Good morning. I hope everyone had a safe July 4th

Today under COVID-19 News I report on the increasing number of people who have not gotten their second dose of an mRNA vaccine. Next is a CDC report on the decline of cancer screening for cervical and breast cancer especially during the early stage of the pandemic.

Under Journal Review I start with the publication outlying the National Breast and Cervical Cancer Early Detection Program which provides cancer screening services to women with low income and inadequate health insurance during the pandemic which was the basis for the CDC report mentioned under COVID-19 News. Next is a prepublication posting on the impact of the J&J vaccine on the neutralization of variants. The third article reviewed patients with cerebral venous sinus thrombosis prior to the COVID-19 pandemic showing baseline thrombocytopenia was uncommon, and heparin-induced thrombocytopenia and platelet factor 4/heparin antibodies were rare The last article suggests that the increased mortality among Black patients hospitalized with COVID-19 is associated with the hospitals at which Black patients disproportionately received care.

Have a great week.

Ed

COVID-19 News

CDC: 15M have missed their second dose Washington Post July 3, 2021
Nearly 15 million people or more than 1 in 10 have missed their second dose per CDC. As of June 16, nearly 11% of people eligible for their second shot have missed the recommended window. This is up from 8% earlier in the year. The major reasons given include mistakenly believing that they only need one dose, avoiding potential side effects after second dose, and others who simply missed their appointment.
Comment: completing vaccination is critical in protecting individuals against the delta variant. A study reviewed several weeks ago in the Briefing founds that the Pfizer vaccine was only 33% effective against the variants in preventing symptomatic disease after one dose; however, was 88% effective after the second dose.

Sharp Declines in Breast and Cervical Cancer Screening CDC June 30, 2021
The total number of cancer screening tests received by women through CDC's National Breast and Cervical Cancer Early Detection Program (Early Detection Program) declined by 87% for breast cancer and 84% for cervical cancer during April 2020 as compared with the previous 5-year averages for that month.

Screening declines observed in the Early Detection Program coincided with the rapid increase of COVID-19 cases in spring 2020. Factors that might have contributed to the declines during this time include screening site closures and the temporary suspension of breast and cervical cancer screening services due to COVID-19. The requirement or recommendation to stay at home and the fear of contracting COVID-19 also likely deterred individuals from seeking health care services, including cancer screening.

