decisions should be made only after consultation with and at the direction of your treating physician(s).

Copyright © 2021 PinnacleCare International, LLC. All rights reserved.

No part of this material may be reproduced in any form, or by any means, without the prior written consent of PinnacleCare International, LLC.



infection with the flu has been found to either increase the severity of the illness, facilitate transmission, or crowd out other infections so only flu is spreading. To date, the COVID-19 pandemic has eliminated the spread of flu, but it is not known if this was due to masking and other public health measures or because of an interaction between the viruses.

This winter there are a large number of individuals who are immune to COVID-19 from vaccination or infection, and they are likely to be less cautious than last year during the 2020-2021 flu season, allowing the flu to reemerge.

Seasonal flu typically kills 290,000 to 650,000 people a year worldwide (Jones, 2021). In the United States, the yearly average of deaths is in the tens of thousands, but there were only 646 flu related deaths in the 2020-2021 season, and only one of the deaths was a pediatric case.

The level of public health measures to prevent respiratory disease transmission has waxed and waned throughout the pandemic, but decline in flu has persisted despite the variable lifting of social interventions to curb the spread of SARS-CoV-2. Richard Webby at St. Jude Children's Research Hospital in Memphis, Tennessee suggests that the **reduction in international travel** may be a large contributing factor. New outbreaks have not been seeded as people travel from one country to another.

COVID-19 Transmission

Mask Use

There have been numerous studies that have found that there is a difference in the number of new COVID-19 cases in counties in the United States that have enacted mask mandates. Because of the way the studies are designed, there can be differences between the residents in a county or complicating factors in the way the cases are counted that allow for some individuals to doubt the results.

A well-designed study that was performed in India allowed for an investigation that included a control group, allowing for a direct comparison of the magnitude of the reduction to the risk of transmission of SARS-CoV-2 occurs with mask-use (Peeples, 2021 and Abaluck et al., 2021). The results of the study were released ahead of their publication in a peer reviewed journal due to the importance of the results. The study included 341,830 adults in 600 villages in rural Bangladesh. Approximately half of the households in the study were in a village that had an active program in place to promote mask use while the other half were not. There were differences in the content of the promotions that also allowed the evaluation of the difference between cloth masks and surgical masks in addition to different types of strategies to promote mask usage. The active promotion and surveillance of mask use occurred for eight weeks with an additional two weeks of surveillance after the campaigns finished.

The information provided in this report is not intended to represent a complete compilation of all treatment options available nor is it to be interpreted as medical advice. The information is intended to serve solely as a guide to facilitate a discussion between you and your medical provider(s). Medical decisions should be made only after consultation with and at the direction of your treating physician(s).

Copyright © 2021 PinnacleCare International, LLC. All rights reserved.

No part of this material may be reproduced in any form, or by any means, without the prior written consent of PinnacleCare International, LLC.

**The promotion of masks included a number of strategies, including**

- Free household distribution of surgical or cloth masks
- Distribution of masks and promotion at markets and mosques
- Mask advocacy by imams during Friday prayers
- Role modeling by local leaders
- Promoters periodically monitoring passers-by and reminding people to put on masks
- Village police accompanying mask promoters
- Providing monetary rewards or certificates to villages if mask-wearing rate improves
- Public signaling of mask-wearing using signs, text message reminders, messaging emphasizing either altruistic or self-protection motives for mask-wearing
- Extracting verbal commitments from households

The level of mask usage was determined by direct observations by individuals stationed in the community to count the number of people wearing masks. Different color masks were distributed to different groups to determine if different strategies were more effective.

There was an increase in the proportion of individuals participating in proper mask wearing from 13% in villages without promotion to 42% in villages where strategies were enacted to promote mask usage.

The increase in mask use was most evident in mosques, with an increase in usage of 37.6 percentage points while other areas of observation had increases that ranged from 25 to 29 percentage points.

Observers also recorded physical distancing tendencies in the villages. At the start of the pandemic, there were concerns that use of masks would lead to a lax adherence to other practices to reduce transmission. Based on the evidence collected during the trial, there were increases in distancing behavior (defined as being at least one arm's length away from the nearest person) in areas with mask promotion.

There was a larger variation across locations in the change in physical distancing, but there was an overall increase of 5.2 percentage points between control villages and those that received promotion for the use of masks.

The largest change in physical distancing was observed in markets, and there was no change in physical distancing in mosques during group prayers.

There were also differences in the results from different strategies of promotion. For example, laws that set forth a legal sanction if masks were not worn did not have a large effect as evidenced by the fact that the use of masks was required by law in public areas in Bangladesh during the entire study. The researchers had local police position themselves in some areas where mask promotions were taking place, and the police presence also did not affect the level of mask use. Other strategies beyond free dispersal of masks that had no additional effect on

The information provided in this report is not intended to represent a complete compilation of all treatment options available nor is it to be interpreted as medical advice. The information is intended to serve solely as a guide to facilitate a discussion between you and your medical provider(s). Medical decisions should be made only after consultation with and at the direction of your treating physician(s).

Copyright © 2021 PinnacleCare International, LLC. All rights reserved.

No part of this material may be reproduced in any form, or by any means, without the prior written consent of PinnacleCare International, LLC.



mask usage included text reminders, public signage commitments, monetary or non-monetary incentives, altruistic messaging, or verbal commitments.

Instead, “the implicit social sanction from the mask promoter themselves, or the awkwardness or embarrassment of that conversation was the key mechanism at play in increasing mask usage.”

At the time the preprint of the study was released, the ten-week observation period had not finished in all the villages.

However, in the villages where the entire observation period had elapsed, there was no evidence that the impact of the intervention decreases over time, and mask-use continued as similar levels after active promotion ceased.

There was an increase in mask use by 27.2 percentage points in the first week of the intervention and there difference in the level of mask use measured by the tenth week was not statistically significant. This continuation of mask use extended two weeks after active promotion of mask wearing had ended.

Importantly, there was a decrease in the number of symptomatic cases of COVID-19 in villages where mask wearing was more prevalent due to the active interventions.

The number of symptomatic cases decreased by 9%, and the overall decrease in the number of cases is expected to be higher if asymptomatic cases were counted. The drop in the number of new cases of COVID-19 was larger when surgical masks were promoted and used (11%) compared to cloth masks (5%), but both did have a statistically significant effect.

