COVID-19 Evidence Digest 4/14/21

Characteristics and Disease Severity of US Children and Adolescents Diagnosed With COVID-19 (JAMA Network Open)

Bottom Line: Of 2430 pediatric patients hospitalized with COVID-19, almost 1/3rd had severe COVID-19.

Details: This cohort study estimated associations between clinical and demographic characteristics and severe COVID-19 (requiring treatment in an IFU or step-down unit, use of invasive mechanical ventilation, or resulting in death) among hospitalized pediatric patients using discharge data from 869 medical facilities. Data on patients ≤18 with an inpatient or emergency department encounter with a COVID-19 discharge diagnosis from 3/1/20-10/31/20 were analyzed. Of 20,714 pediatric patients with COVID-19, over half were girls (53%), 54% were between 12-18 years of age, 39% were Hispanic or Latino individuals, and 24% were non-Hispanic Black individuals. Of those patients hospitalized with COVID-19 (n=2430), 31% (n=756) experienced severe COVID-19. There was an association of severe COVID-19 among patients with 1 or more chronic conditions (adjusted odds ratio = 3.27); in 2-5 year-olds (AOR=1.53) and 6-11 year-olds (AOR=1.53) vs 12-18 year-olds; and in male vs female patients (AOR=1.52).

Key Takeaways:

- In this study, an increased association between severe COVID-19 and children 2-11 vs 12-18 years of age was observed. An abundance of caution, rather than disease severity, may explain this finding, which nonetheless has implications for clinical and resource planning decisions.
- Findings suggest that male sex and existing chronic conditions are independently associated with severe COVID-19.
- Limitations include: inability to differentiate between risk factors associated with severe COVID-19 vs multisystem inflammatory syndrome in children; the fact that chronic conditions could be co-occurring, underlying, or resulting from COVID-19 illness; and potential underdiagnosis of particular chronic conditions in medical records.

Inhaled Budesonide in the Treatment of Early COVID-19 (STOIC): A Phase 2, Open-Label, Randomised Controlled Trial (Lancet)

Bottom Line: Taking an inhaled steroid medication within the first week of mild COVID-19 symptom onset may reduce the need for subsequent urgent medical care and reduce recovery time.

Details: This study looked at whether the use of inhaled glucocorticoids (steroid medication) among patients with chronic respiratory disease could explain their underrepresentation in patients hospitalized with COVID-19 and whether this medication may be an effective treatment for early COVID-19. An open-label phase 2 randomized controlled trial was conducted in England to compare inhaled budesonide with usual care in adults within 7 days of mild COVID-19 symptom onset from 7/16/20-12/9/20; mild symptoms were defined as new onset fever and cough and/or loss of smell, without needing supplemental oxygen. 146 participants were randomized to the budesonide (n=73) or usual care group (n=73) by age (≤40 years or >40 years), sex, and having 1 or fewer or 2 or more comorbidities. Patients in the budesonide group received it in dry

powder form via a turbohaler at 800 µg per actuation, and were asked to take two inhalations 2x per day until symptoms resolved. Study outcomes of interest were COVID-19-related urgent care or ED visits, or hospitalizations. Both per-protocol (PP; only includes data from patients who completed treatment as intended; n=139) and intention to treat (ITT; includes all patients who received treatment, regardless of whether they received or finished it) analyses were conducted. In ITT analysis, 3% of participants receiving budesonide needed subsequent care vs 15% of patients in the control group, which was a statistically significant difference. In the PP analysis, treatment did not decrease the need for subsequent care. Based on the ITT analysis, 8 patients would need to be treated with budesonide in order for 1 to not need subsequent care. Moreover, participants in the treatment group had fewer days with a fever, were less likely to have symptoms 14 and 28 days later, and recovered 1 day faster, on average, than the control group; 7% of treatment group participants (n=5) reported self-limiting adverse events.

Key Takeaways:

- This study has several limitations, including that it assessed the need for subsequent medical care, nor mortality, and enrolled patients were generally healthy compared to the general population, thus limiting the generalizability of findings to sicker patients with mild COVID-19.