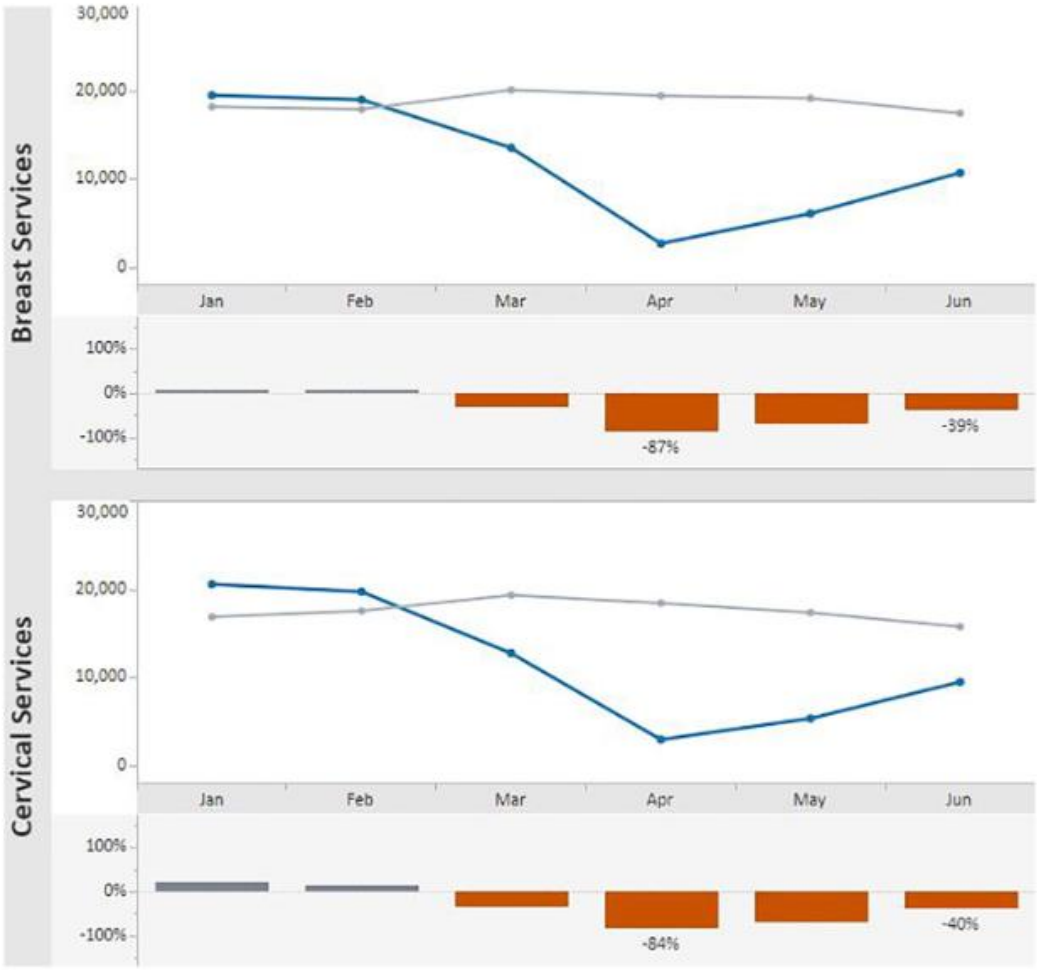
Comment: Prolonged delays in screening related to the COVID-19 pandemic may lead to delayed diagnoses, poor health consequences, and an increase in cancer disparities among women already experiencing health inequities. This is just another non-Covid-19 unintended consequence. See below

Journal Review

COVID-19 impact on screening test volume through the National Breast and Cervical Cancer early detection program(NBCCEDP), January–June 2020, in the United States Preventive Medicine published online June 30, 2021

doi.org/10.1016/j.ypmed.2021.106559

The National Breast and Cervical Cancer Early Detection Program (NBCCEDP) provides cancer screening services to women with low income and inadequate health insurance. They examined COVID-19's impact on NBCCEDP screening services during January-June 2020. They found the total number of NBCCEDP-funded breast and cervical cancer screening tests declined by 87% and 84%, respectively, during April 2020 compared with the previous 5-year averages for that month. The extent of declines varied by geography, race/ethnicity, and rurality. In April 2020, screening test volume declined most severely in HHS Region 2 - New York (96% for breast, 95% for cervical cancer screening) compared to the previous 5-year averages. The greatest declines were among American Indian/Alaskan Native women for breast cancer screening (98%) and Asian Pacific Islander women for cervical cancer screening (92%). Test volume began to recover in May and, by June 2020, NBCCEDP breast and cervical cancer screening test volume was 39% and 40% below the 5-year average for that month, respectively. However, breast cancer screening remained over 50% below the 5-year average among women in rural areas. NBCCEDP programs re-ported assisting health care providers resume screening.