Another recently released, peer-reviewed study looked more closely at the level of protection provided by different mask types (Adenaiye et al., 2021). The researchers investigated the level of viral RNA in blood samples, saliva samples, nasal swabs samples, breath samples, and swabs of participants’ cellphones. **Each of the 57 participants had an active infection** with SARS-CoV-2 based on PCR-based testing of nasal or saliva swabs, and 49 (86%) did not have antibodies (**seronegative**) at the time of their initial diagnosis, suggesting they had not previously been infected. The remaining 14% of the participants had antibodies (**seropositive**) at the time of diagnosis, suggesting a previous infection. All of the cases were asymptomatic or had mild symptoms at the time of the study. Similar studies investigating the effectiveness of masks were performed earlier during the pandemic using either saline to approximate aerosols or individuals with less contagious respiratory illnesses (e.g. rhinovirus).

Test samples of nasal swabs, saliva, cell-phone surface, and aerosols were collected at two-day intervals. Aerosols were measured during a 30-minute exhaled breath collection with and without masks. Provided surgical masks were used in one test and personal masks provided by the participant were used in another. Participants were asked to vocalize by singing the Happy Birthday Song, yelling “Go Terps”, or repeating the alphabet.

The frequency of detection of viral RNA in aerosols was greatest **two to five days after onset of symptoms** or first positive test in asymptomatic participants. There was approximately two-

The information provided in this report is not intended to represent a complete compilation of all treatment options available nor is it to be interpreted as medical advice. The information is intended to serve solely as a guide to facilitate a discussion between you and your medical provider(s). Medical decisions should be made only after consultation with and at the direction of your treating physician(s).

Copyright © 2021 PinnacleCare International, LLC. All rights reserved.

No part of this material may be reproduced in any form, or by any means, without the prior written consent of PinnacleCare International, LLC.



times more viral RNA observed in the fine aerosols particles compared to the large aerosol particles, which is consistent with the data showing that SARS-CoV-2 is transmitted through the air as well as through droplets. Additionally, the researchers were able to grow virus collected from fine aerosols, proving that **infectious virus is present**.

Individuals infected with the Alpha variant had much larger amounts of viral RNA shedding compared to those with infections from early variants of SARS-CoV-2.

Measurements showed that there was 100-times more virus in large aerosols and 73-times more virus in fine aerosols for individuals infected with the Alpha variant compared to those with previous versions of the virus. The proportion of participants with detectable viral RNA in different areas and the variant causing the infection is shown in Table 1.

Table 1. Proportion of participants with evidence of viral RNA in different tests.

Sample Type	Variant	Proportion of participants with detectable viral RNA in all collected samples
Nasal Swab	Alpha variant	100%
	Other	100%
Saliva	Alpha variant	100%
	Other	99%
Fomites (cellphone swab)	Alpha variant	100%
	Other	49%
Large aerosol droplets	Alpha variant	100%
	Other	19%
Fine aerosol droplets	Alpha variant	100%
	Other	31%

Regardless of mask type, there was a statistically significant reduction in the amount of virus shedding in aerosols.

Overall, use of a mask led to a 77% reduction in the amount of viral shedding through large droplets and a 48% reduction in the amount of viral shedding through fine aerosols.

Masks were similarly useful in reducing the amount of both large droplets and fine aerosols for both the Alpha variant and previous version of the virus.

The information provided in this report is not intended to represent a complete compilation of all treatment options available nor is it to be interpreted as medical advice. The information is intended to serve solely as a guide to facilitate a discussion between you and your medical provider(s). Medical decisions should be made only after consultation with and at the direction of your treating physician(s).

Copyright © 2021 PinnacleCare International, LLC. All rights reserved.
No part of this material may be reproduced in any form, or by any means, without the prior written consent of PinnacleCare International, LLC.



Importantly, the researchers concluded from the evidence in the study that people with mild or asymptomatic SARS-CoV-2 infections released infectious aerosols in their exhaled breath.

The results comparing the reduction of viral particles with and without masks indicate that community-wide masking even with loose-fitting masks can reduce viral aerosols in indoor air **by half**, making a significant contribution to reducing the spread of COVID-19.

A study by the St. Louis city health department in collaboration with Saint Louis University also investigated the effect of mask use on the transmission of SARS-CoV-2 in students attending in-person classes (Rebmann et al., 2021). The study was conducted between January and May, 2021 at which time the **Alpha** variant was becoming the most prevalent variant. Universal masking inside and outside was required on campus with faculty and staff reminding those not in compliance to wear a mask. Individuals who did not comply were not allowed to continue to attend in-person classes. During the study period, a modified contact tracing and quarantine program was instigated. If a student was found to have COVID-19, the contact tracing team determined the number of close contacts of the student. Close contacts were defined as a single encounter in which the two persons were within six feet of each other for at least 15 minutes during a 24-hour period regardless of the location. If either person in the encounter was not wearing a mask, the individuals involved were required to quarantine. If both individuals were masked, quarantine was not required, but those involved were instructed to monitor their symptoms. All close contacts were tested for COVID-19 using PCR-based testing within five to seven days after the exposure occurred regardless of mask use.

During the study period, there were 9,335 student-based tests performed, and 2.8% were positive for COVID-19, corresponding to 265 individuals. The majority of the tests were performed for screening in asymptomatic individuals. There were 378 close contacts identified from the students who tested positive. Of the close-contact encounters, 6.9% of the students reported that all encounters were with masked individuals, and 93.1% reported that at least one exposure occurred without a mask. There were 116 positive tests from close contacts, which corresponds to 30% of contacts.

The rate of positive tests was higher in those who had had at least one close contact with someone without a mask compared to those who had encounters with people wearing masks.

Out of 352 encounters that occurred without mask usage, there were 114 positive tests, corresponding to **32.4%**. Of the 26 encounters that occurred when all individuals were masked, there were two positive tests, corresponding to **7.7%**. Additionally, there were **no positive tests in contacts who were fully vaccinated** while 33% of unvaccinated contacts and 20.8% of partially vaccinated contacts tested positive.

The two individuals who tested positive after exposure to SARS-CoV-2 from masked contacts were not required to quarantine while awaiting test results, and no additional cases were connected to them. The authors suggest that using the modified quarantine method allows for a reduction in the negative effects associated with quarantine while also reducing transmission.

The information provided in this report is not intended to represent a complete compilation of all treatment options available nor is it to be interpreted as medical advice. The information is intended to serve solely as a guide to facilitate a discussion between you and your medical provider(s). Medical decisions should be made only after consultation with and at the direction of your treating physician(s).

Copyright © 2021 PinnacleCare International, LLC. All rights reserved.

No part of this material may be reproduced in any form, or by any means, without the prior written consent of PinnacleCare International, LLC.



Students who know they will not have to quarantine if their exposures occurred while masked may also be more compliant with mask mandates.

Evaluation of the conditions of the encounters of students during in-person learning at a college campus showed that universal masking and having fewer encounters in close contact with persons with COVID-19 prevents the spread of SARS-CoV-2.

