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COVID-19 – Impact on Mental Health, Russian Vaccine, Other Vaccines, and Transmission from Healthcare Workers

Since there continues to be multiple publications, rather than wait until Wednesday, I put together 4 articles. The first articles highlight how this pandemic has impacted mental health. The next 2 article are reports on vaccines including the Russian vaccine many of us have heard about. The last article is a very important contribution by colleagues in Boston on risk of SARS-CoV-2 transmission from infected HCWs. Investigators were only able to find only 1 clear case of SARS-CoV-2 transmission from a HCW to a patients. (<1%) This event occurred prior to implementation of universal masking for patients and providers hence the current risk to patients appears to be very low. This is very reassuring.

Ed

Prevalence of Depression Symptoms in US Adults Before and During the COVID-19 Pandemic JAMA Netw Open published online September 2, 2020

1400 adults were surveyed about depressive symptoms in March and April. Their results were compared with 5000 who completed the National Health and Nutrition Examination Survey in 2017–2018. Depression symptoms defined using the Patient Health Questionnaire-9 cutoff of 10 or higher. Categories of depression symptoms were defined as none (score, 0-4), mild (score, 5-9), moderate (score, 10-14), moderately severe (score, 15-19), and severe (score, 20). Overall, 9% of participants had depression symptoms pre-pandemic, and 28% had such symptoms during the pandemic. The prevalence of all levels of depression were higher during the pandemic (e.g., severe depression: 5.1% vs. 0.7% pre-pandemic). Among those with the lowest incomes, nearly half had depressive symptoms during the pandemic.

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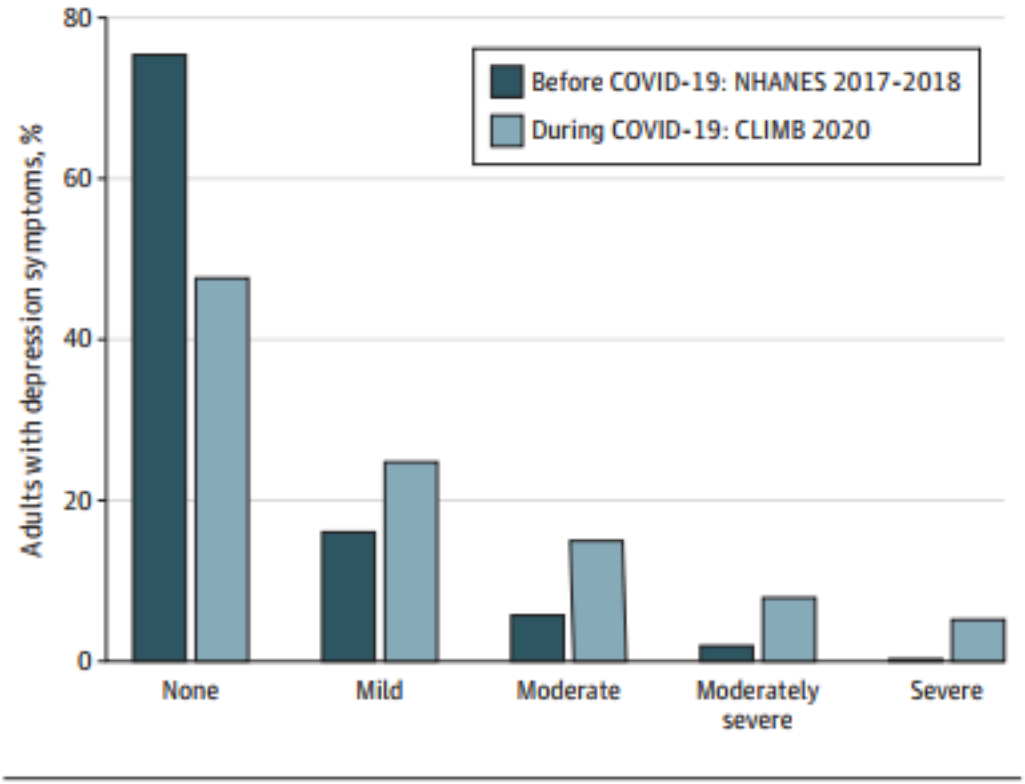
Figure. Depression Symptoms in US Adults Before and During the Coronavirus Disease 2019 (COVID-19) Pandemic



Comment: The findings are consistent with other studies showing a substantial burden of psychological distress following COVID-19. In this population-representative survey study of US adults, they found that prevalence of depression symptoms was more than 3-fold higher during COVID-19. It is important to recognize the potential for the mental health consequences of COVID-19 to be large in scale and to recognize that these effects can be long lasting. This is another example of the non-COVID-19 related medical consequences of this pandemic.

