COVID-19 Evidence Digest 11/20/20

SARS-CoV-2 Neutralizing Antibody LY-CoV555 in Outpatients with Covid-19 (NEJM)

Bottom line: Infusion of a one-time dose of neutralizing monoclonal antibody in outpatients with mild to moderate COVID-19 was shown to speed up the decline of SARS-CoV-2 in the nasopharynx.

Details: 452 outpatients diagnosed with mild or moderate COVID-19 were randomly assigned to receive one infusion of one of 3 doses of monoclonal neutralizing antibody (700mg, 2800mg or 7000mg) or placebo. The COVID-19 viral load (level of virus detected in a nasopharyngeal swab) was 3.4 times significantly lower at day 11 after COVID-19 diagnosis for patients who received the 2800mg infusion as compared to patients who received placebo. The other doses also decreased viral load but to a lesser degree and not statistically significant. Patients who received any dose of the neutralizing antibody infusion had slightly less severe symptoms than those who received placebo. There were fewer hospitalizations or emergency room visits in patients who received any dose of the neutralizing antibody (1.6%) compared to placebo (6.3%).

Key Takeaways:

- One of three tested doses (the 2800mg dose) of a monoclonal antibody that works by blocking attachment of the SARS-CoV-2 virus to its target was shown to decrease the level of virus at a faster rate than placebo in patients with mild to moderate COVID-19 in the outpatient setting.
- Patients who received any dose of this monoclonal antibody (LY-CoV555) were also less likely to be hospitalized or visit the emergency department and there were no serious adverse events reported.

Disparities in Post-Intensive Care Syndrome During the COVID-19 Pandemic: Challenges and Solutions (NEJM)

Bottom Line: Healthcare systems should invest in preventing COVID-19 infection, developing systems to ensure hospitalized patients diagnosed with COVID-19 have adequate medical care after discharge, and build stronger long-term community supports to address the disproportionate burden of COVID-19 post intensive care syndrome (PICS) amongst vulnerable populations in the United States.

Details: Black, Latinx and Native American communities have experienced increased COVID-19 infection rates, likely due to increased representation amongst essential workers, limited testing availability and multigenerational housing. Increased infection rates are compounded by higher rates of complications once diagnosed. Increased rate of medical comorbidities and differential access to healthcare, in addition to structural factors including poverty and racial bias from providers, are likely reasons for these differences.

Differential rates of post-intensive care syndrome is also witnessed amongst racial minorities. Post-intensive care syndrome (PICS) refers to a range of symptoms that affect individuals requiring care in critical care settings, including neurocognitive deficits, fatigue, muscle weakness and PTSD. Vulnerable populations may experience higher rates of this condition due to unequal access to long-term rehabilitation facilities and skilled nursing facilities.

In order to close the gap, authors recommend a three-pronged approach that prevents critical illness, provides short-term care options for individuals diagnosed with COVID, and develops long-term community support. Systems can prevent severe illness by adopting widespread testing and a rigorous contact tracing program, ensuring safe quarantine options for infected or exposed individuals, providing masks and cleaning products, and developing an equitable vaccine distribution plan when it is available.

Healthcare systems can develop post-discharge clinics specializing in PICS with a multidisciplinary care team and ensuring all patients have access. Policy changes are necessary to ensure that insurance plans cover post-acute care services and that undocumented persons are eligible for insurance that covers these options. Additionally, healthcare systems should develop meaningful relationships with community-based organizations in order to earn the trust of disadvantaged populations.

Key Takeaways:

- Systems level factors are at the root of inequities in COVID diagnosis, infection complications and PICS in vulnerable patient populations in the United States.
- Healthcare systems can attenuate these effects by focusing on strategies known to decrease disease spread, create robust, equitable post-discharge care plans for patients, and invest in long-term community relationships.

Hospital-Acquired SARS-CoV-2 Infection: Lessons for Public Health (JAMA)

Bottom Line: Although hospital transmission of COVID-19 is rare with universal masking requirements and it is not necessary for patients to delay seeking care when needed, healthcare workers still face risk. Provisions should be put in place to ensure the safety of healthcare workers.

Details: Since the start of the COVID-19 pandemic, there has been concern about hospital-acquired infection with earlier studies demonstrating hospital transmission leading to several clusters. Because of this concern, many hospital-settings have limited elective visits and procedures and less patients are showing up for emergency illness like stroke, tuberculosis, and hyperglycemic episodes.

There is increasing evidence that hospital transmission of COVID-19 is rare with universal masking (universal use of surgical masks by patients and healthcare staff) even with increased cases in the community. One study of 12 hospitals and over 75,000 employees found that COVID-19 positivity decreased from 15% to 11% three weeks after universal masking was implemented. Another study based on contact-tracing found no convincing evidence of hospital transmission among patients after implementing universal masking. These findings highlight that universal masking is effective in controlling COVID-19 transmission and that should not delay care and urgent health care needs.

