Good morning and TGIF

Under COVID-19 News the report from CDC that B.1.1.7 (UK) is now the most common variant in United States. A new Rand report shows a decline in trust in the CDC. Last is another AZ vaccine update on the troubled vaccine which is hampering vaccinations in Europe and elsewhere.

Under Journal Review the first two articles look at impact of psychiatric disorders and outcomes from COVID-19. The third article is a small observational trial on tocilizumab. The last article is a very nice review on performance of saliva, oropharyngeal swabs, and nasal swabs for SARS-CoV-2 Molecular Detection.

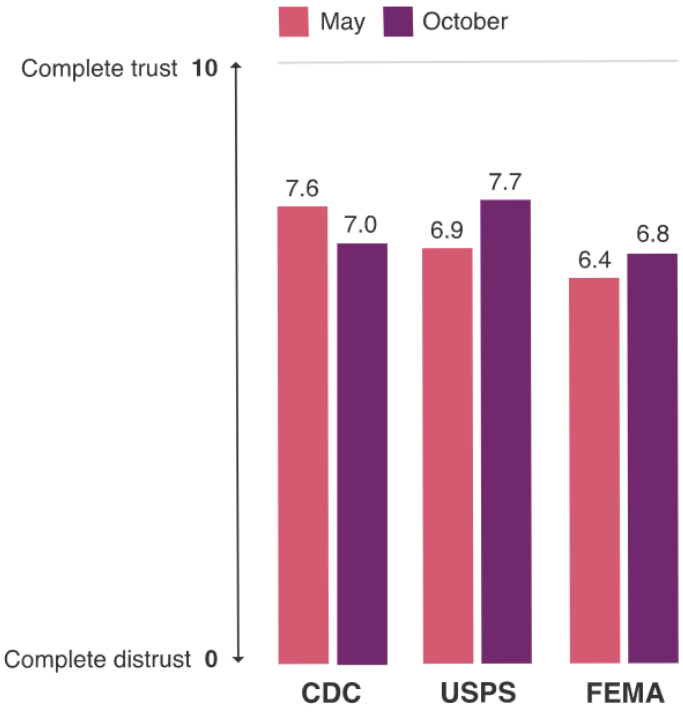
Have a great weekend

Ed

COVID-19 News

B117 COVID-19 Variant in the US
B.1.1.7 is now the most common variant in United States, according to CDC Wednesday. The variant may be partly responsible for recent spike in cases. Young adults, kids in youth sports, and people associated with daycare centers are among the new cases. These populations are not likely to have been vaccinated and may be taking more risks as states loosen restrictions. In Michigan vaccinated people account for 4.6 cases per 100,000 [residents] in Michigan, compared to 345 cases per 100,000 among unvaccinated people. Michigan follows Florida with most B.1.1.7 variants.

Rand Survey



Comment: One picture is worth a thousand words! Sadly, trust in CDC has declined and now is below USPS (Postal Service). It is true that the CDC did botch the initial testing rollout and messaging has become politicized and at times inconsistent, but we need a strong CDC that we can trust. The men and women I have worked with over the years are hardworking and dedicated excellent public health officials who always go the extra mile in protecting the public against new and emerging infectious diseases. They have always come through despite underfunding. Let us hope we have learned our lesson and we will adequately fund our public health agency, so we are better prepared for the next emerging infectious disease.

AstraZeneca Vaccine Update

Vaccine advisors from two regulatory groups in Europe today shared their latest investigation findings into blood clots in some AstraZeneca-Oxford COVID-19 vaccine recipients, with both finding a possible link. Experts from the European Medicines Agency (EMA) and the United Kingdom's Medicines and Healthcare Products Regulatory Agency (MHRA) both emphasized that the benefits of the vaccine continue to outweigh any risks. The WHO vaccine safety group reviewed the latest information from the EMA, MHRA, and other countries and said the link is plausible but not confirmed.

