PINNACLECARE

Medical Intelligence Report

Date: June 22, 2021

Topic: COVID-19 Vaccination of Children

Overview

The overarching goal of SARS-CoV-2 vaccination programs is to stop transmission of the virus and attain control of the pandemic. To achieve this goal, it is necessary to reduce the number of individuals who are susceptible to the virus, thereby interrupting transmission. Early decisions about who would receive the first doses of a limited supply were made to protect those who were also at the most risk for poor outcomes if infected. Now that vaccine supply is no longer an issue in the United States, the focus becomes stopping transmission throughout the population. Because SARS-CoV-2 is highly transmissible through airborne particles from both symptomatic and non-symptomatic individuals, continued outbreaks will occur in the United States and abroad unless 70% to 80% of the local population can no longer be infected (Gostin et al., 2021). With the increased transmissibility of new variants, such as Alpha (previously known as B.1.1.7) and Delta, some researchers have predicted that the levels of immunity will need to be even higher, around 90% (Aschwanden, 2021).

As of June 20, 2021, there were still at least 11,138 new cases of COVID-19 a day with 18,024 people currently hospitalized and 300 deaths a day due to COVID-19.

This is far below the heights of the pandemic, but with only about 50% of the United States population vaccinated, there are still a large number of individuals susceptible to the virus (New York Times, 2021). Recent evaluations of new cases of COVID-19 indicate that while the rate of new infections in vaccinated individuals has been greatly reduced, the rate of infection in unvaccinated individuals has not changed since the surge experienced in January, 2021 (Keating and Shapiro, 2021).

In other words, people who have not been vaccinated for COVID-19 continue to get sick at the same rate as before the vaccine campaign began, and transmission has only slowed in those who are vaccinated.

The danger of increased transmission in an unvaccinated population from the Delta variant can be seen in Britain where the virus has already become widespread (Van Beusekom, 2021). Researchers in England have been randomly testing individuals in the population to measure the prevalence of the disease as asymptomatic cases may be missed by testing of individuals who seek tests on their own (Riley et al, 2021). The analysis of the screening showed that there was a 50% surge in positive tests in England between the two most recent sampling periods,

April 15 to May 3 and May 20 to June 7, 2021. During the earlier sampling period between April 15 and May 3, 2021, the proportion of positive tests in the random screening was 0.1%, and the proportion of positive tests increased in the most recent period to 0.15% (corresponding to the period from May 20 to June 7, 2021).

Importantly, in the most recent period, children aged five to twelve and young adults aged 18 to 24 were five times more likely to test positive than those 65 or older with a prevalence of 0.35% and 0.36%, respectively.

People younger than 50 were 2.5 times more likely to be infected than older individuals, 0.2% versus 0.08%. At the start of the study, 60% of the cases were due to the Delta variant, and by the end 90% were due to the Delta variant. The surge, led by infections in the young, has led to a delay in the relaxation of restrictions in the country. Steven Riley, Professor of Infectious Disease Dynamics at Imperial College London, stated that "Even though we are seeing the highest infection prevalence in younger people who are less susceptible to COVID-19, if this growth continues it will drive up infections in older, more vulnerable people, as the vaccines are not 100% effective and not everyone has been fully vaccinated." As of June 16, 2021, the CDC estimates that 10% of the cases of COVID-19 in the United States are due to the Delta variant (Soucheray, 2021). This is up from 2.7% of cases on May 22 in the United States. The time observed in England to double the amount of cases from the Delta variant was eleven days. Using this replication rate, the majority of COVID-19 cases in the United States will be due to the extremely transmissible Delta variant by the end of July.

The two methods available to acquire immunity from a virus are a previous infection or vaccination. In healthy individuals, natural infection by SARS-CoV-2 leads to a strong immune response that currently is expected to be long lasting based on the presence of long-lived antibody producing cells detected in the bone marrow of individuals who have recovered from COVID-19 (Turner et al, 2021). However, some individuals become severely ill from the infection, requiring hospitalization and treatment in the intensive care unit. Others have mild or no symptoms but develop long lasting disabilities months after the infection has resolved. Severe disease is more likely to occur in those with certain chronic medical conditions, but researchers have not found a common link that would allow them to predict those who are more likely to have long-term effects after infection or which children progress from mild COVID-19 to the much more serious MIS-C inflammatory syndrome. It is also not known what the age threshold is that helps to protect young children from infection and the most severe symptoms.