Antibody Persistence through 6 Months after the Second Dose of mRNA-1273 Vaccine for Covid-19 (NEJM)

Bottom Line: In this study of 33 adults who received both doses of the Moderna vaccine, neutralizing antibody levels were high 6 months after the second dose.

Details: In this study, blood was taken for antibody testing from 33 adults enrolled in Moderna's clinical trials for the COVID-19 vaccine 180 days after receiving their second dose. Binding antibody levels were well above the detectable limit for all age groups, though antibodies were slightly lower for ≥56 year-olds (92,451 geometric mean end-point titers (GMTs) for 18-55 year olds vs 62,424 GMTs and 49,373 GMTs for 56-70 year-olds and ≥71 year-olds, respectively). Blood from these participants was also able to neutralize live SARS-CoV-2, though again, GMTs were lower in 56 to ≥71 year-olds.

Key Takeaways:

- Findings from this study suggest that the Moderna COVID-19 vaccine provides durable protection 6 months after the second dose; however, how effective the vaccine is against variants of interest/concern and how long immunity lasts warrant further study.

Evidence for Increased Breakthrough Rates of SARS-CoV-2 Variants of Concern in BNT162b2 mRNA Vaccinated Individuals (medRxiv – pre-print)

Bottom Line: Findings from this pre-print study of individuals with documented SARS-CoV-2 infection following receipt of the Pfizer-BioNTech COVID-19 vaccine suggest an increased occurrence of B.1.351 and B.1.1.7 variants of concern in vaccine breakthrough infections in fully vaccinated and partially vaccinated individuals, respectively,

necessitating both mass vaccination with two doses and continued non-pharmaceutical interventions to control the spread of SARS-CoV-2.

Details: This study examined whether B.1.351 and B.1.1.7 variants of concern can break through protection conferred by the Pfizer-BioNTech COVID-19 vaccine in a real-world setting. Individuals with documented SARS-CoV-2 infection (symptomatic or asymptomatic) were identified within a large Israeli health care organization. Enrolled individuals included: 1) vaccinees (cases) who had a positive PCR test between 14 days after the first vaccine dose and a week after the second dose (partial effectiveness); 2) vaccinees (cases) with a positive PCR test at least 1 week after the second dose (full effectiveness); and 3) unvaccinated control participants who were matched with participants in #1 and #2 categories on similar demographic characteristics, including date of PCR test. RNA from PCR samples were collected to perform genome sequencing for 813 samples (149 pairs of full effectiveness-controls, 247 pairs of partial effectiveness-controls and samples from matches that were not successfully sequenced). B.1.1.7 was the predominant virus strain and B.1.351 was only present in <1% of the sample. There was no statistically significant difference in rates of B.1.1.7 in full effectiveness cases vs unvaccinated controls; however, a significantly higher proportion of B.1.351 was found in full effectiveness cases vs unvaccinated controls (5.4% vs 0.7%, respectively; odds ratio of 8:1). Alternatively, there was a significantly higher B.1.1.7 rate in partial effectiveness cases vs unvaccinated controls (odds ratio of 26:10); analysis could not be done with B.1.351 among this group, as numbers were too small.

Key Takeaways:

- In this case-control study of individuals with documented SARS-CoV-2 infection following receipt of the Pfizer-BioNTech COVID-19 vaccine, those infected at least a week after their second dose were disproportionately infected with the B.1.351 variant, whereas those infected two weeks after the first dose and 1 week after the second dose were disproportionately infected with the B.1.1.7 variant.
- Authors hypothesize that breakthrough cases in this study may be due to the ability of B.1.1.7 to produce higher viral loads or immune evasion of both variants.
- Confounders/limitations include: small sample sizes for the wild type virus and B.1.351 variant (due both to the substantial increase in B.1.1.7 and low prevalence of B.1.351 in Israel during the study period); not controlling for behavioral differences among vaccinees; and limitations in sequencing that prevented sequencing of very low viral load samples.