As of April 4th, European Union surveillance had received 169 reports of CVST and 53 reports of splanchnic vein thrombosis among 34 million vaccinees. All of the events occurred after the first vaccine dose, and 19 people died. The blood clot cases were among 20.2 million in the United Kingdom who had been vaccinated, for an overall risk of 4 in 1 million. As for the mechanism, it is thought that the vaccine may trigger an immune response leading to an atypical heparin-induced-thrombocytopenia-like disorder. Currently, it is not possible to identify specific risk factors. Most events occurred in people < age 60.

Comment: In response to the new analysis, a number of countries now recommend not giving the AstraZeneca vaccine to people under 30(UK) and under 50(Australia). These reports certainly complicate vaccinations efforts in Europe and beyond. The US is not dependent on the AstraZeneca vaccine.

Journal Review

6-Month Neurological and Psychiatric Outcomes in 236,379 Survivors of COVID-19: A Retrospective Cohort Study Using Electronic Health Records

Lancet Psychiatry published online April 6, 2021
doi.org/10.1016/S2215-0366(21)00084-5

Among 236,379 US COVID-19 patients, the researchers found that 33.6% of survivors developed a neurologic or psychological condition within 6 months after testing positive for coronavirus and that for 12.8%, it was their first such condition. The most common psychiatric conditions were anxiety (17.4%) and mood disorders (13.7%), while neurologic conditions included ischemic stroke (2.1%), and dementia (0.7%). No significant association was found between COVID-19 and increased risk of parkinsonism or Guillain-Barre syndrome.

Severe COVID-19 was also associated with a higher prevalence of neurologic or psychological disorders. For instance, 38.7% of those who were hospitalized had a neurologic or psychological diagnosis, compared with 46.4% admitted to the intensive care unit (ICU) and 62.3% who had delirium at some point during their infection. Compared with a matched cohort of people who had the flu or any

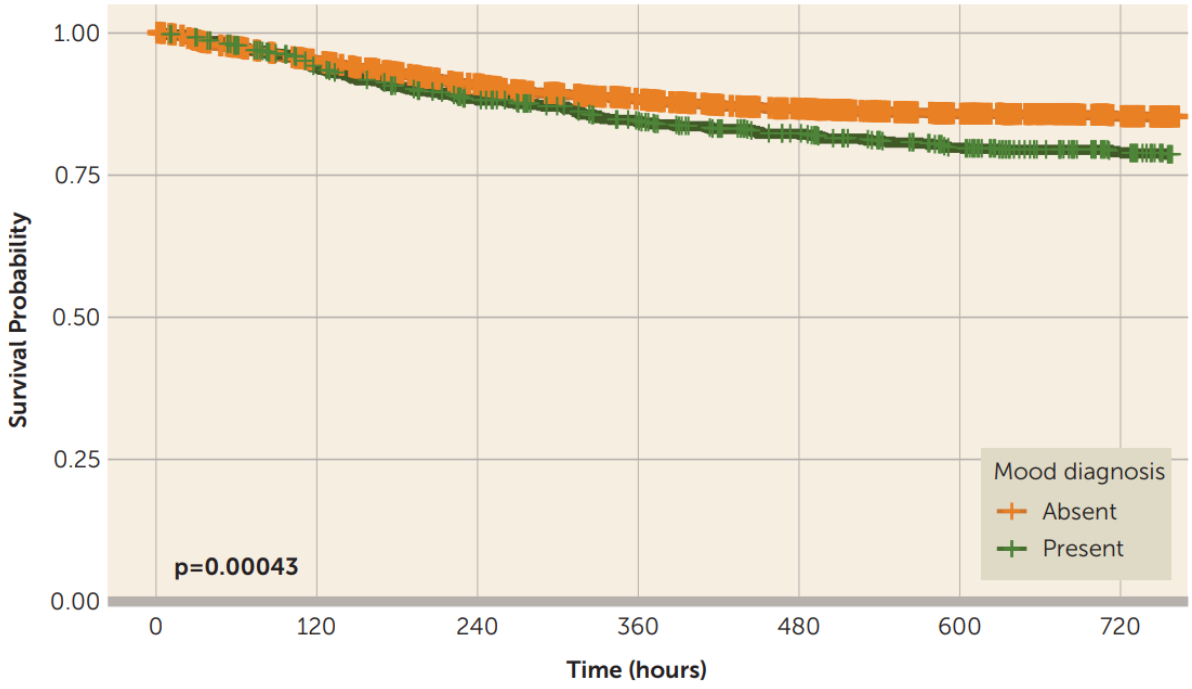
respiratory infection, those who had COVID-19 were associated with a 44% and 16% increased risk, respectively (95% confidence interval, 1.40 to 1.47 and 1.14 to 1.17).