Because of the unknowns associated with natural infection, even for healthy individuals, vaccination is the safest way to acquire immunity to SARS-CoV-2 and stop the transmission and thereby the pandemic.

That is to say, the current push for vaccination of children is not for their own protection from infection by SARS-CoV-2, per se, but rather to remove a susceptible population in order to control the pandemic. Until transmission is controlled throughout the world, there continues to be the risk of more transmissible or more pathogenic strains of the virus developing. However, getting the vaccine also removes the risk of potential life-long effects that can occur from a serious case of COVID-19 or the less understood Long COVID.

Clinical Trials and Studies of the Vaccines

The Pfizer-BioNTech vaccine was given an Emergency Use Authorization (EAU) for use of the vaccine in adolescents aged 12 to 15 on May 10, 2021 by the FDA, and the Moderna vaccine filed for an EAU for use in adolescents aged 12 to 17 with the FDA on May 25, 2021.

Assessment of the Pfizer-BioNTech Vaccine

The Emergency Use Authorization of the Pfizer-BioNTech vaccine was based on information reviewed by the FDA from an ongoing Phase 1/2/3 trial that has enrolled approximately 46,000 participants, including 2,260 participants who were 12 through 15 years of age (FDA Coronavirus, 2021, FDA Pfizer, 2021, and Frenck et al., 2021). The response to the vaccine was specifically compared to a group of participants aged 16 to 25 who received the vaccine at the same time and a placebo group that received a shot of saline instead of the vaccine. The participants were followed for two months after receiving the second dose of the vaccine in order to observe adverse reactions and measure the immune response.

The antibody response in participants 12 to 15 was at least as high as the response observed for participants aged 16 to 25. The vaccine was 100% effective in preventing COVID-19 based on no COVID-19 cases in the vaccinated group compared to 16 cases in the unvaccinated group.

Overall the safety profile was considered good. The following is the complete summary of the incidences observed and is more detail than is typically reported. Usually only issues that are serious or related to the treatment are highlighted, but a misrepresentation of some of the results from the trial has led to confusion about the frequency of adverse reactions to the vaccine. Therefore, all of the safety information from the clinical trial is listed here.

There were no deaths from reactions to the vaccine and no cases of vaccine-associated enhanced COVID-19 symptoms. Injection-site reactions were reported by 91% of participants with the most frequent symptom being pain. Systemic reactions were also common in the first week after each dose of the vaccine. The most common systemic reactions reported were fatigue (78%), headache (76%), chills (49%), muscle pain (42%), fever (24%), and joint pain (20%). Some participants also experienced diarrhea and vomiting. Systemic reactions were generally more frequent and severe after dose two compared with dose one.

> **These systemic reactions are the flu-like symptoms most people experience as their immune system responds to the components of the vaccine and begins producing antibodies.**

During the study period, seven (or 0.6%) of vaccinated participants and one (or 0.1%) unvaccinated participant developed enlarged lymph nodes within two to ten days after receiving a dose. The lymph nodes affected were mainly in the arm and neck area. In 50% of those

affected, the symptoms resolved within one to ten days. The remaining were ongoing at the cutoff of the study period for application of the EAU to the FDA. Three additional cases were reported that began more than 28 days after the second dose and were found to not be related to the vaccine. One of the later cases was associated with a known case of mononucleosis.

There were six hypersensitivity reactions reported in vaccinated participants, corresponding to 0.53%, and ten reactions in unvaccinated participants, corresponding to 0.89%. The majority of reactions were skin reactions with hives being the most common symptom.

Severe, local or systemic reactions within seven days following either the first or second dose of vaccine were reported by 10.7% of vaccine recipients. A severe event was defined as Grade 3 on the clinical trial rating system, which means that there were significant symptoms requiring any use of prescription pain reliever or prevented daily activity. The most common Grade 3 symptoms reported by vaccine recipients were fatigue (3.5%), fever (3.0%), headache (2.7%), chills (2.1%), and injection site pain (1.5%).

The researchers also recorded serious adverse events that occurred during the trial. The definition of a serious adverse event is an untoward medical occurrence that resulted in death, was life-threatening, required inpatient hospitalization or prolongation of existing hospitalization, or resulted in persistent disability or incapacity.