The CDC also published two studies on mask use in schools and universities that indicate that school districts without a universal masking policy in place were more likely to have COVID-19 outbreaks (CDC, 2021). One of the reports investigated the incidence of COVID-19 cases in schools in two Arizona counties. The authors compared the number of cases at schools that started the year with universal masking compared to those that had later requirements or incomplete masking. There were 21% of the schools in the counties that had an early requirement, 30.9% that had a later ask requirement, and 48% had no mask requirement.

Schools without mask requirements were 3.5-times more likely to have COVID-19 outbreaks than schools that started the year with universal mask requirements.

The CDC also investigated the difference in the number of pediatric COVID-19 cases in counties with and without school mask requirements (Budzyn, et al., 2021). Counties with conflicting school mask requirements were excluded from this analysis; only those counties with the same known mask requirements for all schools were included. Data for 16.5% of the 3,142 counties in the United States were included in the analysis.

Counties without school mask requirements experienced larger increases in pediatric COVID-19 case rates after the start of school compared with counties that had school mask requirements.

Transmission during Airline Flights

The risk of SARS-CoV-2 transmission on airline flights has been difficult to ascertain. The closeness to other passengers along with the extended durations traveling together would suggest an increased risk of transmission, but the use of masks and high levels of ventilation while on the plane may offset those risks.

Researchers in China determined the attack rate (proportion of people who become ill) and the upper and lower levels of risk for transmission of SARS-CoV-2 between travelers on airplanes (Hu et al., 2021). The study included 5797 passengers who flew on 177 flights departing from Wuhan City before the start of the lockdown in January, 2020. There were 175 individuals who were ill on the planes (index cases) who could have spread the virus to other passengers.

The authors found that the overall risk is relatively low, although it varies by seat distance from the index case and the length of time traveled together.

Based on the variation of conditions, the highest attack rate for the whole plane was 0.6%, and the lowest attack rate was 0.33%. Each index case would infect between 0.19 and 0.10 other

The information provided in this report is not intended to represent a complete compilation of all treatment options available nor is it to be interpreted as medical advice. The information is intended to serve solely as a guide to facilitate a discussion between you and your medical provider(s). Medical decisions should be made only after consultation with and at the direction of your treating physician(s).

Copyright © 2021 PinnacleCare International, LLC. All rights reserved.

No part of this material may be reproduced in any form, or by any means, without the prior written consent of PinnacleCare International, LLC.



people. As might be expected, the highest risk of transmission was observed for passengers directly next to the index case.

The attack rate in the seats immediately adjacent to the index case was 9.2% with a 25-fold increase in relative risk of transmission compared to other seats on the plane.

Longer flight times also increased the risk. The attack rate increased from 0.7% to 1.2% with an increase in the flight time from two hours to 3.3 hours.

Many countries require COVID-19 testing for international travel, but it is unknown how well this practice controls transmission because individuals at the early stages of COVID-19 may be contagious after testing negative (Tande et al, 2021). Researchers, in collaboration with Delta Airlines, investigated the level of exposure and transmission associated with international travel that requires a negative COVID-19 test within 72 hours of departure.

The study included **9,853 passengers** with a negative SARS-CoV-2 PCR performed within 72 hours of departure from December, 2020 through May, 2021, at the Atlanta airport and JFK airport in New York. Flights starting from Atlanta or New York and arriving in Rome or Milan were part of the study. The average community infection rate in the United States was 1.1% during the study period. The average number of passengers on each flight was 76 with an average seating capacity of 289 and load factor of 26% (a measure of the percentage of available seating capacity that has been filled with passengers).

All passengers had submitted proof of a negative COVID-19 test administered within 72 hours of their arrival at the airport. After the passengers passed through airport security, they were tested using the BinaxNOW antigen test. Any individuals with a positive antigen test was subsequently tested with rapid PCR-based testing. Any passengers who had a positive PCR-based test were categorized as positive and not allowed to board. Upon arrival in Italy, passengers were tested again with a rapid antigen test (STANDARD Q COVID-19 Ag, SD BIOSENSOR), and any positive tests were confirmed with PCR-based testing.

There were four passengers who tested positive before boarding the plane to Italy who were not allowed to fly. This corresponds to 0.04% of the passengers in the study. There were no false-positive rapid antigen tests before the flight. Testing in Italy, after the flight, identified one additional individual who was positive by antigen and PCR-based testing, corresponding to 0.01% of the passengers in the study. There were twelve false-positive antigen tests in Italy.

Therefore, a single PCR-based test performed within 72 hours of initial departure led to a frequency of active infection of less than 1 in 1,000 passengers identified on rapid antigen testing at the airport.

The authors conclude that a single molecular test performed within 72 hours of departure can decrease the rate of active infection on board a commercial aircraft to a level that is several orders of magnitude below active community infection rates. Additional measures, including mask use at the airport and onboard the plane, an increase in frequency of air exchanges and enhanced cleaning, physical distancing during deplaning activities, increasing vaccination rates among travelers and exclusion of symptomatic individuals, further enhances safety. The

The information provided in this report is not intended to represent a complete compilation of all treatment options available nor is it to be interpreted as medical advice. The information is intended to serve solely as a guide to facilitate a discussion between you and your medical provider(s). Medical decisions should be made only after consultation with and at the direction of your treating physician(s).

Copyright © 2021 PinnacleCare International, LLC. All rights reserved.

No part of this material may be reproduced in any form, or by any means, without the prior written consent of PinnacleCare International, LLC.



vaccination rate was low in the United States at the time of the study, suggesting that current risks may be even lower.

Implementing additional testing at the time of the flight is unlikely to increase the level of safety from transmission during international flights.

Update on COVID-19 Treatments

Updates on three antiviral medications for the treatment of COVID-19 were released. Two, molnupiravir and remdesivir, act directly on the virus to prevent replication of new copies. The third, baricitinib, reduces the inflammatory response and has been repurposed from use to treat rheumatoid arthritis.

Baricitinib

Baricitinib is the first immunomodulatory treatment found to reduce COVID-19 mortality in a placebo-controlled trial (Kalil, 2021 and Marconi et al., 2021). The medication was originally developed for treatment of rheumatoid arthritis and reduces certain immune and inflammatory responses.

Between June 11, 2020, and Jan 15, 2021, 1525 participants were randomly assigned to receive either baricitinib or the standard of care, which at the time included systemic corticosteroids, such as dexamethasone, and antivirals, including remdesivir. The efficacy was evaluated by determining the proportion of participants who progressed to high-flow oxygen, non-invasive ventilation, invasive mechanical ventilation, or death by day 28 after the start of treatment. Fewer individuals who received baricitinib met these conditions, with 27.8% of participants receiving baricitinib and 30.5% receiving placebo progressing to use of high-flow oxygen, non-invasive ventilation, invasive mechanical ventilation, or death. This difference was not found to be statistically significant, however. When the proportion of individuals who died was evaluated separately, use of baricitinib did cause a statistically significant reduction.