Phase 1–2 Trial of a SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine N Engl J Med published online September 2, 2020

This is a randomized, placebo-controlled, phase 1–2 trial to evaluate the safety and immunogenicity of the rSARS-CoV-2 vaccine (in 5-µg and 25-µg doses, with or without Matrix-M1 adjuvant, and with observers unaware of trial-group assignments) in 131 healthy adults. In phase 1, vaccination comprised two intramuscular injections, 21 days apart. The primary outcomes were reactogenicity to assess safety; and IgG anti–spike protein response. Secondary outcomes included unsolicited adverse events, wild-type virus neutralization (microneutralization assay), and T-cell responses (cytokine staining). IgG and microneutralization assay results were compared with 32 (IgG) and 29 (neutralization) convalescent serum samples from patients with Covid-19, most of whom were symptomatic. We performed a primary analysis at day 35. Most adverse events were mild or moderate. By day 35, vaccine with adjuvant produced an immune response that exceeded that observed in convalescent plasma of hospitalized COVID-19 patients. The Matrix-M1 adjuvant induced CD4+ T-cell responses that were biased toward a Th1 phenotype.

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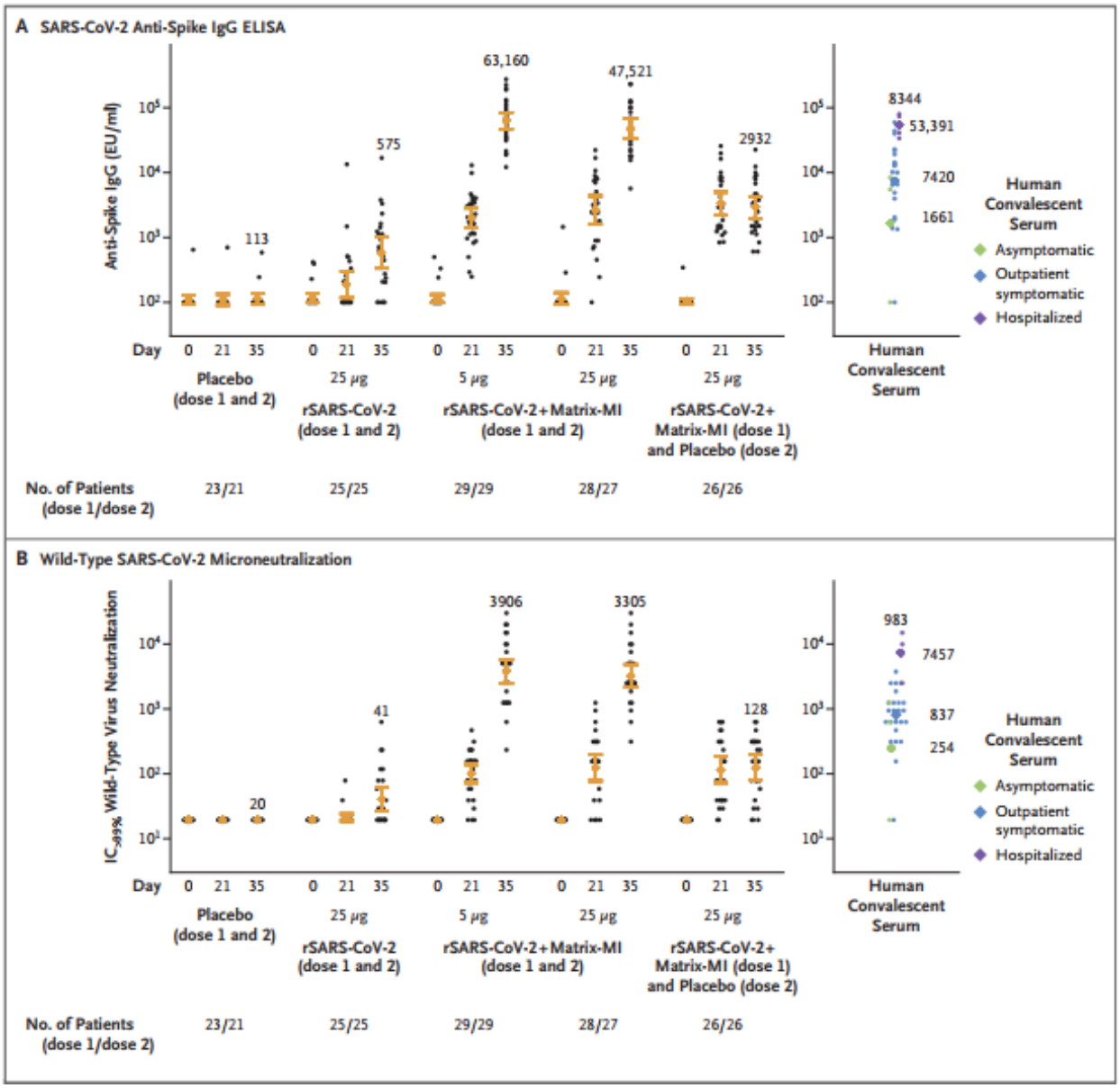