The serious adverse events that were reported include

Vaccine Group

- Exacerbation of depression in 3 participants with pre-existing anxiety or depression
- One participant reported generalized neuralgia (nerve pain), and was later diagnosed with functional abdominal pain
- One participant with a history of ADHD and recent anxiety and depression diagnoses was hospitalized for suicidal ideation

Placebo Group

- Two participants were hospitalized for appendicitis

There were more occurrences of serious adverse events recorded in the group receiving the vaccine (0.4%) compared to those not receiving the vaccine (0.2%).

The number of serious events that occurred, however, was very low. The rate of serious events observed in the clinical trial was similar to the frequency that is observed during daily life in the general population for both the placebo and vaccinated group of participants.

There were two participants in the group that received the vaccine that withdrew from the study before receiving the second dose and none in the placebo group that withdrew. One participant withdrew due to a high fever after the first dose and was included as a non-serious adverse event. The fever resolved after two days. The second participant withdrew due to exacerbation of pre-existing anxiety and depression, which was included as a serious adverse event.

There were no cases of Bell's palsy or facial paralysis in any of the participants. There was one participant that received the vaccine and one participant that received the placebo that experienced a deep vein thrombosis (blood clot). Both cases were found to be unrelated to the vaccine. Data collected after the end of the official study period indicates that there were four cases of deep vein thrombosis in participants who received the vaccine and three in those in the placebo group in the intervening time period. Two of the cases in vaccinated individuals have resolved and were due to pre-existing diabetes in one case and a sports related injury in the other. The remaining two instances had progression to pulmonary embolism and symptoms have since resolved, but the cause of the blood clots has not been determined as of the time of the report to the FDA. The researchers state, however, that "the clinical features of these thromboembolic serious adverse events do not appear to be similar to cases of thrombosis with thrombocytopenia syndrome (TTS) reported following adenovirus-vectored COVID-19 vaccines." In the TTS cases, the characteristics were very specific both in where the clots formed and the severity of the clotting.

Overall, the frequency of non-serious adverse events was higher in the vaccinated group compared to the group that received the placebo, 24% versus 4.7%, and this discrepancy is due to the high amount of local and systemic reactions to the vaccine (e.g. fever, aches) as the immune system responded.

Advisory Committee on Immunization Practices Recommendation

Once the FDA certifies that the vaccine is effective and safe by issuing an EUA or other type of approval, the Advisory Committee on Immunization Practices (ACIP) develops recommendations on the use of the vaccine (CDC-How CDC, 2020). The ACIP is a federal advisory committee made up of medical and public health experts that holds regular meetings about newly approved vaccines. The ACIP evaluated the information from the EUA to decide whether to recommend the use of the vaccine for individuals aged 12 to 15 and published their findings (CDC ACIP, 2021).

They determined that there was a large anticipated effect of the vaccine on the risk of symptomatic COVID-19 among those aged 12 to 15 year who received two doses of the Pfizer-BioNTech vaccine. They also found that the undesirable effects were expected to be small. Specifically, the risk of serious adverse events was low, but slightly more common in the vaccine than the placebo group.

The shortcomings acknowledged in the ACIP evaluation

- The length of efficacy of the vaccine was not determined because the follow-up period was only two months. However, longer-term efficacy from the adult trial and strong vaccine effectiveness observed during use after authorization in adults suggest that short-term efficacy will translate to longer-term efficacy.
- There was also a concern because the available evidence does not provide certainty that rare or serious adverse events that may occur in a large population were observed during the trial due to the short follow-up and small sample size. The ACIP stated that surveillance after authorization will be critical to detect any rare, serious adverse events which were not identified in the clinical trial.

After assessment, the ACIP determined that the "desirable consequences clearly outweigh undesirable consequences in most settings."

The time period for observation in this trial is shorter than typically used for the approval of a new medication. While the initial studies are completed, the participants in the studies continue to be observed to determine if there are any issues that develop over time.

Vaccine monitoring of the numerous vaccines developed for multiple uses over the years has historically shown that side effects generally happen within six weeks of receiving a vaccine dose.

Events that occur further away from vaccination are harder to connect as having been caused by the vaccine as so many other things have happened in the meantime. For this reason, the FDA required each of the authorized COVID-19 vaccines to be studied for at least two months (eight weeks) after the final dose (CDC Safety, 2021).