Data from the World Health Organization suggests that healthcare workers contribute to 1 in 7 COVID-19 cases worldwide. This data must be interpreted carefully because (1) much of the data was collected before universal masking requirements, (2) possible community transmission, and (3) increased testing among healthcare workers. However, the risk of transmission among healthcare workers is concerning given the evidence of inadequate space

to social distance in hospital settings, and unmasked patients despite universal masking. Hospitals should focus on several strategies to minimize risk and provide a safe environment for healthcare workers. This includes: sufficient supply of masks to staff and patients, eye protection, adequate and well-ventilated break space for staff, staggered breaks, decreased shared space between healthcare workers and patients in patient rooms, statutory sick leave, and regular and quick COVID-19 testing for healthcare workers.

Key Takeaways:

- Patients should not be discouraged from seeking necessary health care in hospital settings with well-implemented mask requirements.
- Both healthcare workers and patients should be provided with sufficient supply of masks given their effectiveness in reducing transmission.
- Healthcare workers should be provided with proper and well-ventilated break space, staggered breaks, sick leave, eye protection, and regular testing with quick turnaround.

Fluvoxamine vs Placebo and Clinical Deterioration in Outpatients With Symptomatic COVID-19: A Randomized Clinical Trial (JAMA)

Bottom Line: In a small randomized trial, patients quarantining at home with COVID-19 who received fluvoxamine had lower rates of clinical deterioration than those receiving placebo.

Details: Fluvoxamine is a selective serotonin reuptake inhibitor that may reduce the inflammatory immune response by binding to S1R receptors. In this double-blind, placebo-controlled, randomized clinical trial, 152 outpatient adults with confirmed COVID-19 were randomized to receive either fluvoxamine or placebo for 15 days. Eligible patients were symptomatic within 7 days of the first dose of medication, had oxygen saturation over 92% on room air, and did not have severe underlying lung, heart, or liver disease. The primary outcome of clinical deterioration was defined by (1) shortness of breath or hospitalization for shortness of breath or pneumonia and (2) oxygen saturation less than 92%. At 15 days, clinical deterioration occurred in 0 of 80 patients in the fluvoxamine group and in 6 of 72 patients in the placebo group (absolute difference, 8.7% [95% CI, 1.8%-16.4%]).

Key Takeaways:

- In this preliminary study, adult outpatients with symptomatic COVID-19 treated with fluvoxamine had a lower likelihood of clinical deterioration over 15 days compared with placebo.
- Larger randomized trials with longer follow-up would be needed to more definitively determine clinical efficacy.

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Effectiveness of Adding a Mask Recommendation to Other Public Health Measures to Prevent SARS-CoV-2 Infection in Danish Mask Wearers (Annals of Internal Medicine)*

Bottom Line: This randomized controlled trial found that provision of surgical masks and a recommendation to wear them in community settings did not reduce SARS-CoV-2 infection among wearers by more than 50% in Denmark, a study setting with low infection rates, some social distancing measures, and uncommon community mask wearing.

Details: Available evidence suggests that wearing masks reduces transmission of SARS-CoV-2, though it remains unclear to what extent this is due to reduced transmission onwards from infected mask wearers (source control), protection of uninfected wearers (protective effect), or both. This randomized controlled trial purported to assess whether recommending wearing surgical masks for use outside the home by uninfected adults when in contact with others reduced their risk of acquiring SARS-CoV-2 infection, as measured by a positive antibody test (immunoglobulin M and G), polymerase chain reaction (PCR) test, or hospital diagnosis at 1 month. The study took place in Denmark during a time where social distancing measures were in effect but mask wearing in community settings was uncommon and not recommended (Apr-May 2020). Eligible participants were community members 18 or older who reported being outside the home with others for at least 3 hours a day, did not wear masks for occupational purposes, and did not have current or prior symptoms of diagnosis of COVID-19. Participants were randomized to the mask or control group; the mask group received a package of 50 disposable surgical masks (filtration rate: 98%) and instructed to wear a mask when outside the home around others for the next month; instructions for how to correctly wear a mask were provided. Both groups received instructions and materials for how to get antibody tests at the start of the study and 1 month later, as well as materials/instructions for collecting a sample for polymerase chain reaction (PCR) testing at 1 month and if COVID-like symptoms emerged during follow up. 3030 and 2994 participants were randomized to the intervention (mask wearing) and control groups; 4862 (81%) completed the study. SARS-CoV-2 infection occurred in 1.8% (n=42) and 2.1% (n=53) of mask and control group participants, respectively, with a -0.3 % between group difference (95% CI, -1.2-0.4%; P=0.38; odds ratio, 0.82 [CI = 0.54-1.23]; P=0.33). While the difference was not statistically significant, CIs were associated with a 46% reduction to 23% increase in infection, so results are inconclusive. Limitations identified by the author team include: inconclusive results, missing data, variable reported adherence to mask wearing (46%-54% adherence to mask wearing as recommended and occasionally or not as recommended, respectively), and self-reported test results. Additional critiques of this study have also been offered, most notably in this commentary, including low incidence of SARS-CoV-2 infections in Denmark during the study period that may have made assessing differences between groups difficult to detect; limited generalizability to settings with widespread mask use, lack of sufficient power to detect subgroup differences (e.g., by occupation, length of time outside the home around others); and the use of antibody tests to diagnose COVID-19, given variability in accuracy of tests. Perhaps most importantly, this study has been critiqued for its characterization of assessing the effectiveness of mask wearing, when it more accurately assessed the impact of providing and recommending use of masks.