Overall, 80.4% of the cohort was not hospitalized, 19.6% was, 3.8% needed ICU treatment, and 2.6% developed encephalopathy.

Comment: This study raises several important questions: will severe, enduring, and less common conditions such as psychoses behave more like neurological disorders or common mental disorders? Among the COVID-19 cohort, a first diagnosis of a psychotic disorder was substantially more common in patients hospitalized with COVID-19 (HR 2·77, 95% CI 1·99–3·85), and most especially in those with encephalopathy (5·62, 2·93–10·77), than in those who were not hospitalized. This link with encephalopathy may be important. The affected patients were, on average, 53 years old (population mean age 46 years, SD 19·7), so patients with first-onset psychosis were likely to have been much older than cases of schizophrenia and related disorders with a peak age of onset in early adulthood. The findings could be consistent with the psychoses being triggered by external causes but, more likely, they could be exacerbations of pre-existing conditions possibly unknown to the physician. Additionally, an association between psychosis (and dementia) and encephalopathy could be due to reverse causality. Unfortunately, many of the disorders identified in this study tend to be chronic or recurrent, so we can anticipate that the impact of COVID-19 may persist for many years. The findings are robust given the sample size, the propensity score matching, and the results of the sensitivity and secondary analyses. However, this review is limited to an electronic health records study, which inherently has unknown completeness of records, no validation of diagnoses, and limited information on socioeconomic and lifestyle factors.

Mood Disorders and Outcomes of COVID-19 Hospitalizations
Am J Psych published online
doi: 10.1176/appi.ajp.2020.20060842
This is a retrospective cohort reviewed from the electronic health records of two academic medical centers and four community hospitals between February 15 and May 24, 2020. Associations between history of mood disorder and in-hospital mortality and hospital discharge home were examined using regression models among any hospitalized patients with positive tests for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Among 2,988 admitted individuals, 717 (24.0%) had a prior mood disorder diagnosis. In Cox regression models adjusted for age, sex, and hospital site, presence of a mood disorder prior to admission was associated with greater in-hospital mortality risk beyond hospital day 12 (crude hazard ratio=2.156, 95% CI=1.540, 3.020; fully adjusted hazard ratio=1.540, 95% CI=1.054, 2.250). A mood disorder diagnosis was also associated with greater likelihood of discharge to a skilled nursing facility or other rehabilitation facility rather than home (crude odds ratio=2.035,95%CI=1.661, 2.493; fully adjusted odds ratio=1.504, 95% CI=1.132, 1.999).



Comment: Hospitalized individuals with a history of mood disorder may be at risk for greater COVID-19 morbidity and mortality and are at increased risk of need for post-acute care. Further studies should investigate the mechanism by which these disorders may confer elevated risk. There are several limitations to this study. While use of EHRs allows for detection of symptoms—for example, via natural language processing applied to clinical notes, they're limited to an electronic health records study, which inherently has unknown completeness of records, no validation of diagnoses by actual chart review, and dependent on documentation of neuropsychiatric symptoms. There is no control group, so they cannot determine the extent to which adverse outcomes may reflect nonspecific consequences of severe illness in general. The mechanism by which a preexisting mood disorder may influence hospital course and outcome merits further investigation in large clinical cohorts.