Additionally, possible side effects from the vaccine are still being recorded using a different method than a clinical trial, the Vaccine Adverse Event Reporting System, which is described in detail below. The number of people in the world who have received the Pfizer-BioNTech vaccine far outnumbers the size of a typical clinical trial used for FDA approval of a new treatment, allowing for identification of rare side effects that would not have been evident in even the largest trials. For example, over 170 million doses of the Pfizer-BioNTech COVID-19 vaccine have been given in the United States from December 2020, through June 2021, and Israel has given over 10 million doses of the Pfizer-BioNTech vaccine.

Post-Authorization Screening of the Pfizer-BioNTech Vaccine

As stated by the ACIP, the safety data collected during clinical trials is just the start of safety monitoring of vaccines. The Department of Health and Human Services, CDC, and FDA collect reports of adverse events that occur after vaccination from healthcare providers and individuals even after a vaccine is being used by the general public. The reporting system, called the

Vaccine Adverse Event Reporting System (VAERS), allows researchers to collate the data and watch for trends that would indicate if there are rare side effects that are occurring.

However, not all of the medical events experienced soon after vaccination are attributable to the vaccine.

Coincidental events can occur around the time a vaccine is given that are not caused by the vaccine. For example, some of the participants in the clinical trial described above had to be hospitalized for appendicitis soon after their first dose of placebo. However, the placebo from the trial did not cause the appendicitis, it just occurred at around the same time period. In a similar way, many of the events submitted to the VAERS end up being coincidental events. Physicians are also required to report any patient deaths that occur within a certain timeframe after vaccination. Therefore, anyone who dies of any cause after being vaccinated would be reported to the VAERS so that any patterns can be identified. However, there is no evidence that the cause of death for any of the individuals who have been reported to the VAERS was related to their vaccination.

Researchers must sift through the reports to VAERS to find adverse events that are occurring at a higher rate than random chance. They then investigate if there is a potential mechanism of action for the vaccine to cause the event. The process is difficult because when an event is rare, it can be hard to determine whether the cause is the vaccine or other unrelated events.

During the first month of the vaccination campaign for COVID-19, December 14, 2020 to January 13, 2021, there were 13,794,904 COVID-19 vaccine doses given and the VAERS received 6,994 reports of adverse events (Gee et al., 2021). Among all reports, 90.8% were classified as non-serious, and there were 113 deaths reported, which was 1.6% of all the reports. Headache (22.4%), fatigue (16.5%), and dizziness (16.5%) were the most frequently reported symptoms after vaccination. In individuals who were not residents of long-term care facilities, there were 31 deaths that occurred within 20 days of vaccination. In 16 cases, the cause of death has been determined and was found to be from underlying heart disease, cancer, stroke, probable pulmonary embolism, and otherwise frail health. The remaining cases are still under investigation.

There have been three serious adverse events associated with vaccination for COVID-19 identified through post-authorization screening.

There were cases of anaphylaxis associated with both the Pfizer-BioNTech and Moderna vaccines. In the first month, there were a total of 62 reports of anaphylaxis. Researchers also identified a severe blood clotting condition associated with the adenovirus-vector vaccines from AstraZeneca-Oxford and Johnson & Johnson. The condition caused by the reaction is life-threatening, but the symptoms are now recognized and treatments are available.

The more recent adverse event identified is associated with the Pfizer-BioNTech vaccine. Reporting systems in Israel and the United States identified cases of myocarditis, or inflammation of the heart muscles, that occurred after vaccination.

Public health officials in Israel have issued a press release describing several incidences of myocarditis after vaccination for COVID-19 with the Pfizer-BioNTech vaccine (IMOH, 2021).

Based on the report, the symptoms observed were usually a mild illness characterized by chest pains, shortness of breath, or rapid heart palpitations. There were a total of 275 cases of myocarditis from any cause reported in Israel between December, 2020 and May, 2021, and 148 of these cases occurred near vaccination for COVID-19, making them potentially associated with vaccination.

Characteristics of individuals with myocarditis around the time of COVID-19 vaccination

- 27 cases occurred after the first dose
- 121 cases occurred after the second dose
- Those were affected were mainly younger men between 16 and 19
- Most cases were treated in the hospital for up to 4 days
- 95% were considered mild cases

The Israeli officials concluded that “There is some probability for a possible link between the second vaccine dose and the onset of myocarditis among young men aged 16 to 30.”