The proportion of participants that died within 28 days of starting the treatment was 8% for baricitinib and 13% for the placebo, which corresponds to a 38.2% relative reduction in mortality.

The frequency of side effects reported were similar in the two groups. The frequency of serious infections also occurred at a similar rate, 9% versus 10%, which is important to monitor with immunomodulatory medication.

Molnupiravir

Merck announced the interim results from their clinical trial investigating the effect of the antiviral medication molnupiravir on COVID-19. (Merck, 2021). The medication is in the same class as remdesivir and mimics the subunits (called ribonucleic acids) that make up the genome of certain viruses. Molnupiravir is administered orally as a pill rather than by infusion as with

The information provided in this report is not intended to represent a complete compilation of all treatment options available nor is it to be interpreted as medical advice. The information is intended to serve solely as a guide to facilitate a discussion between you and your medical provider(s). Medical decisions should be made only after consultation with and at the direction of your treating physician(s).

Copyright © 2021 PinnacleCare International, LLC. All rights reserved.

No part of this material may be reproduced in any form, or by any means, without the prior written consent of PinnacleCare International, LLC.



remdesivir. The medication was shown to be active against a number of coronavirus family members when tested in cells grown in the laboratory (Sheahan et al., 2020). However, there have been numerous potential treatments for COVID-19 that looked promising when tested on cultured cells that did not later show an effect when used in people.

Since the initial report, results from a Phase 2 and interim results from a Phase 3 study have become available (Merck, 2021b and Fischer, 2021). In the Phase 2 trial, there were 202 participants with COVID-19 who were not in the hospital that were treated with differing doses of molnupiravir. On the third day after the start of treatment, 1.9% of individuals receiving 800 mg of molnupiravir were producing virus compared to 16.7% of those in the placebo group. The safety and tolerability profile was also found to be good.

Based on the Phase 2 results, molnupiravir was found to be the first direct-acting antiviral shown to be highly effective at reducing nasopharyngeal SARS-CoV-2 infectious virus and viral RNA.

The Phase 3 trial of molnupiravir was organized by Merck and included 775 at risk, non-hospitalized, adult participants with mild-to-moderate COVID-19 (Merck, 2021). To be eligible, participants also needed to be within five days of symptom onset. Each of the participants had at least one risk factor that is associated with poor disease outcome. The study sites were located at more than 170 sites worldwide with participants in Argentina, Brazil, Canada, Chile, Colombia, Egypt, France, Germany, Guatemala, Israel, Italy, Japan, Mexico, Philippines, Poland, Russia, South Africa, Spain, Sweden, Taiwan, Ukraine, the United Kingdom, and the United States.

The interim analysis of the results indicates that the medication reduced the risk of hospitalization or death by approximately 50%.

Through 29 days following the start of treatment, there were no deaths in the group taking molnupiravir while there were eight deaths out of 377 participants in the placebo group. There was no change in the efficacy based on the timing of symptom onset or the type of risk factor present.

Molnupiravir also demonstrated consistent efficacy across viral variants Gamma, Delta, and Mu.

Genomic sequencing was performed for approximately 40% of the participants in the study, and 80% of the cases in the trial were the Delta, Gamma, or Mu variant.

Fewer subjects discontinued study therapy due to an adverse event in the molnupiravir group (1.3%) compared to the placebo group (3.4%).

The results were so compelling that the independent trial monitoring committee suggested to the FDA that the trial be halted early due to positive results. The trial had recruited more than 90% of the intended number of participants at the time, and this early stoppage is not expected to affect the veracity of the study. Merck announced that they are in the process of submitting the information on the new medication to the FDA for Emergency Use Authorization. Merck has a procurement agreement with the United States government to supply approximately 1.7

The information provided in this report is not intended to represent a complete compilation of all treatment options available nor is it to be interpreted as medical advice. The information is intended to serve solely as a guide to facilitate a discussion between you and your medical provider(s). Medical decisions should be made only after consultation with and at the direction of your treating physician(s).

Copyright © 2021 PinnacleCare International, LLC. All rights reserved.
No part of this material may be reproduced in any form, or by any means, without the prior written consent of PinnacleCare International, LLC.



million courses of the medication. The company also entered into non-exclusive, voluntary licensing agreements for molnupiravir with five established Indian generics manufacturers to accelerate availability of molnupiravir in India and in other low- and middle-income countries.

Remdesivir

Gilead, the maker of remdesivir (marketed as Veklury) published a press release reporting the results from a Phase 3 randomized, double-blind, placebo-controlled trial to evaluate the efficacy and safety of a three-day course of remdesivir for treatment of COVID-19 in non-hospitalized patients at high risk for disease progression (Gilead, 2021).

There was an 87% reduction in COVID-19 related hospitalization or death within 28 days of the start of treatment compared to placebo.

Use of remdesivir also reduced the need for medical visits due to COVID-19 or death compared to the placebo. No deaths were observed during the study for either the group receiving remdesivir or the placebo.

The safety profile was similar between remdesivir and the placebo, with the most common treatment emergent adverse events in participants taking remdesivir being nausea and headache.

A study of remdesivir in hospitalized participants was also published and appeared in the Lancet Infectious Diseases (Ader et al., 2021). The medication was infused daily for up to ten days during the trial. Dosing was discontinued after five days if participants were well enough to be discharged. There were 429 participants that received remdesivir and 428 who received the standard of care.

There was no statistically significant difference at day 15 in hospitalized individuals after the start of treatment on patient condition based on the WHO scale.

There was also no statistically significant difference in the occurrence of adverse events between the two groups.

Based on this study, the authors concluded that “no clinical benefit was observed from the use of remdesivir in patients who were admitted to hospital for COVID-19, were symptomatic for more than seven days, or required oxygen support.”

COVID-19 in Pregnancy

The CDC issued an **urgent health advisory** in regards to the effects of COVID-19 in pregnant women on September 29, 2021. It has been found that there is an increased risk to both the mother and baby for poor outcomes.

The information provided in this report is not intended to represent a complete compilation of all treatment options available nor is it to be interpreted as medical advice. The information is intended to serve solely as a guide to facilitate a discussion between you and your medical provider(s). Medical decisions should be made only after consultation with and at the direction of your treating physician(s).

Copyright © 2021 PinnacleCare International, LLC. All rights reserved.
No part of this material may be reproduced in any form, or by any means, without the prior written consent of PinnacleCare International, LLC.



Specifically, pregnant women with symptomatic COVID-19 have a two-fold risk of admission into intensive care and a 70% increased risk of death.

