Another week! Autumn is in full swing.

Today under Covid-19 News I start with an abstract from ID Week on use of MCA in select hospitalized patients. Next is a WHO report that deaths due to TB are on the rise again due to Covid-19. The last is the recent FDA panel approval of half-dose of Moderna as a booster.

Under Journal Review the pre-publication NIH study on evaluating homologous and heterologous booster vaccinations which could pave the way for an expanded booster rollout. The last two articles remind us of another unintended consequence of the pandemic – depression and anxiety disorders. We have already reported on increase opioid use, overdoses, suicides, etc.

Have a wonderful weekend.

Ed

COVID-19 News

ID Week Abstract LB4
In this study, hospitalized patients were enrolled if they were receiving low-flow or no supplemental oxygen. Patients were randomized in a 1:1:1 ratio to receive either 2.4 grams or 8 grams of casirivimab and imdevimab (n=360) or placebo (n=160). Patients who were seronegative and were treated with casirivimab and imdevimab saw a relative risk reduction (RRR) in patients who died or needed MV by day 28 (10.3% treated vs 15% placebo). Additionally, there was a 55.6% (6.7 treated vs 15% placebo) and 35.9% (7.3% treated vs 11.5% placebo) RRR in mortality in the treatment group.

Comment: I included this abstract since it suggests MCA may have a role early in patients on no oxygen or low-flow oxygen. To date MCA has not been recommended for inpatients who test positive for Covid-19. Since most of us are testing all admissions, we are picking up infection for patients being hospitalized for non-Covid-19 reasons in patients who may be at high risk for progression.

WHO Estimates 1.5 Million People Died in 2020
Estimated deaths from tuberculosis—the deadliest infectious disease until the emergence of Covid-19—increased for the first time in more than a decade last year according to the WHO Thursday, blaming severe disruptions in treatment and diagnosis caused by the pandemic. United Nations' health agency estimated that around 1.5 million people died last year of the disease. That is up from 1.4 million estimated TB deaths in 2019.

Comment: I included this report to highlight another unintended consequence of the pandemic.

FDA Advisory Committee Recommends Authorization of Moderna COVID-19 Vaccine Booster
The FDA's independent Vaccines and Related Biological Products Advisory Committee voted to unanimously recommended the agency authorize a booster dose for Moderna's COVID-19 two-dose vaccine. The dose will be a 50-milligram dose — half the dose used in the primary series of shots

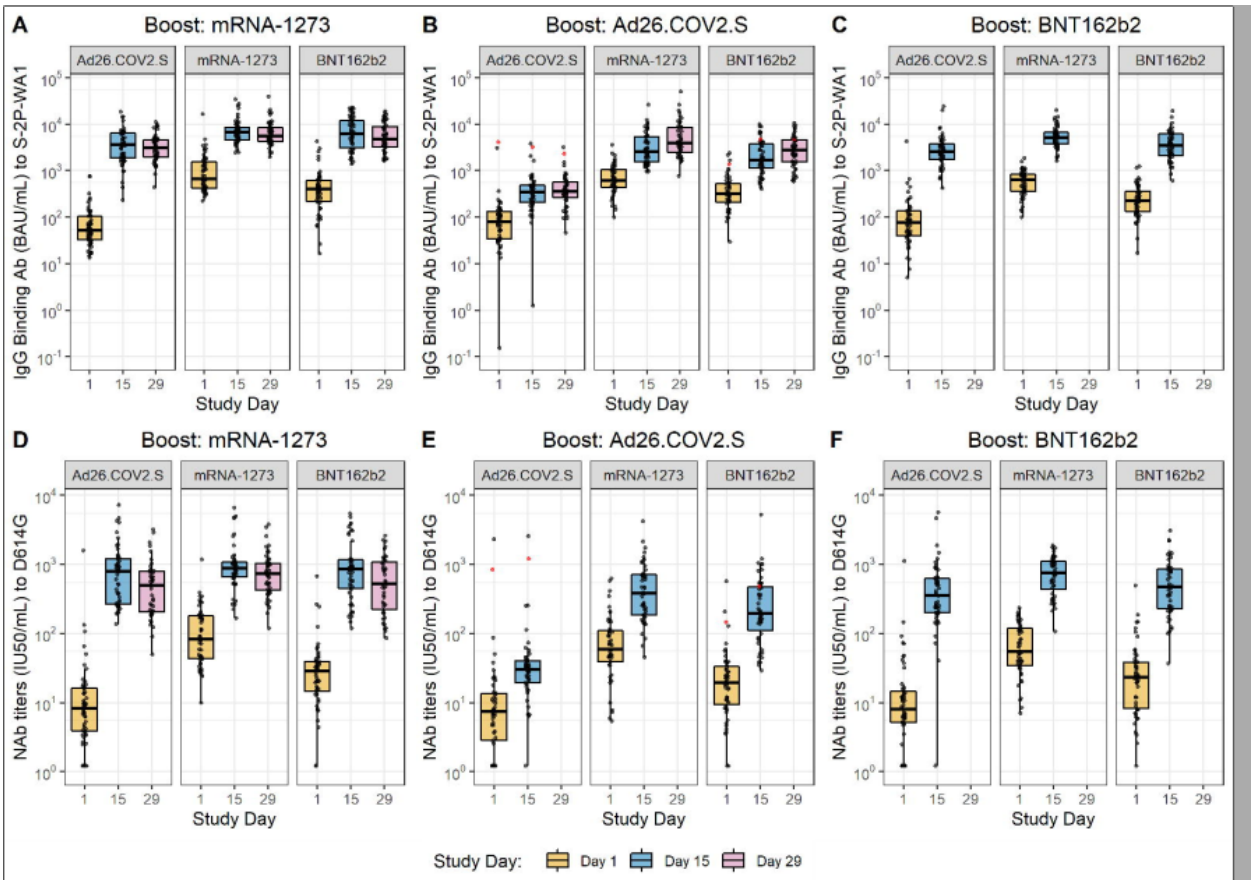
The booster guidance states:

- A person should receive the booster at least six months after completion of the two-dose regimen
- Individuals 65 years of age and older
- Individuals 18 to 64 who are at high risk of severe COVID
- Individuals in that same age group whose work or institutional exposure puts them at a high risk for contracting COVID

Comment: Members of the FDA's vaccine-advisory panel supported Moderna's booster dose even though the evidence for it was from a small study and had mixed results. Dr Patrick Moore a member of the committee said, "The data itself is not strong, but it is certainly going in the direction that is supportive of this vote." ACIP is scheduled to meet Oct. 20 to weigh endorsing an additional Moderna dose before it becomes available to the public. J&J is next today.

Journal Review

Heterologous SARS-CoV-2 Booster Vaccinations – Preliminary Report
medRxiv published online October 13, 2021 article provided by Josh Septimus
doi.org/10.1101/2021.10.10.21264827
The investigators evaluated homologous and heterologous booster vaccination in persons who had received an EUA Covid-19 vaccine regimen. This was an open-label clinical trial conducted at ten U.S. sites. Adults who received one of three EUA Covid-19 vaccines at least 12 weeks prior to enrollment and had no reported history of SARS-CoV-2 infection received a booster injection with one of three vaccines (Moderna, J&J, or Pfizer; nine combinations). The primary outcomes were safety, reactogenicity, and humoral immunogenicity on study days 15 and 29. 458 individuals were enrolled: 154 received Moderna, 150 received J&J, and 154 received Pfizer booster vaccines. Reactogenicity was similar to that reported for the primary series. Injection site pain, malaise, headache, and myalgia occurred in more than half the participants. Booster vaccines increased the neutralizing activity against a D614G pseudovirus (4.2-76-fold) and binding antibody titers (4.6-56-fold) for all combinations; homologous boost increased neutralizing antibody titers 4.2-20-fold whereas heterologous boost increased titers 6.2-76-fold. Day 15 neutralizing and binding antibody titers varied by 28.7-fold and 20.9-fold, respectively, across the nine prime-boost combinations. Specifically, the investigators found that those who got a J&J followed by Moderna saw their antibody levels rise 76-fold within 15 days, whereas those who received another dose of J&J saw only a fourfold rise in the same period. A Pfizer booster raised antibody levels in J&J recipients 35-fold. (See below)