Cases of myocarditis around the time of vaccination for COVID-19 have also been reported in the United States (Soucheray, 2021). Based on the data collected, the cases are mild, often follow the second dose of mRNA vaccine, and are seen more often in males than females. Less information has been released than in the report from Israel. Officials at the CDC stated in a report on June 10, 2021 in *STAT News*, that there had been 573 cases of myocarditis and pericarditis reported to the VAERS after individuals received their second dose and 216 after their first dose from people of all age groups (Joseph, 2021). There had been 79 cases at the time from the 2.3 million individuals 16 to 17 years of age who had received doses. The typical frequency of myocarditis in this age group would suggest a group this size would have two cases, suggesting that the number is higher than normal. The official also said not all of the cases had been verified yet, but continued investigation is warranted. There were also reports from the United States Department of Defense of 14 cases of myocarditis, and the European Medicines Agency (The European equivalent to the FDA), said they had received 107 reports of myocarditis following vaccination with the Pfizer-BioNTech vaccine (Vogel and Couzin-Frankel, 2021).

Researchers and physicians mention that the side effect seems to be very rare and is treatable, but that parents and pediatricians should be aware of youngsters with chest pain, shortness of breath, or rapid heart palpitations that occur after vaccination for COVID-19.

Researchers in Israel published a more detailed case study of seven of the cases of myocarditis detected in individuals between the ages of 16 and 18 (Snapiri et al., 2021). The cases were identified between January and February of 2021 at three pediatric medical centers in Israel. All of the individuals were male and started to have chest pain within one to three days after vaccination with the Pfizer-BioNTech vaccine. Six of the individuals were affected after the second dose and the remaining was affected after the first. All of the cases were classified as mild. Four patients were admitted to the pediatric intensive care unit for observation, but none

required cardiovascular or respiratory support. Five children were treated with ibuprofen, one was treated with aspirin, and one did not receive any pharmacologic treatment.

All of the affected individuals tested negative for COVID-19 with repeated PCR-based tests, but the researchers state that it was not possible to rule out a possible connection with a SARS-CoV-2 infection rather than response to the vaccine. There is evidence of similar cardiac effects in adults both during active infection and after the resolution of COVID-19. Thus far myocarditis has only been described in association with the MIS-C condition in children, and none of the individuals in this study showed any sign or symptoms associated with either COVID-19 or MIS-C.

The researchers state that myocarditis has been observed as an adverse effect from other vaccines used in both children and adults, and therefore it is reasonable that this condition may arise after vaccination. No clear mechanism of action or factors associated with the effect were determined in previous cases.

Vaccination after COVID-19 Infection

It is currently recommended that individuals who have had COVID-19 also get vaccinated (Raw et al., 2021). Vaccination has been shown to cause a further increase in the strength of the immune response and also may confer additional protection from variants, such as Beta (previously B.1.351), which are able to avoid the immune response. There is no evidence of an increased risk of serious adverse events in individuals who have recovered from COVID-19. Some individuals experience more flu-like symptoms after the first dose compared to those who have not previously had COVID-19. For instance, fever, fatigue, muscle aches, joint pain, and swollen lymph nodes have been reported.

There have been preliminary reports that some individuals experiencing symptoms of Long COVID have had a relief of symptoms after vaccination, but further study is needed to determine the extent of the effects.

Complications from COVID-19

While children are less likely to become severely ill from infection with SARS-CoV-2, there is still an increased risk of hospitalization compared to previous years. A recent study of the hospitalization rates of adolescents aged 12 to 17 years of age showed that most COVID-19–associated hospitalizations do occur in adults, but severe disease occurs in all age groups (Havers et al., 2021).

There were 376 hospitalized adolescents who had a positive COVID-19 test between January 1 and March 31, 2021 based on information from COVID-NET, a surveillance program that includes 14 states and covers approximately 10% of the United States population. There were 172 of this group who were analyzed separately because the primary reason for admission to the hospital might not have been directly COVID-19 related, e.g. obstetrics, trauma, or inpatient surgery, but they tested positive due to procedural screening.

Out of the remaining 204 individuals, 70.6% had one or more underlying medical conditions. The most common conditions included obesity (35.8%), chronic lung disease, such as asthma, (30.9%), and neurologic disorders (14.2%).

After admission to the hospital for treatment of COVID-19, 31.4% required treatment in the intensive care unit, and 4.9% required invasive mechanical ventilation.

The COVID-19–associated hospitalization rates for adolescents between the ages of 12 and 15 during October 1, 2020 through April 24, 2021, which corresponds to the typical flu-season, were 2.5 to 3 times higher than influenza-associated hospitalization rates from the three recent influenza seasons, corresponding to 2017–18, 2018–19, and 2019–20.