As of September 27, 2021, there have been more than 125,000 cases of COVID-19 in pregnant women with more than 22,000 requiring treatment in the hospital for COVID-19 symptoms and 161 maternal deaths. Of the total number of deaths, 22 occurred in August, 2021. Of those who were hospitalized for treatment of COVID-19, 97% were not vaccinated.

There is also an increased risk to the baby, and officials have observed an increase in pre-term birth, stillbirth, and admission to the intensive care unit of newborns with COVID-19.

Overall, the CDC reports that there were 266 pregnancy losses from women diagnosed with COVID-19. However, only 25 states and territories reported information, meaning that the nationwide total is much more. In Mississippi, the state health department has identified 72 stillbirths among women with COVID-19 since the start of the pandemic (Shammas, 2021). At a press conference, officials also reported that these fetal deaths occurred after 20 weeks of gestation (a total pregnancy is 40 weeks), and the number of cases was **twice the rate observed in a normal year**.

A study at four university hospitals in Europe investigated the outcome of pregnancy based on the stage in which the infection occurred (Badr et al., 2021). There were 10,925 pregnant women included in the study, and 393 (3.60%) had confirmed infections with SARS-CoV-2. The outcomes reported included adverse obstetric outcomes such as eclampsia, HELLP (hemolysis, elevated liver enzymes, low platelet count) syndrome, unscheduled cesarean delivery, deep venous thrombosis (DVT), pulmonary embolism, pregnancy loss, or maternal death. The adverse effects on the baby that were reported include low birthweight, neonatal intensive care unit admission, APGAR score of less than seven at five minutes of life, respiratory distress, or neonatal death. The criteria for neonatal intensive care unit admission were gestational age at birth of less than 32 weeks, birthweight of under 1,500 grams (3.3 pounds), signs of respiratory distress, abnormal or unstable blood pressure, metabolic problems needing central venous access placement and intensive care, perinatal asphyxia, and need for exchange-transfusion (removal of an individual's blood and replacement with donor's blood).

The researchers found that adverse obstetric outcomes occurred in 22.75% of participants with COVID-19 versus 19.25% of those not infected while neonatal adverse events occurred for 17.86% of participants with COVID-19 versus 14.28% of those without the virus.

The researchers also looked at the individual outcomes and found that there were increases in preeclampsia, eclampsia, or HELLP syndrome, preterm delivery, cesarean delivery, unscheduled cesarean delivery, postpartum hemorrhage, DVT or pulmonary embolism, fetal distress, admission to the NICU, and APGAR score of less than seven at five minutes. Babies born of mothers with COVID-19 also had lower birthweight.

The increase in obstetric adverse events was higher for individuals infected with SARS-CoV-2 past 20 weeks of pregnancy, and neonatal adverse events were higher for individuals who were infected after 26 weeks of pregnancy.

The information provided in this report is not intended to represent a complete compilation of all treatment options available nor is it to be interpreted as medical advice. The information is intended to serve solely as a guide to facilitate a discussion between you and your medical provider(s). Medical decisions should be made only after consultation with and at the direction of your treating physician(s).

Copyright © 2021 PinnacleCare International, LLC. All rights reserved.

No part of this material may be reproduced in any form, or by any means, without the prior written consent of PinnacleCare International, LLC.



Therefore, gestational age at the time of infection is important for the outcome of the pregnancy, and **infections early have less of an effect on the outcome.**

A previous study reported on the comparison between the placentas of women with COVID-19 and those without an infection. The comparison showed that there was an increased prevalence of abnormalities including villitis (an inflammatory condition that damages the placenta) and vascular underperfusion (lack of sufficient blood flow) to the fetus for women who were positive for SARS-CoV-2 infection. These types of abnormalities are consistent with the outcomes observed in the above study in Europe.

A study assessing the outcome of all births of single babies (e.g. no twins, etc.) in England between May 29, 2020, and January 31, 2021 showed that SARS-CoV-2 at the time of birth was associated with higher rates of fetal death, preterm birth, preeclampsia, and emergency cesarean delivery (Gurol-Urganci et al., 2021). There were 342,080 women included in the study, and 3527 had confirmed COVID-19. The risk of neonatal adverse outcome, need for specialist neonatal care, and prolonged neonatal admission after birth were all higher for infants with mothers with laboratory-confirmed SARS-CoV-2. When the analysis was restricted to pregnancies delivered at term, there were no statistically significant differences in neonatal adverse outcome or neonatal readmission within four weeks of birth. However, babies born at term to mothers with COVID-19 were more likely to have prolonged admission after birth.

The main risk for babies was preterm delivery, and the associated problems, rather than direct influence from the viral infection.

The number of stillbirths around the world have increased during the pandemic (Watson, 2021). In one study in Nepal, reported stillbirths increased from 14 per 1,000 before lockdowns for the pandemic to 21 per 1,000 by the end of May, 2020. This initial increase in the rate of stillbirths was not from complications from COVID-19, but rather from lack of prenatal medical care. There was also a four-fold increase in the number of stillbirths at St. George's Hospital in London.

Information on the safety of vaccination of pregnant women continues to indicate that vaccination is safe and effective at preventing COVID-19 (Van Beusekom, 2021).

Three recent studies all indicate that there is not an increase in the risk of miscarriage in vaccinated women compared to unvaccinated women.

The studies included information on all three authorized vaccines available in the United States.

Vaccine Updates

An analysis by individuals from the Peterson and Kaiser Family Foundation found that insurance companies and government funded health programs, such as Medicare, have spent billions of dollars on medical bills for individuals who were not vaccinated (Amin, 2021). **The average cost of hospitalization for the treatment of COVID-19 is estimated to be \$20,000**, and insurance companies are beginning to reinstate cost sharing for COVID-19 treatment.

The information provided in this report is not intended to represent a complete compilation of all treatment options available nor is it to be interpreted as medical advice. The information is intended to serve solely as a guide to facilitate a discussion between you and your medical provider(s). Medical decisions should be made only after consultation with and at the direction of your treating physician(s).

Copyright © 2021 PinnacleCare International, LLC. All rights reserved.

No part of this material may be reproduced in any form, or by any means, without the prior written consent of PinnacleCare International, LLC.



Based on available data from the CDC and other government departments, there were 287,000 preventable COVID-19 hospitalizations across the three summer months, June, July, and August, 2021.

Preventable hospitalizations were defined as unvaccinated adults who were hospitalized with confirmed COVID-19.

Based on information from the department of Health and Human Services, the approximate proportion of adults hospitalized primarily for COVID-19 over the summer who were not vaccinated was 86%.