Comment: Neutralizing antibody responses after the second vaccination with rSARS-CoV-2 plus Matrix-M1 exceeded values seen in symptomatic Covid-19 outpatients and were of the magnitude seen in convalescent serum from hospitalized patients with Covid-19. The benefit of the Matrix-M1 adjuvant was clear in both the antibody and the T-cell response. The value of the second dose on day 21 for the two-dose rSARSCoV-2 plus Matrix-M1 regimen was clearly demonstrated. This trial was limited by small size of the trial, the limited ethnic diversity (particularly the low number of Black and Latino participants), the younger age of participants, the short period of follow-up, and the participants' good health status. The populations at greatest risk for serious Covid-19 include people with coexisting conditions and older adults, groups will apparently be included in the next phase.

Safety and immunogenicity of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine in two formulations: two open, non-randomised phase 1/2 studies from Russia Lancet published online September 4, 2020

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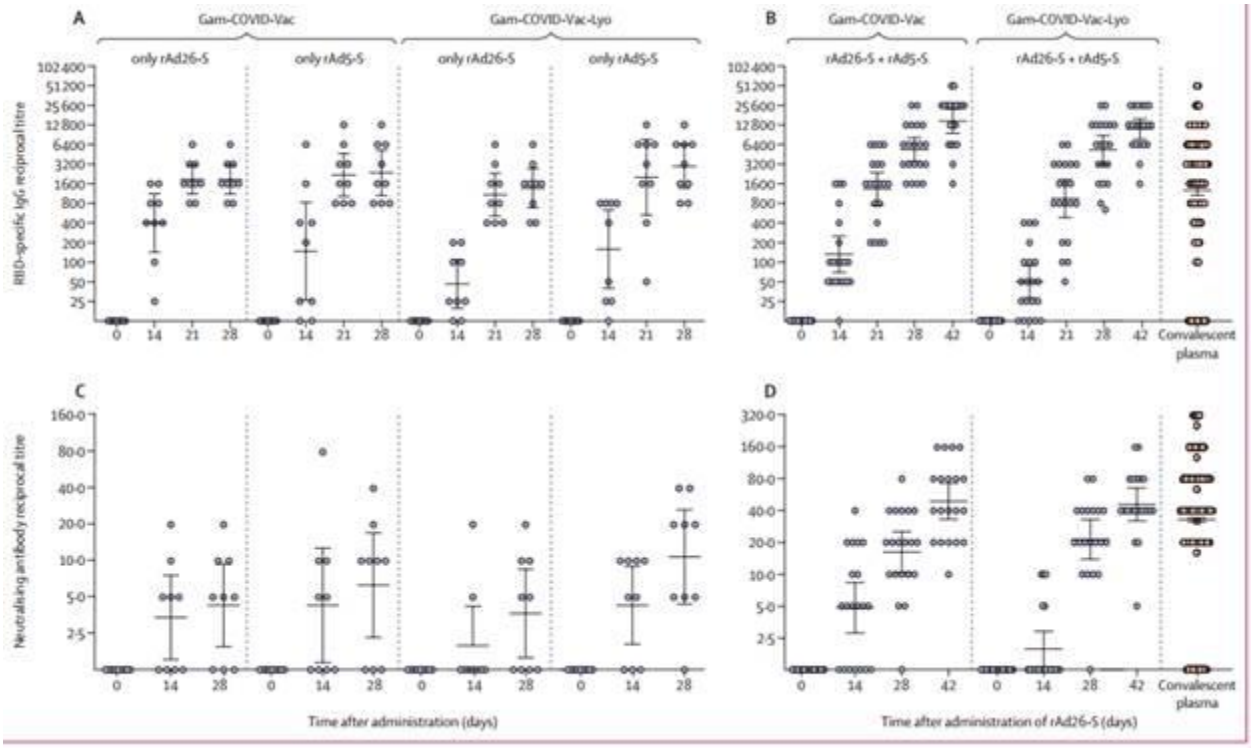
The investigators developed a heterologous COVID-19 vaccine consisting of two components, a recombinant adenovirus type 26 (rAd26) vector and a recombinant adenovirus type 5 (rAd5) vector, both carrying the gene for severe acute SARS-CoV-2 spike glycoprotein (rAd26-S and rAd5-S). They aimed to assess the safety and immunogenicity of two formulations (frozen and lyophilized) of this vaccine.