This indicates that 2.5 to 3 times more individuals aged 12 to 15 will be hospitalized from COVID-19 outbreaks than a normal flu season.

The overall number of individuals in this study only corresponds to 10% of the population of the United States because not all of the states provide information to the surveillance programs, so the overall numbers of adolescents affected will be much higher. The medical conditions found to be associated with poor outcomes, obesity, lung disease or asthma, and neurological disorders are not uncommon in this age group. Neurological disorders can include headaches and migraines, epilepsy, or neuromuscular disorders.

Risk of Long COVID in Children

With the high number of asymptomatic cases of COVID-19 in individuals 18 or under combined with the wide variety of symptoms associated with Long COVID, it has been difficult to determine the prevalence of the disorder (Cooney, 2021).

Researchers currently estimate that between 7% and 20% of children and adolescents who had COVID-19 will be affected by Long COVID.

The disorder affects multiple organ systems such as neurological, respiratory, gastrointestinal, musculoskeletal, cardiovascular, and dermatologic, and so far there is no way to predict who will develop problems after recovering from the initial infection. Age does seem to be a factor, and those over the age of 12 are more likely to develop Long COVID, but there are cases of infants 18 months of age being affected. The range of severity observed so far can span from headache to brain fog to numbness that leaves children unable to walk.

Physicians studying the condition report that it has been even more difficult to treat in children than in adults. Adults have abnormal results on laboratory tests or imaging scans, but children often have normal white blood cell counts in general, normal inflammatory markers, normal pulmonary function tests, normal EKGs, normal X-rays, and normal echocardiograms.

In a study of health records of 1,959,982 people, 23% sought medical treatment for a new condition after have having COVID-19 (Belluck, 2021). The report found that all age groups were affected, including children. The most common new health problems included pain, such

as nerves and muscles; breathing difficulties; high cholesterol; malaise and fatigue; and high blood pressure. Other issues included intestinal symptoms; migraines; skin problems; heart abnormalities; sleep disorders; and mental health conditions like anxiety and depression. Of those with long-term symptoms after COVID-19, 27% had mild or moderate symptoms and 19% were asymptomatic during the initial infection.

Risk of Infection for Unvaccinated Individuals

The rate of new cases is 73% higher for unvaccinated individuals compared to the national average, which includes the rate for both vaccinated and unvaccinated individuals.

The rate of hospitalization and death for unvaccinated people also remains high, at levels nearly the same as it was two to three months ago (Keating and Shapiro, 2021).

In other words, the pandemic is spreading as fast among the unvaccinated as it did during the winter surge.

There are six states where the average new daily deaths per one million unvaccinated residents is 50% higher than the overall national rate that includes both vaccinated and unvaccinated individuals. Additionally, the death rate for unvaccinated individuals has remained at the same level, rather than declining as it has in those who have been vaccinated, meaning that unvaccinated people are not safer.

Facilities across the United States have reported that they are seeing only unvaccinated individuals admitted to the hospital for treatment for COVID-19 (Edwards, 2021). A national spokesperson for the American Academy of Pediatrics also stated that the children in her hospital that were sick were all unvaccinated. The only breakthrough infections, that is infections after being vaccinated for COVID-19, have been in individuals with compromised immune systems.

Data from Maryland indicates that unvaccinated young adults in the state have the same infection rate as they had during the January surge in COVID-19 cases (Keating and Shapiro, 2021). Furthermore, the risk of hospitalization among those who are infected is more than double the risk reported in January, which is thought to be due to the spread of variants of the virus. Officials in Washington state have also reported an increased risk of hospitalization for unvaccinated residents. For example, unvaccinated individuals over 65 years old were 11-times more likely to be hospitalized and those 45 to 64 were 18-times more likely to require hospitalization for COVID-19.

In Colorado, the Delta variant accounts for 40% of the cases as of the first week of June, and the spread of Delta has occurred more quickly than that of Alpha (previously known as B.1.1.7) (Ingold, 2021). In Mesa County, Colorado, it is thought that all cases of COVID-19 are being caused by Delta at this point. At the beginning of the month, the county released a public health alert warning of widespread transmission that was occurring mainly in children ages ten to 19 with high levels in those under ten as well.