Comment: All booster vaccines were immunogenic in subjects irrespective of the primary EUA regimen. The fold increases from baseline in both binding and neutralizing antibody titers were similar or greater after heterologous boosts compared to homologous boosts. There were no safety concerns identified. All groups, with the exception of the homologous J&J prime-boost group, achieved post-boost neutralizing geometric mean IU50/mL levels of >100, which has correlated with 90.7% vaccine efficacy. The neutralizing activity post-boost against the Delta variant was about 3-fold lower compared to D614G (ancestral strain), and this decrement was similar regardless of primary vaccine series. This is similar to the lower neutralization values for Delta compared to D614G. The sample size is insufficient for inter-group comparisons (nine groups of roughly 50 people each), and the demographics of those studied are not representative of the US population. In addition, volunteers were not randomized. The immunogenicity data are limited to immune responses through Study Day 29, and only serologic responses were reported. The good news: it appears that if a vaccine is approved or authorized as a booster, an immune response will be generated regardless of the primary Covid-19 vaccination regimen. Whether the FDA might authorize the mix-and-match approach, and how, is unclear.

Global Prevalence and Burden of Depressive and Anxiety Disorders in 204 Countries and Territories in 2020 Due to the COVID-19 Pandemic

Lancet published October 8, 2021

doi.org/10.1016/ S0140-6736(21)02143-7

The authors conducted a systematic review of data reporting the prevalence of major depressive disorder and anxiety disorders during the COVID-19 pandemic and published between Jan 1, 2020, and Jan 29, 2021. They searched PubMed, Google Scholar, preprint servers, grey literature sources, and

consulted experts. Eligible studies reported prevalence of depressive or anxiety disorders that were representative of the general population during the COVID-19 pandemic and had a pre-pandemic baseline. We used the assembled data in a meta-regression to estimate change in the prevalence of major depressive disorder and anxiety disorders between pre-pandemic and mid-pandemic (using periods as defined by each study) via COVID-19 impact indicators (human mobility, daily SARS-CoV-2 infection rate, and daily excess mortality rate). They used final prevalence estimates and disability weights to estimate years lived with disability and disability-adjusted life-years (DALYs) for major depressive disorder and anxiety disorders.

The authors found 48 studies that met inclusion criteria (46 studies met criteria for major depressive disorder and 27 for anxiety disorders). Two COVID-19 impact indicators, specifically daily SARS-CoV-2 infection rates and reductions in human mobility, were associated with increased prevalence of major depressive disorder for daily SARS-CoV-2 infection and anxiety disorders. Females were affected more by the pandemic than males for major depressive disorder and for anxiety disorders and younger age groups were more affected than older age groups for major depressive disorder. They estimated an additional 53·2 million (44·8 to 62·9) cases of major depressive disorder globally (an increase of 27·6% [25·1 to 30·3]) due to the COVID-19 pandemic, such that the total prevalence was 3152·9 cases (2722·5 to 3654·5) per 100000 population.