The design was a non-randomized phase 1/2 studies at two hospitals in Russia. They enrolled healthy adult volunteers (men and women) aged 18–60 years to both studies. In phase 1 of each study, they administered intramuscularly on day 0 either one dose of rAd26-S or one dose of rAd5-S and assessed the safety of the two components for 28 days. In phase 2 of the study, which began no earlier than 5 days after phase 1 vaccination, we administered intramuscularly a prime-boost vaccination, with rAd26-S given on day 0 and rAd5-S on day 21. Primary outcome measures were antigen-specific humoral immunity (SARS-CoV-2-specific antibodies measured by ELISA on days 0, 14, 21, 28, and 42) and safety. Secondary outcome measures were antigen-specific cellular immunity (T-cell responses and interferon-γ concentration) and change in neutralizing antibodies (detected with a SARS-CoV-2 neutralization assay)

The vaccines produced humoral and cellular immune responses in healthy adults. IgG responses were elicited in all participants, with geometric mean titers significantly higher than those reported in people who have recovered from COVID-19. Antibodies to SARS-CoV-2 glycoprotein and neutralizing antibodies increased significantly at day 14 and continued to increase throughout the observation period. Specific T-cell responses peaked at day 28 after vaccination. Both vaccine formulations were safe and well tolerated. The most common adverse events were pain at injection site (44 [58%]), fever (38 [50%]), headache (32 [42%]), asthenia (21 [28%]), and muscle and joint pain (18 [24%]). Most adverse events were mild, and no serious adverse events were detected.



Comment: The findings reported indicate that a heterologous rAd26 and rAd5 vector-based COVID-19 vaccine is safe and immunogenic in healthy adults. Limitations of the study include the short duration of follow-up (42 days), the low number of participants (n=76), and no placebo or control vaccine. Further

research is needed to evaluate the vaccine in different populations, including older age groups, individuals with underlying medical conditions, and people in at-risk groups

Low risk of COVID-19 among patients exposed to infected healthcare workers Clin Infect Dis published online September 5, 2020

The investigators conducted healthcare-based contact tracing for all patients and healthcare workers who tested positive for COVID-19 at a large academic medical center in Boston from March 1-June 10, 2020. They were able to identify all patients potentially exposed to each COVID-19 case starting from the date of symptom onset and continuing until the last day of exposure; on 4/4/20, the hospital modified their protocol to also include patients exposed in the 48 hours prior to symptom onset as per evolving science. An exposure was defined as ≥10 cumulative minutes of face-to-face contact within 6 feet, during which at least one person was not wearing a mask.[CDC has modified to 15 minutes]
All exposed patients were notified of their exposure and assessed for symptoms including cough, shortness of breath, fever, chills, muscle pain, sore throat, and/or new loss of taste or smell. During the first two months of the study period, they referred all symptomatic patients for testing. However starting in May they referred all exposed patients for testing regardless of symptom status in accordance with revised state guidance. Exposed patients were asked to self-quarantine for 14 days after their exposure and to report any new symptoms. At the end of the 14-day follow-up period, all patients were reassessed via telephone for ambulatory patients and via electronic healthcare record review for inpatients. COVID-19 was considered healthcare-associated if an exposed patient tested positive for SARS-CoV-2 within 14 days of a healthcare exposure. Initial hospital policy only required HCW to wear personal protective equipment when seeing patients with symptoms concerning for COVID-19; however, universal masking of HCWs was required starting on 3/25/2020 and patient masking was implemented on 4/6/2020.