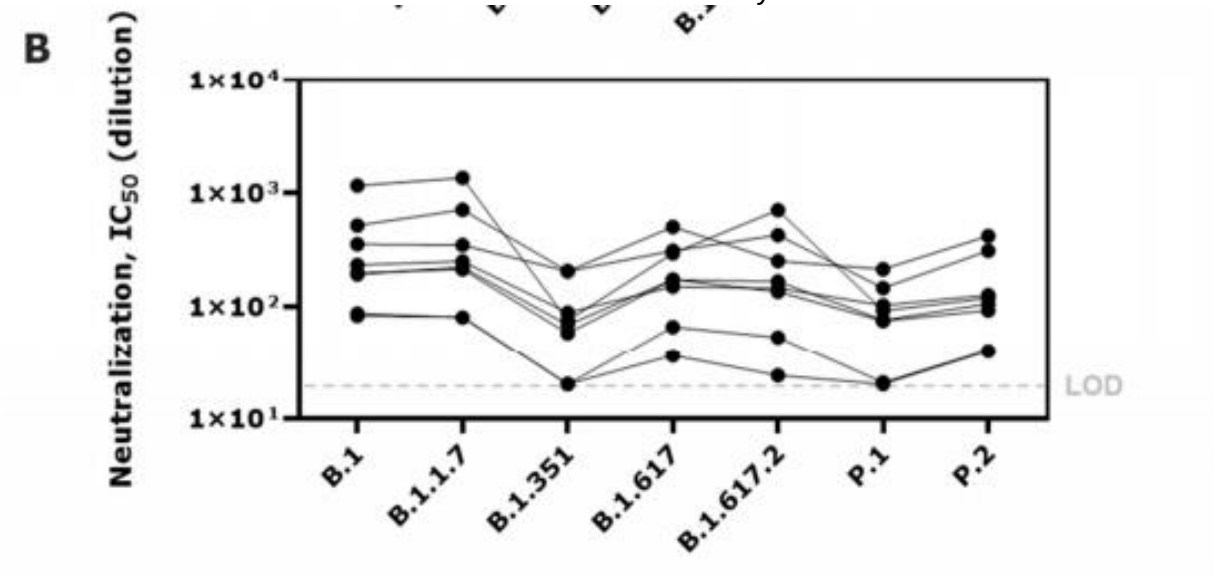


Comment: The COVID-19 pandemic dramatically reduced cancer screening in the U.S in early spring 2020, including among NBCCEDP clients. The data show, however, that among the women who are served by the NBCCEDP, screening recovered in a similar way to insured populations, and, overall, by June was roughly 60% of pre-COVID-19 levels. The declines in breast cancer screening test volume due to COVID-19 identified in this study may lead to later stage breast cancer diagnosis and mortality while declines in cervical cancer screening may result in increased cervical cancer incidence, later stage diagnoses, and mortality, furthering cancer disparities among this population.

Ad26.COV2.S elicited neutralizing activity against Delta and other SARS-CoV-2 variants of concern bioRxiv published online July 1, 2021
doi.org/10.1101/2021.07.01.450707

Participants of phase 3 ENSEMBLE trial were immunized with one dose of J&J vaccine. For measuring the breadth of neutralization against tested SARS-CoV-2 spike variants, SARS-CoV-2 spike-
neutralizing antibody titers were measured in psVNA against several SARS-CoV-2 spike variant.

These data showed that the Johnson & Johnson single-shot COVID-19 vaccine elicited neutralizing antibody activity against the Delta variant at an even higher level than what was recently observed for the Beta (B.1.351) variant in South Africa where high efficacy against severe/critical disease was demonstrated, but lower than Alpha (B.1.1.7). Geometric mean neutralization titers (GMT) were observed against all variants. The neutralization titers against B.1.1.7 and B.1 were similar and reduced against all other variants tested, ranging from 1.5 (B.1.617) to 3.6 (B.1.351) . The Beta (B.1.351) and Gamma (P.1) variants, with mutations at positions 417, 484 and 501 in the receptor binding domain (RBD), showed the largest reduction in neutralization sensitivity (3.6-fold and 3.4-fold respectively). The Delta (B.1.617.2) variant, with mutations at positions 452 and 478 in the RBD, still demonstrated a 1.6-fold reduction in neutralization sensitivity and increased over time.