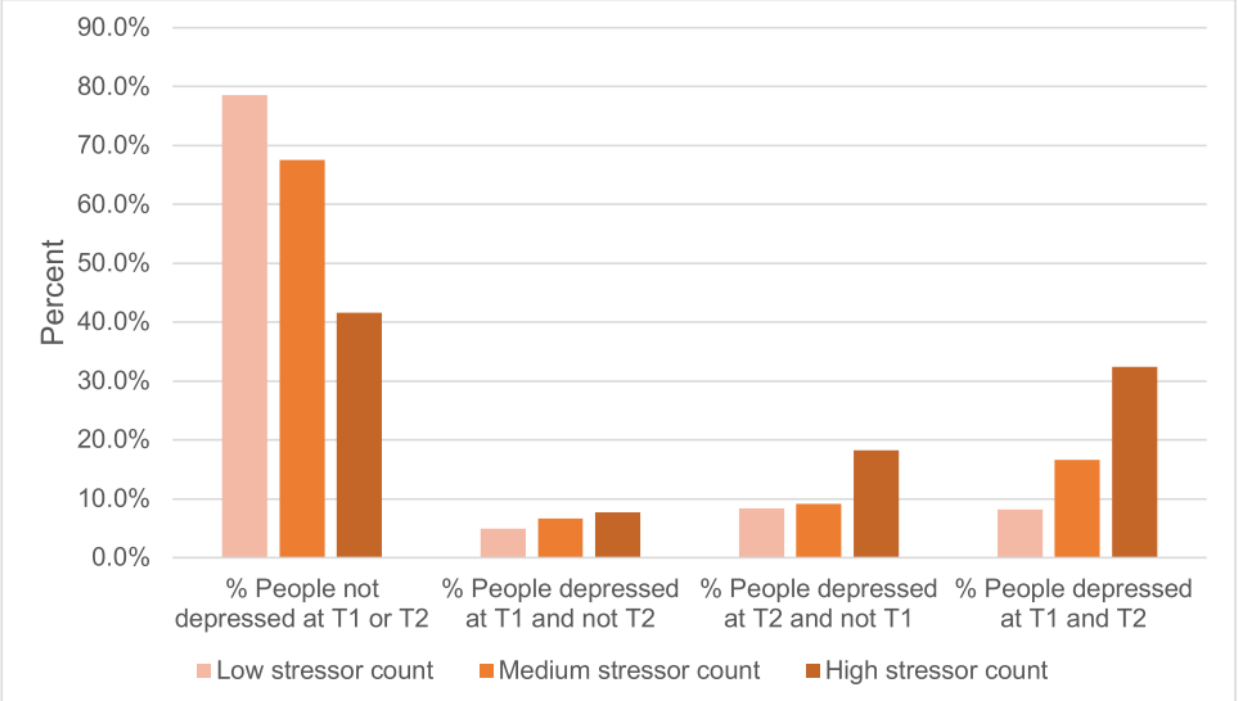
Comment: The authors estimated a significant increase in the prevalence of both major depressive disorder (with an estimated additional 53·2 million [95% uncertainty interval 44·8–62·9] cases worldwide—i.e., a 27·6% [25·1–30·3] increase) and anxiety disorders (76·2 million [64·3–90·6] additional cases—i.e., a 25·6% [23·2–28·0] increase) since before the pandemic. These findings are more concerning because depressive and anxiety disorders were already leading causes of disability worldwide. The study is unable to identify what is causing the increased burden of major depressive disorder and anxiety. In particular, the relative contributions to the prevalence of depression and anxiety disorders of direct consequences of COVID-19 illness and interventions, such as measures used to curb the propagation of the virus (e.g., lockdowns) was difficult to link to outcomes, but logically may have contributed. (See next article)

Persistent Depressive Symptoms During COVID-19: A National, Population-Representative, Longitudinal Study of U.S. Adults

Lancet Reg Health – Americas published online October 9, 2021
doi.org/10.1016/j.lana.2021.100091

The investigators assessed how depressive symptoms changed among U.S. adults over the course of the pandemic and identified the key risk factors for these symptoms. They studied a nationally representative group of U.S. adults ages 18 years and older surveyed in March-April 2020 (Time 1; N=1441) and March-April 2021 (Time 2; N=1161) in the COVID-19 and Life Stressors Impact on Mental Health and Well-being study (CLIMB). The Patient Health Questionnaire-9 (PHQ-9) was used to define elevated depressive symptoms (cut-off ≥10) and depressive symptoms score (0-27).

The prevalence of elevated depressive symptoms persisted from 27.8% in 2020 (95% CI: 24.9, 30.9) to 32.8% in 2021 (95% CI: 29.1, 36.8). Over time, the central drivers of depressive symptoms were low household income, not being married, and experiencing multiple stressors during the COVID-19 pandemic. The odds ratio of elevated depressive symptoms for low income relative to high income persons increased from 2.3 (95% CI: 1.2, 4.2) in 2020 to 7.0 (95% CI: 3.7, 13.3) in 2021.



Comment: The burden of depressive symptoms in the US adult population has clearly increased over the course of the pandemic. Mental health gaps grew between populations with different assets and stressor experiences during the COVID-19 pandemic were also identified. They had a follow up rate of 81.1%. Non-responders at T2 were more likely to be younger (ages 18-39), non-married, have lower income, and have reported elevated depressive symptoms at T1 than responders. This suggests that these findings may actually underestimate the full burden of depressive symptoms at the population level at T2. The data in this study did not include information about whether participants were on antidepressants or were receiving psychotherapy; therefore, they were unable to comment on the dynamics between access to treatment and depressive symptoms over time. While there has been much attention focusing on the prevention and treatment of SARS-CoV-2 infection, these two studies highlight the impact of mental health at the population level and that socioeconomic inequities in mental health are widening.