References

Aschwanden C. Five reasons why COVID herd immunity is probably impossible. *Nature*. 2021 Mar;591(7851):520-522. doi: 10.1038/d41586-021-00728-2. PMID: 33737753.

Belluck P. Many Post-Covid Patients Are Experiencing New Medical Problems, Study Finds. *The New York Times*. Published June 15, 2021. Accessed June 16, 2021 at https://www.nytimes.com/2021/06/15/health/covid-19-patients.html

CDC. ACIP Evidence to Recommendations for Use of Pfizer-BioNTech COVID-19 Vaccine under an Emergency Use Authorization. Published May 14, 2021. Accessed June 16, 2021 at https://www.cdc.gov/vaccines/acip/recs/grade/covid-19-pfizer-biontech-etr-12-15-years.html

CDC. How CDC Is Making COVID-19 Vaccine Recommendations. Updated November 9, 2020. Accessed on November 13, 2020 at https://www.cdc.gov/coronavirus/2019-ncov/vaccines/recommendations-process.html

CDC. Safety of COVID-19 Vaccines. Published June 8, 2021. Accessed June 16, 2021 at https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/safety-of-vaccines.html

Cooney E. As more kids go down the 'deep, dark tunnel' of long Covid, doctors still can't predict who is at risk. *STAT News*. Published June 10, 2021. Accessed June 16, 2021 at https://www.statnews.com/2021/06/10/as-more-kids-get-long-covid-doctors-still-cant-predict-who-is-at-risk/

FDA. Coronavirus (COVID-19) Update: FDA Authorizes Pfizer-BioNTechCOVID-19 Vaccine for Emergency Use in Adolescents in Another Important Action in Fight Against Pandemic. Published May 10, 2021. Accessed June 16, 2021 at https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-pfizer-biontech-covid-19-vaccine-emergency-use

FDA. Pfizer-BioNTech COVID-19 Vaccine EUA Amendment Review Memorandum. Published April 9, 2021. Accessed June 16, 2021 at https://www.fda.gov/media/148542/download

Frenck RW Jr, Klein NP, Kitchin N, Gurtman A, Absalon J, Lockhart S, Perez JL, Walter EB, Senders S, Bailey R, Swanson KA, Ma H, Xu X, Koury K, Kalina WV, Cooper D, Jennings T, Brandon DM, Thomas SJ, Türeci Ö, Tresnan DB, Mather S, Dormitzer PR, Şahin U, Jansen KU, Gruber WC; C4591001 Clinical Trial Group. Safety, Immunogenicity, and Efficacy of the BNT162b2 Covid-19 Vaccine in Adolescents. *N Engl J Med*. 2021 May 27:NEJMoa2107456. doi: 10.1056/NEJMoa2107456. Epub ahead of print. PMID: 34043894; PMCID: PMC8174030.

Gee J, Marquez P, Su J, Calvert GM, Liu R, Myers T, Nair N, Martin S, Clark T, Markowitz L, Lindsey N, Zhang B, Licata C, Jazwa A, Sotir M, Shimabukuro T. First Month of COVID-19 Vaccine Safety Monitoring - United States, December 14, 2020-January 13, 2021. *MMWR Morb Mortal Wkly Rep*. 2021 Feb 26;70(8):283-288. doi: 10.15585/mmwr.mm7008e3. PMID: 33630816.

Gostin LO, Shaw J, Salmon DA. Mandatory SARS-CoV-2 Vaccinations in K-12 Schools, Colleges/Universities, and Businesses. *JAMA*. 2021 Jun 7. doi: 10.1001/jama.2021.9342. Epub ahead of print. PMID: 34096972.

Havers FP, Whitaker M, Self JL, Chai SJ, Kirley PD, Alden NB, Kawasaki B, Meek J, Yousey-Hindes K, Anderson EJ, Openo KP, Weigel A, Teno K, Monroe ML, Ryan PA, Reeg L, Kohrman A, Lynfield R, Como-Sabetti K, Poblete M, McMullen C, Muse A, Spina N, Bennett NM, Gaitán M, Billing LM, Shiltz J, Sutton M, Abdullah N, Schaffner W, Talbot HK, Crossland M, George A, Patel K, Pham H, Milucky J, Anglin O, Ujamaa D, Hall AJ, Garg S, Taylor CA; COVID-NET Surveillance Team. Hospitalization of Adolescents Aged 12-17 Years with Laboratory-Confirmed COVID-19 - COVID-NET, 14 States, March 1, 2020-April 24, 2021. *MMWR Morb Mortal Wkly Rep*. 2021 Jun 11;70(23):851-857. doi: 10.15585/mmwr.mm7023e1. PMID: 34111061.