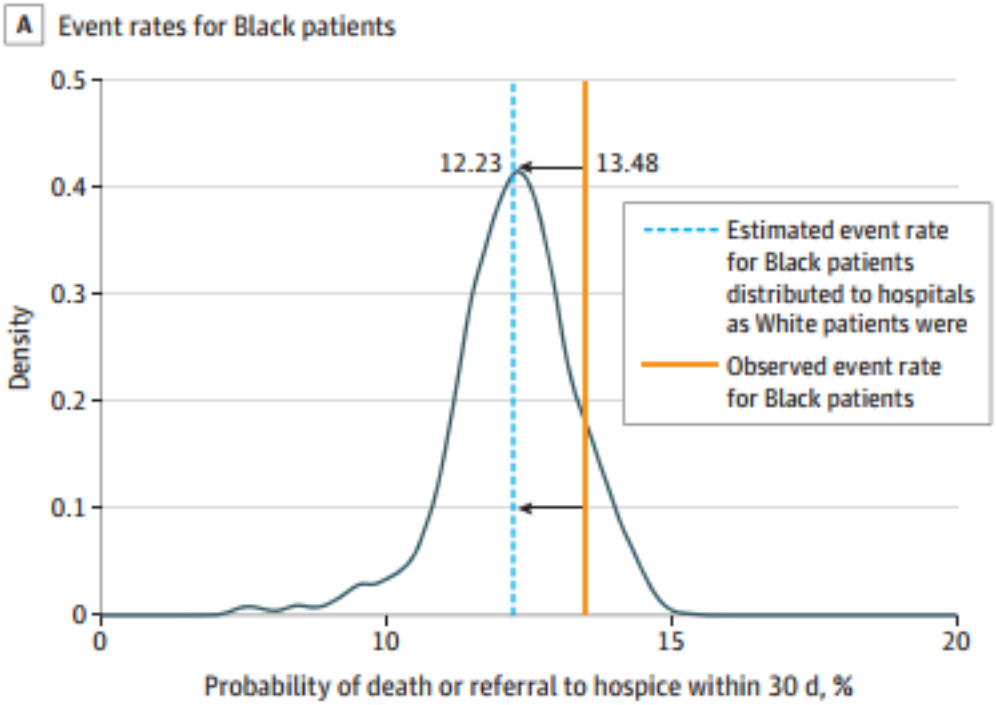
Comment: As compared to the neutralizing activity in Ad26.COV2.S (J&J) elicited immune sera against the B.1 virus, neutralizing activity was reduced against the Beta (B.1.351) and Gamma (P.1) variants than against the rapidly spreading Delta (B.1.617.2) variant. These results are in line with recently published studies in which sera from subjects who received the Moderna, Pfizer, or AZ vaccines were tested for neutralizing activity against VOCs. For all the vaccines, the reduction in neutralization titer was greater for the Beta (B.1.351) than observed for the Delta (B.1.617.2) variant. The study also demonstrated the neutralizing antibody response does not wane for at least 8 months. Humoral and cellular immune responses generated by the J&J single-shot COVID-19 vaccine lasted through at least eight months. In the ENSEMBLE trial, J & J's single-dose COVID-19 vaccine was 85 percent effective against severe/critical disease and demonstrated protection against hospitalization and death. The vaccine was consistently effective across all regions studied globally, including in South Africa and Brazil. There is no real-world data showing how protective the J&J vaccine is against the new Delta variant. However, UK studies show that two doses of either the Pfizer or AstraZeneca vaccines are significantly more protective against the variant than one so adding a second J&J dose or one of the mRNA vaccines might provide broader protection.

Frequency of Thrombocytopenia and Platelet Factor 4/Heparin Antibodies in Patients With Cerebral Venous Sinus Thrombosis Prior to the COVID-19 Pandemic JAMA published online July 2, 2021
doi:10.1001/jama.2021.9889