The total proportion of people hospitalized who tested positive for COVID-19 who were unvaccinated was 98.6%, which includes asymptomatic individuals incidentally diagnosed by screening for other procedures. There were **32,000** preventable COVID-19 hospitalizations in June, **68,000** in July, and **187,000** in August.

Using the average cost of treatment, it is estimated that from June through August, 2021, preventable COVID-19 hospitalizations among **unvaccinated adults cost \$5.7 billion**. The cost of COVID-19 outpatient treatment costs can average \$500 to \$1,000 per person compared to a pre-pandemic typical outpatient office visit estimated to cost \$105 on average. The increase in costs has allowed employers, such as Delta Airlines, to charge extra fees for unvaccinated employees. Not included in the cost reported above is the contribution of unvaccinated individuals spreading SARS-CoV-2 to others who may then also need to be treated.

The authors of the study conclude that adults can largely avoid the potential out-of-pocket costs, and severe illness, by getting the free vaccine.

Vaccination of Children Ages Five to Eleven

Pfizer announced their clinical trial results investigating the use of the Pfizer-BioNTech vaccine in children (Herper, 2021). The dose given to children aged five to eleven is lower than that used in older individuals, but there was an encouraging level of antibodies produced with a similar safety profile to that observed for volunteers aged eleven to 18 years.

Comparisons of the placebo group, vaccinated individuals aged five to eleven, and vaccinated individuals aged eleven to 18 showed that there was similar levels of antibody production after the two smaller doses.

Pfizer filed for an Emergency Use Authorization with the FDA on September 28, 2021. The FDA has scheduled a meeting of the Vaccines and Related Biological Products Advisory Committee (VRBPAC) on October 28, 2021 to discuss the findings.

Effectiveness of Pfizer-BioNTech in Adolescents

The effectiveness of the Pfizer-BioNTech vaccine in adolescents (aged 12 to 15) was evaluated in Israel between the date of its authorization in this age group, June 2, 2021, and August 26,

The information provided in this report is not intended to represent a complete compilation of all treatment options available nor is it to be interpreted as medical advice. The information is intended to serve solely as a guide to facilitate a discussion between you and your medical provider(s). Medical decisions should be made only after consultation with and at the direction of your treating physician(s).

Copyright © 2021 PinnacleCare International, LLC. All rights reserved.

No part of this material may be reproduced in any form, or by any means, without the prior written consent of PinnacleCare International, LLC.



2021 (Glatman-Freedman et al., 2021). By the end of the study period, 46.1% of those eligible had received the first dose of the vaccine, and 31.2% had received both doses. The start of the vaccination campaign for this age group coincided with the spread of the **Delta** variant in Israel.

The researchers found that vaccine effectiveness against laboratory-confirmed SARS-CoV-2 infection was 55.3% in the first week after the second dose, 87.1% in the second week, 91.2% in the third week, and 88.2% in the fourth week. The differences in the vaccine effectiveness in the second week after the second dose and beyond were not statistically significant.

The data shows that vaccine effectiveness increases during the first week after vaccination, and then becomes stable at a value of 91.5% against SARS-CoV-2 infection with the Delta variant.

During the study period, none of the vaccinated individuals had been hospitalized. During the same period, 26 unvaccinated participants were hospitalized out of 8,144 who tested positive for COVID-19, corresponding to 0.32%. None of the participants in either group had died by the end of the study.

The level of protection from infection with the Delta variant of SARS-CoV-2 in adolescents is similar to that previously reported for adults.

References

Abaluck J et al., Normalizing Community Mask-Wearing: A Cluster Randomized Trial In Bangladesh. *NBER Working Paper Series*. Published April, 2021. Accessed September 30, 2021 at <https://www.nber.org/papers/w28734>

Adenaiye OO, Lai J, de Mesquita PJB, Hong F, Youssefi S, German J, Tai SS, Albert B, Schanz M, Weston S, Hang J, Fung C, Chung HK, Coleman KK, Sapoval N, Treangen T, Berry IM, Mullins K, Frieman M, Ma T, Milton DK; University of Maryland StopCOVID Research Group. Infectious SARS-CoV-2 in Exhaled Aerosols and Efficacy of Masks During Early Mild Infection. *Clin Infect Dis*. 2021 Sep 14:ciab797. doi: 10.1093/cid/ciab797. Epub ahead of print. PMID: 34519774.

Ader F, Bouscambert-Duchamp M, Hites M, Peiffer-Smadja N, Poissy J, Belhadi D, Diallo A, Lê MP, Peytavin G, Staub T, Greil R, Guedj J, Paiva JA, Costagliola D, Yazdanpanah Y, Burdet C, Mentré F; DisCoVeRy Study Group. Remdesivir plus standard of care versus standard of care alone for the treatment of patients admitted to hospital with COVID-19 (DisCoVeRy): a phase 3, randomised, controlled, open-label trial. *Lancet Infect Dis*. 2021 Sep 14:S1473-3099(21)00485-0. doi: 10.1016/S1473-3099(21)00485-0. Epub ahead of print. PMID: 34534511; PMCID: PMC8439621.

Agha R, Avner JR. Delayed Seasonal RSV Surge Observed During the COVID-19 Pandemic. *Pediatrics*. 2021 Sep;148(3):e2021052089. doi: 10.1542/peds.2021-052089. Epub 2021 Jun 9. PMID: 34108234.

The information provided in this report is not intended to represent a complete compilation of all treatment options available nor is it to be interpreted as medical advice. The information is intended to serve solely as a guide to facilitate a discussion between you and your medical provider(s). Medical decisions should be made only after consultation with and at the direction of your treating physician(s).

Copyright © 2021 PinnacleCare International, LLC. All rights reserved.

No part of this material may be reproduced in any form, or by any means, without the prior written consent of PinnacleCare International, LLC.



Amin K, Cox C. Unvaccinated COVID-19 hospitalizations cost billions of dollars. *Peterson-KFF Health System Tracker*. Published September 14, 2021. Accessed September 30, 2021 at <https://www.healthsystemtracker.org/brief/unvaccinated-covid-patients-cost-the-u-s-health-system-billions-of-dollars/>

Badr DA, Picone O, Bevilacqua E, Carlin A, Meli F, Sibiude J, Mattern J, Fils JF, Mandelbrot L, Lanzone A, De Luca D, Jani JC, Vivanti AJ. Severe Acute Respiratory Syndrome Coronavirus 2 and Pregnancy Outcomes According to Gestational Age at Time of Infection. *Emerg Infect Dis*. 2021 Oct;27(10):2535-2543. doi: 10.3201/eid2710.211394. Epub 2021 Aug 5. PMID: 34352196; PMCID: PMC8462348.