Between 3/1/2020 and 6/10/2020, 238 patients met our exposure criteria; all exposures were to infected healthcare workers (n=60), none were due to patient-to-patient exposures. One quarter of exposures (60/238) occurred in the outpatient or emergency department setting, the rest in the inpatient setting. 15 patients were exposed twice hence there were 253 exposures overall. The median number of exposed patients per our exposure criteria was 3, interquartile range (1.75-5). In 87 exposures, neither the infected provider nor the exposed patient wore a mask, and in 166 exposures, only the infected healthcare worker wore a mask. Follow-up at 14 days after exposure was available for 226/253 exposures (89%). Testing was performed after 92/253 exposures. Only 2 patients tested positive for SARS-CoV-2. The first was exposed to a physician for 30 minutes during an outpatient visit on the day the physician's symptoms began; neither the patient nor physician were masked. A second patient tested positive 6 days following exposure to a nurse for more than 10 minutes in the perioperative setting; only the nurse was masked. However, this patient also had an intimate household contact who tested positive on same day that they were exposed to the infected healthcare worker. Considering that the patient was exposed to their household member before they were exposed to the infected healthcare worker and that the highest risk of transmission occurs among household contacts, They I think correctly attributed this exposure to the patient's household contact.

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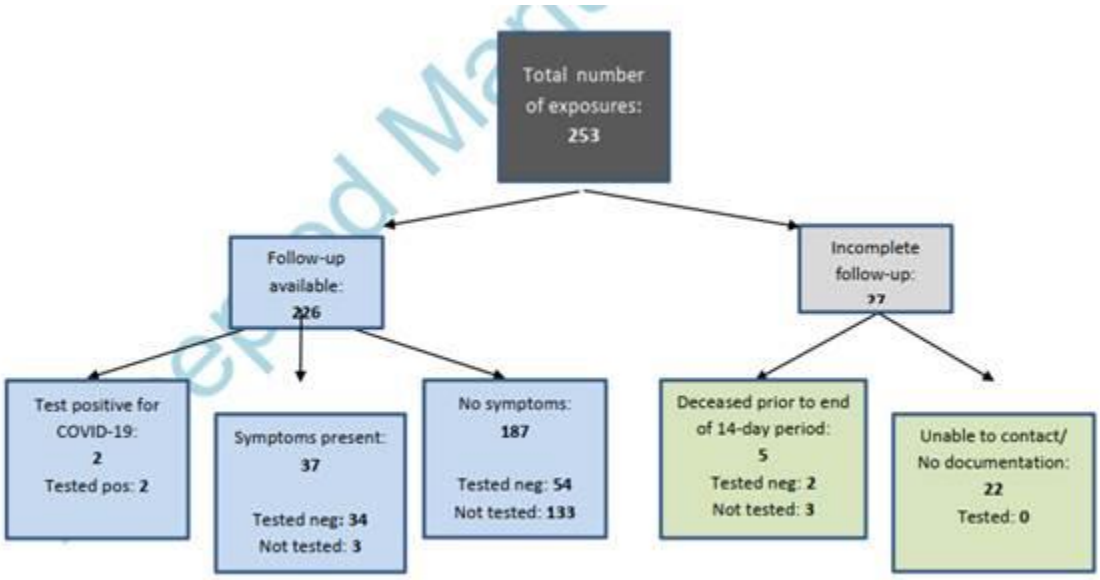

Comment: Investigators were only able to find 1 clear case of SARS-CoV-2 transmission from a HCW to a patients. (<1%) This event occurred prior to implementation of universal masking for patients and providers hence the current risk to patients appears to be very low. Current literature confirms that the risk of transmission is closely tied to duration and intimacy of contact, and likely varies based on viral burden, symptoms, PPE use, proximity, duration of contact, and quality of ventilation. Limitation of the current study includes that mask use and testing requirement evolved over time and many exposed asymptomatic patients were not tested. Nonetheless, this observation provides reassurance that transmission from healthcare workers to patients is rare and that patients should feel safe resuming routine care, particularly in hospitals and clinics with evidenced-based infection prevention are implemented.