Early Tocilizumab Dosing is Associated with Improved Survival in Critically Ill Patients Infected with Severe Acute Respiratory Syndrome Coronavirus-2
Crit Care Exploration published online
DOI: 10.1097/CCE.0000000000000395
This is an observational multicenter cohort study including 23 acute care hospitals in four states. One-hundred eighteen patients admitted between March 13, 2020, and April 16, 2020. Eighty-one patients received tocilizumab, and 37 were untreated and served as a control group. The main outcome was mortality and was analyzed by timing of tocilizumab dosing. Early dosing was defined as a tocilizumab dose administered prior to or within 1 day of intubation. Late dosing was defined as a dose administered greater than 1 day after intubation. A control group that was treated only with standard of care, and without tocilizumab, was used for comparison.

Early tocilizumab therapy was associated with a statistically significant decrease in mortality as compared to patients who were untreated (p = 0.003). Dosing tocilizumab late was associated with an increased mortality compared with the untreated group (p = 0.006).

Logistic Regression With Mortality as the Outcome—Late Tocilizumab Versus No Tocilizumab

Coefficient	OR	95% CI	*t*	*p*
Tocilizumab given late	3.513	(1.15–11.97)	2.133	0.033
Age	1.059	(1.01–1.11)	2.316	0.021
Gender (male)	0.973	(0.32–2.82)	−0.050	0.960
Race (non-White)	2.631	(0.89–8.26)	1.718	0.086
Comorbidities present	0.823	(0.19–3.55)	−0.262	0.793
Steroids	1.353	(0.44–4.1)	0.536	0.592

Comment: This is a relatively small observational series and should be interpreted cautiously. Despite this, the results of this trial are consistent with results from REMAP CAP and RECOVERY – early tocilizumab in the first 24 hours when patients progress to vapotherm or MV improves outcomes, but later treatment does not.

Performance of Saliva, Oropharyngeal Swabs, and Nasal Swabs for SARS-CoV-2 Molecular Detection: A Systematic Review and Meta-analysis
J Clin Microbiol published online January 27, 2021
The authors system searched PubMed, Google Scholar, medRxiv, and bioRxiv (last retrieval October 1st, 2020) for comparative studies of alternative specimen types [saliva, oropharyngeal (OP), and nasal (NS) swabs] versus NP swabs for SARS-CoV-2 diagnosis using nucleic acid amplification testing (NAAT). A logistic-normal random-effects meta-analysis was performed to calculate % positive alternative-specimen, % positive NP, and % dual positives overall and in sub-groups. The QUADAS 2 tool was used to assess bias.

The authors identified 25 saliva, 11 NS, 6 OP, and 4 OP/NS studies meeting inclusion criteria. Three specimen types captured lower % positives [NS (82%, 95% CI: 73-90%), OP (84%, 95% CI: 57-100%), saliva (88%, 95% CI: 81 – 93%)] than NP swabs, while combined OP/NS matched NP performance (97%, 95% CI: 90-100%).

Comment: This is a nice review I found when updating my slide deck on diagnostics. NP swabs remain the gold standard for diagnosis of SARS-CoV-2, although alternative specimens look promising. Much remains unknown about the impact of variations in specimen collection, processing protocols, and population (pediatric vs. adult, late vs. early in disease course) and head-to-head studies of sampling strategies are still needed. Most studies utilized reverse transcription polymerase chain reaction (RT-PCR) assays, only one study used reverse transcription loop-mediated isothermal amplification (RT-LAMP), and two studies used transcription mediated amplification (TMA). IDSA revised recommendations on COVID-19 testing suggest that rapid RT-PCR assays be used instead of rapid isothermal NAATs when COVID-19 is suspected in symptomatic individuals since isothermal NAAT may have lower sensitivity. This was the conclusion in a recent Cochrane analysis, but results may vary by manufacturer. Cepheid-Xpert Xpress may be more sensitive than Abbott-ID NOW.