Ingold J. The Delta coronavirus variant is exploding across Colorado. That's bad news for unvaccinated people. *The Colorado Sun*. Published June 21, 2021 Accessed on June 21, 2021 at https://coloradosun.com/2021/06/21/coronavirus-delta-variant-vaccination/

Israeli Ministry of Health. Surveillance of Myocarditis (Inflammation of the Heart Muscle) Cases Between December 2020 and May 2021 (Including). Published June 2, 2021. Accessed June 2, 2021 at https://www.gov.il/en/departments/news/01062021-03

Joseph A. U.S. health officials report higher-than-expected heartinflammation cases following Covid-19 vaccination. *STAT News*. Published June 10, 2021. Accessed June 16, 2021 at https://www.statnews.com/2021/06/10/officials-higher-than-expected-heart-inflammation-cases-covid-19-vaccination/

Keating D, Shapiro L. The unseen covid-19 risk for unvaccinated people. *The Washington Post.* Published May 21, 2021. Accessed May 28, 2021 at https://www.washingtonpost.com/health/interactive/2021/covid-rates-unvaccinated-people/

The New York Times. Coronavirus in the U.S.: Latest Map and Case Count. *The New York Times.* Updated June 21, 2021. Accessed June 21, 2021 at https://www.nytimes.com/interactive/2021/us/covid-cases.html

Raw RK, Kelly CA, Rees J, Wroe C, Chadwick DR. Previous COVID-19 infection, but not Long-COVID, is associated with increased adverse events following BNT162b2/Pfizer vaccination. *J Infect*. 2021 May 29:S0163-4453(21)00277-2. doi: 10.1016/j.jinf.2021.05.035. Epub ahead of print. PMID: 34062184; PMCID: PMC8164507.

Riley S et al., REACT-1 round 12 report: resurgence of SARS-CoV-2 infections in England associated with increased frequency of the Delta variant. Published June 17, 2021. Accessed June 21, 2021 at https://spiral.imperial.ac.uk/handle/10044/1/89629

Snapiri O, Rosenberg Danziger C, Shirman N, Weissbach A, Lowenthal A, Ayalon I, Adam D, Yarden-Bilavsky H, Bilavsky E. Transient Cardiac Injury in Adolescents Receiving the BNT162b2 mRNA COVID-19 Vaccine. *Pediatr Infect Dis J.* 2021 Jun 2. doi: 10.1097/INF.0000000000003235. Epub ahead of print. PMID: 34077949.

Soucheray S. CDC: Delta variant now 10% of US COVID-19 cases. *CIDRAP News*. Published June 16, 2021. Accessed June 21, 2021 at https://www.cidrap.umn.edu/news-perspective/2021/06/cdc-delta-variant-now-10-us-covid-19-cases

Soucheray S. COVID-19 cases drop sharply across US. *CIDRAP News*. Published May 24, 2021. Accessed May 25, 2021 at https://www.cidrap.umn.edu/news-perspective/2021/05/covid-19-cases-drop-sharply-across-us

Turner JS, Kim W, Kalaidina E, Goss CW, Rauseo AM, Schmitz AJ, Hansen L, Haile A, Klebert MK, Pusic I, O'Halloran JA, Presti RM, Ellebedy AH. SARS-CoV-2 infection induces long-lived bone marrow plasma cells in humans. *Res Sq* [Preprint]. 2020 Dec 31:rs.3.rs-132821. doi: 10.21203/rs.3.rs-132821/v1. Update in: Nature. 2021 May 24;: PMID: 33398264; PMCID: PMC7781328.

Van Beusekom M. Youth, Delta variant behind UK COVID surge. *CIDRAP News*. Published June 17, 2021. Accessed June 21, 2021 at https://www.cidrap.umn.edu/news-perspective/2021/06/youth-delta-variant-behind-uk-covid-surge

Vogel G, Couzin-Frankel J. Israel reports link between rare cases of heart inflammation and COVID-19 vaccination in young men. *Science*. Published June 1, 2021. Accessed on June 2, 2021 at https://www.sciencemag.org/news/2021/06/israel-reports-link-between-rare-cases-heart-inflammation-and-covid-19-vaccination