The investigators set out to determine the frequencies of admission thrombocytopenia, heparin-induced thrombocytopenia, and presence of platelet factor 4/heparin antibodies in patients diagnosed with cerebral venous sinus thrombosis(CVST) prior to the COVID-19 pandemic. This analysis was a retrospective review reviewing consecutive sample of 865 patients with cerebral venous sinus thrombosis from 1987 to 2018. Baseline thrombocytopenia was observed in 8.4% of
patients, and heparin-induced thrombocytopenia was diagnosed in 0.1%. In a convenience sample subset of 93 patients with plasma available for additional laboratory analysis (including 8 who had
thrombocytopenia), none had platelet factor 4/heparin antibodies.
Comment: Cases of CVST in combination with thrombocytopenia have been reported within 4 to 28 days of vaccination with the AstraZeneca and J&J vaccines. An immune-mediated response associated with platelet factor 4/heparin antibodies has been proposed as the underlying mechanism. Clinical data for this cohort were collected retrospectively, and information on race/ethnicity was not obtained. Baseline platelet count was not always available, nor was the underlying cause of thrombocytopenia identified or investigated in all cases and patients were not routinely screened for HIT; nonetheless in patients with CVST prior to the COVID-19 pandemic, baseline thrombocytopenia was uncommon, and heparin-induced thrombocytopenia and platelet factor 4/heparin antibodies were rare. These findings may strengthen the possible association between adenovector vaccines and CVST with thrombocytopenia.

Patient and Hospital Factors Associated With Differences in Mortality Rates Among Black and White US Medicare Beneficiaries Hospitalized With COVID-19 Infection JAMA Netw Open 2021;4:e2112842. doi:10.1001/jamanetworkopen.2021.12842

The authors set out to examine differences in COVID-19 hospital mortality rates between Black and White patients and to assess whether the mortality rates reflect differences in patient characteristics by race or by the hospitals to which Black and White patients are admitted. They used a cohort to assessed Medicare beneficiaries admitted with a diagnosis of COVID-19 to 1188 US hospitals from January 1, 2020, through September 21, 2020. The primary outcome was inpatient death or discharge to hospice within 30 days of admission. They estimated the association of patient-level characteristics with differences in mortality or discharge to hospice among Black and White patients. To examine the association with the hospital itself, they further adjusted for the specific hospitals to which patients were admitted. In this cohort study of over 44,000 adult Medicare beneficiaries admitted with COVID-19 to 1188 US hospitals, odds of 30-day inpatient mortality or discharge to hospice were 11% higher for Black patients than for White patients after adjustment for patient sociodemographic and clinical characteristics. That difference was largely eliminated when adjustment was made for the hospital where care was received.



Comment: This study's findings suggest that the increased mortality among Black patients hospitalized with COVID-19 is associated with the hospitals at which Black patients disproportionately received care. Why do hospitals that care disproportionately for Black patients have worse outcomes for COVID-19? Many hospitals in predominantly Black communities continue to face financial challenges and limited resources. Hospitals that serve these communities, also have uneven schools and limited job opportunities are associated with lower income. Communities with lower incomes have more people working in jobs that do not offer health insurance, and a higher proportion of the insured population is covered by Medicaid. This means that hospitals in these communities must operate with lower revenues because of increased burden of charity care and an adverse payer mix, meaning that they have few resources for staffing, training, and quality improvement activities. There is rarely, if ever, a single cause for disparities in health. Rather, differences are usually due to a combination of factors, including lack of health insurance, financial and nonfinancial barriers to care, low health literacy, differential treatment by clinicians, distrust, where people receive care to name a few. Structural racism pervades our society in other ways that appear to have contributed to the COVID-19 mortality differences reported in this article. This analysis was restricted to Medicare Advantage beneficiaries from a single US insurer, a group that is largely older than 65 years and unevenly distributed across the US geographically and demographically. Nevertheless, this study reflects, to my knowledge, the largest and most comprehensive sample of US hospitals to date. Second, they were unable to measure out-of-hospital mortality rates for individuals with COVID-19. We must address this racial disparity and the uneven resourcing and quality of hospitals that provide care to a disproportionate number of Black patients.

Ed Septimus, MD, FACP, FIDSA, FSHEA

Therapeutics Research and Infectious Disease Epidemiology, Department of Population Medicine
Harvard Medical School and Harvard Pilgrim Health Care Institute
281-714-5689 |eseptimus@gmail.com