Branswell H. Winter is coming, again: What to expect from Covid-19 as the season looms. *STAT News*. Published September 20, 2021. Accessed September 21, 2021 at <https://www.statnews.com/2021/09/20/winter-is-coming-again-what-to-expect-from-covid-19-as-the-season-looms/>

Budzyn SE, Panaggio MJ, Parks SE, et al. Pediatric COVID-19 Cases in Counties With and Without School Mask Requirements — United States, July 1–September 4, 2021. *MMWR Morb Mortal Wkly Rep* 2021;70:1377–1378. DOI:<http://dx.doi.org/10.15585/mmwr.mm7039e3>

CDC. Studies Show More COVID-19 Cases in Areas Without School Masking Policies. Published September 24, 2021. Accessed September 29, 2021 at <https://www.cdc.gov/media/releases/2021/p0924-school-masking.html>

CDC Statement. CDC Statement on Pregnancy Health Advisory. Published September 29, 2021 at <https://www.cdc.gov/media/releases/2021/s0929-pregnancy-health-advisory.html>

CDC Health Network. Increased Interseasonal Respiratory Syncytial Virus (RSV) Activity in Parts of the Southern United States. Published June 10, 2021. Accessed September 30, 2021 <https://emergency.cdc.gov/han/2021/han00443.asp>

Fischer W, Eron JJ, Holman W, Cohen MS, Fang L, Szewczyk LJ, Sheahan TP, Baric R, Mollan KR, Wolfe CR, Duke ER, Azizad MM, Borroto-Esoda K, Wohl DA, Loftis AJ, Alabanza P, Lipansky F, Painter WP. Molnupiravir, an Oral Antiviral Treatment for COVID-19. *medRxiv* [Preprint]. 2021 Jun 17:2021.06.17.21258639. doi: 10.1101/2021.06.17.21258639. PMID: 34159342; PMCID: PMC8219109.

Gilead. Veklury® (Remdesivir) Significantly Reduced Risk of Hospitalization in High-Risk Patients with COVID-19. Published September 22, 2021 at <https://www.gilead.com/news-and-press/press-room/press-releases/2021/9/veklury-remdesivir-significantly-reduced-risk-of-hospitalization-in-highrisk-patients-with-covid19>

Glatman-Freedman A, Hershkovitz Y, Kaufman Z, Dichtiar R, Keinan-BokerL, Bromberg M. Effectiveness of BNT162b2 vaccine in adolescents during outbreak of SARS-CoV-2 Delta variant infection, Israel, 2021. *Emerg Infect Dis*. 2021 Dec [date cited]. <https://doi.org/10.3201/eid2711.211886>

The information provided in this report is not intended to represent a complete compilation of all treatment options available nor is it to be interpreted as medical advice. The information is intended to serve solely as a guide to facilitate a discussion between you and your medical provider(s). Medical decisions should be made only after consultation with and at the direction of your treating physician(s).

Copyright © 2021 PinnacleCare International, LLC. All rights reserved.
No part of this material may be reproduced in any form, or by any means, without the prior written consent of PinnacleCare International, LLC.



GuroI-Urganci I, Jardine JE, Carroll F, Draycott T, Dunn G, Fremeaux A, Harris T, Hawdon J, Morris E, Muller P, Waite L, Webster K, van der Meulen J, Khalil A. Maternal and perinatal outcomes of pregnant women with SARS-CoV-2 infection at the time of birth in England: national cohort study. *Am J Obstet Gynecol*. 2021 May 20:S0002-9378(21)00565-2. doi: 10.1016/j.ajog.2021.05.016. Epub ahead of print. PMID: 34023315; PMCID: PMC8135190.

Herper M. Pfizer Covid-19 vaccine generates robust antibody response in children, without serious safety issues, company says. *STAT News*. Published September 20, 2021. Accessed September 21, 2021 at <https://www.statnews.com/2021/09/20/pfizer-covid-19-vaccine-children/>

Herper M. Remdesivir reduces Covid hospitalizations when given early, study shows. *STAT News*. Published September 22, 2021. Accessed September 22, 2021 at <https://www.statnews.com/2021/09/22/remdesivir-reduces-covid-hospitalizations-when-given-early-in-study/>

Hu M, Wang J, Lin H, Ruktanonchai CW, Xu C, Meng B, Zhang X, Carioli A, Feng Y, Yin Q, Floyd JR, Ruktanonchai NW, Li Z, Yang W, Tatem AJ, Lai S. Risk of SARS-CoV-2 Transmission among Air Passengers in China. *Clin Infect Dis*. 2021 Sep 21:ciab836. doi: 10.1093/cid/ciab836. Epub ahead of print. PMID: 34549275.

Jehn M, McCullough JM, Dale AP, et al. Association Between K–12 School Mask Policies and School-Associated COVID-19 Outbreaks — Maricopa and Pima Counties, Arizona, July–August 2021. *MMWR Morb Mortal Wkly Rep* 2021;70:1372–1373. DOI: <http://dx.doi.org/10.15585/mmwr.mm7039e>

Kalil AC, Stebbing J. Baricitinib: the first immunomodulatory treatment to reduce COVID-19 mortality in a placebo-controlled trial. *Lancet Respir Med*. 2021 Aug 31:S2213-2600(21)00358-1. doi: 10.1016/S2213-2600(21)00358-1. Epub ahead of print. PMID: 34480862; PMCID: PMC8409093.

Kupferschmidt K. Will the pandemic fade into an ordinary disease like the flu? The world is watching Denmark for clues. *Science*. Published September 30, 2021. Accessed October 1, 2021 at <https://www.science.org/content/article/will-pandemic-fade-ordinary-disease-flu-world-watching-denmark-clues>

Marconi VC, Ramanan AV, de Bono S, Kartman CE, Krishnan V, Liao R, Piruzeli MLB, Goldman JD, Alatorre-Alexander J, de Cassia Pellegrini R, Estrada V, Som M, Cardoso A, Chakladar S, Crowe B, Reis P, Zhang X, Adams DH, Ely EW; COV-BARRIER Study Group. Efficacy and safety of baricitinib for the treatment of hospitalised adults with COVID-19 (COV-BARRIER): a randomised, double-blind, parallel-group, placebo-controlled phase 3 trial. *Lancet Respir Med*. 2021 Aug 31:S2213-2600(21)00331-3. doi: 10.1016/S2213-2600(21)00331-3. Epub ahead of print. Erratum in: *Lancet Respir Med*. 2021 Oct;9(10):e102. PMID: 34480861; PMCID: PMC8409066.

Merck. Merck and Ridgeback's Investigational Oral Antiviral Molnupiravir Reduced the Risk of Hospitalization or Death by Approximately 50 Percent Compared to Placebo for Patients with Mild or Moderate COVID-19 in Positive Interim Analysis of Phase 3 Study. Published October 1, 2021. Accessed October 5, 2021 at <https://www.merck.com/news/merck-and-ridgebacks->

The information provided in this report is not intended to represent a complete compilation of all treatment options available nor is it to be interpreted as medical advice. The information is intended to serve solely as a guide to facilitate a discussion between you and your medical provider(s). Medical decisions should be made only after consultation with and at the direction of your treating physician(s).

Copyright © 2021 PinnacleCare International, LLC. All rights reserved.

No part of this material may be reproduced in any form, or by any means, without the prior written consent of PinnacleCare International, LLC.



[investigational-oral-antiviral-molnupiravir-reduced-the-risk-of-hospitalization-or-death-by-approximately-50-percent-compared-to-placebo-for-patients-with-mild-or-moderat/](#)

McGregor G. Highly-vaccinated, but more cases than ever: Singapore shows the world what 'endemic' COVID might look like. *Fortune*. Published September 28, 2021. Accessed October 1, 2021 at <https://fortune.com/2021/09/28/singapore-covid-reopening-record-cases-vaccines/>

New York Times. Coronavirus World Map: Tracking the Global Outbreak. Published October 4, 2021. Accessed on October 4, 2021 at https://www.nytimes.com/interactive/2021/world/covid-cases.html?pageType=LegacyCollection&collectionName=Maps+and+Trackers&label=Maps+and+Trackers&module=hub_Band®ion=inline&template=storyline_band_recirc

Office for National Statistics. Deaths involving COVID-19 by vaccination status, England: deaths occurring between 2 January and 2 July 2021. Published September 13, 2021. Accessed September 29, 2021 at <https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/articles/deathsinvolvingcovid19byvaccinationstatusengland/deathsoccurringbetween2januaryand2july2021>

Peeples L. Face masks for COVID pass their largest test yet. *Nature*. 2021 Sep 9. doi: 10.1038/d41586-021-02457-y. Epub ahead of print. PMID: 34504329.

Rebmann T, Loux TM, Arnold LD, Charney R, Horton D, Gomel A. SARS-CoV-2 Transmission to Masked and Unmasked Close Contacts of University Students with COVID-19 - St. Louis, Missouri, January-May 2021. *MMWR Morb Mortal Wkly Rep*. 2021 Sep 10;70(36):1245-1248. doi: 10.15585/mmwr.mm7036a3. PMID: 34499631; PMCID: PMC8437055.

Schmidt F, Weisblum Y, Rutkowska M, Poston D, Da Silva J, Zhang F, Bednarski E, Cho A, Schaefer-Babajew DJ, Gaebler C, Caskey M, Nussenzweig MC, Hatzioannou T, Bieniasz PD. High genetic barrier to SARS-CoV-2 polyclonal neutralizing antibody escape. *Nature*. 2021 Sep 20. doi: 10.1038/s41586-021-04005-0. Epub ahead of print. PMID: 34544114.

Sen P, Yamana TK, Kandula S, Galanti M, Shaman J. Burden and characteristics of COVID-19 in the United States during 2020. *Nature*. 2021 Aug 26. doi: 10.1038/s41586-021-03914-4. Epub ahead of print. PMID: 34438440.

Sheahan TP, Sims AC, Zhou S, Graham RL, Pruijssers AJ, Agostini ML, Leist SR, Schäfer A, Dinnon KH 3rd, Stevens LJ, Chappell JD, Lu X, Hughes TM, George AS, Hill CS, Montgomery SA, Brown AJ, Bluemling GR, Natchus MG, Saindane M, Kolykhalov AA, Painter G, Harcourt J, Tamin A, Thornburg NJ, Swanstrom R, Denison MR, Baric RS. An orally bioavailable broad-spectrum antiviral inhibits SARS-CoV-2 in human airway epithelial cell cultures and multiple coronaviruses in mice. *Sci Transl Med*. 2020 Apr 29;12(541):eabb5883. doi: 10.1126/scitranslmed.abb5883. Epub 2020 Apr 6. PMID: 32253226; PMCID: PMC7164393.

Shammas B. Stillbirths have doubled during covid in Mississippi. Officials are sounding the alarm. *The Washington Post*. Published September 9, 2021. Accessed on October 7, 2021 at <https://www.washingtonpost.com/health/2021/09/09/pregnant-covid-mississippi/>

The information provided in this report is not intended to represent a complete compilation of all treatment options available nor is it to be interpreted as medical advice. The information is intended to serve solely as a guide to facilitate a discussion between you and your medical provider(s). Medical decisions should be made only after consultation with and at the direction of your treating physician(s).

Copyright © 2021 PinnacleCare International, LLC. All rights reserved.

No part of this material may be reproduced in any form, or by any means, without the prior written consent of PinnacleCare International, LLC.



Tande AJ, Binnicker MJ, Ting HH, Del Rio C, Jalil L, Brawner M, Carter PW, Toomey K, Shah ND, Berbari EF, SARS-CoV-2 Testing Prior to International Airline Travel, December 2020-May 2021, *Mayo Clinic Proceedings* (2021), doi:<https://doi.org/10.1016/j.mayocp.2021.08.019>.

Taquet M, Dercon Q, Luciano S, Geddes JR, Husain M, Harrison PJ. Incidence, co-occurrence, and evolution of long-COVID features: A 6-month retrospective cohort study of 273,618 survivors of COVID-19. *PLoS Med*. 2021 Sep 28;18(9):e1003773. doi: 10.1371/journal.pmed.1003773. PMID: 34582441; PMCID: PMC8478214.

Van Beusekom M. COVID-19 vaccines don't raise miscarriage risk, 3 studies show. *CIDRAP News*. Published September 9, 2021. Accessed September 13, 2021 at <https://www.cidrap.umn.edu/news-perspective/2021/09/covid-19-vaccines-dont-raise-miscarriage-risk-3-studies-show>

The Washington Post. Tracking cases and deaths in the U.S. Updated September 30, 2021. Accessed September 30, 2021 at https://www.washingtonpost.com/graphics/2020/national/coronavirus-us-cases-deaths/?itid=hp_pandemic

Watson C. Stillbirth rate rises dramatically during pandemic. *Nature*. 2020 Sep;585(7826):490-491. doi: 10.1038/d41586-020-02618-5. PMID: 32934376.

The information provided in this report is not intended to represent a complete compilation of all treatment options available nor is it to be interpreted as medical advice. The information is intended to serve solely as a guide to facilitate a discussion between you and your medical provider(s). Medical decisions should be made only after consultation with and at the direction of your treating physician(s).

Copyright © 2021 PinnacleCare International, LLC. All rights reserved.
No part of this material may be reproduced in any form, or by any means, without the prior written consent of PinnacleCare International, LLC.