Key Takeaways:

- This study can be more accurately characterized as an assessment of the impact of providing and recommending use of masks, rather than the effectiveness of mask wearing.
- Importantly, this study does not disprove the effectiveness of widespread mask wearing; given variable adherence despite recommendations and supplies, it does point to additional work needed to increase use and continued reliance on other public health measures to reduce transmission.
- While statistically significant differences in rates of SARS-CoV-2 infection were not detected between mask and control groups, results were inconclusive and numerous limitations have been noted by the study team and others, including: study setting characteristics that limit generalizability (low SARS-CoV-2 cases and with no mask use recommendation), variable reported adherence to mask wearing, self-reported test results, and use of antibody tests to diagnosis COVID-19.

*Denotes a study that has received considerable media attention

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Proportion of Asymptomatic Infection among COVID-19 Positive Persons and Their Transmission Potential: A Systematic Review and Meta-Analysis (PLOS ONE)

Bottom Line: This systematic review of and analysis across studies found high reported rates of asymptomatic SARS-CoV-2 infection and varied though substantial potential to transmit infection to others.

Details: This paper reports findings from a systematic review of and analysis across studies (meta-analysis) on the proportion of asymptomatic SARS-CoV-2 infection at testing and through follow-up and potential to transmit asymptomatic infection to others (measured as the secondary attack rate among close contacts of asymptomatic index patients). Both peer-reviewed and pre-print databases were included in searches for publications up to 6/22/20. Various study designs were included, including case series, cross-sectional, and cohort studies; studies rated low quality were excluded. Asymptomatic infection proportions and 95% confidence intervals (CIs) were estimated by pooling data using meta-analysis approaches, where appropriate. 6,137 studies were evaluated for inclusion; 71 were assessed for quality and 28 were included. Proportion of asymptomatic SARS-CoV-2 infection in general population studies and studies of contacts ranged from 8.2% to 75%. In meta-analysis (conducted in instances where >3 were conducted in the same population and had similar study design and inclusion criteria), asymptomatic infection proportions in nursing home residents and obstetric patients were 54% (42%-65%) and 95% (45%-100%), respectively. Through follow-up, 28% (13%-50%) of nursing home residents and 59% (49%-68%) of obstetric patients remained asymptomatic. Meta-analysis of asymptomatic infection transmission was not possible due to considerable variation in included studies. In 5 transmission studies, 18.8% (18/96) close contacts exposed to an asymptomatic individual were positive for SARS-CoV-2.

Key Takeaways:

- Pooled estimates of asymptomatic SARS-CoV-2 infection could only be calculated for obstetric patients and residents/staff of nursing homes due to variability in study designs and settings, and lack of high-quality studies for other populations; these estimates may not be generalizable to the general population. To better characterize these phenomena, high quality studies in representative general populations are needed.
- Studies to date, while variable in populations, settings, and outcomes, point to the necessity of public health strategies to identify and reduce transmission among asymptomatic persons, including systematic testing of high-risk populations, contact tracing of all contacts, and non-pharmaceutical interventions.

Acute Kidney Injury in a National Cohort of Hospitalized US Veterans with COVID-19 (CJASN)

Bottom Line: This large national study of patients hospitalized with COVID-19 in the Veterans Affairs health care system found approximately 1/3rd had acute kidney injury (AKI), which was associated with longer hospital stays, higher use of mechanical ventilation, and higher risk of death compared to patients without AKI.

Details: This study sought to describe rates of acute kidney injury (AKI) and characterize associated predictors and outcomes of AKI among US veterans hospitalized with COVID-19. Department of Veterans Affairs (VA) health care system patients with a lab-confirmed SARS-CoV-2 test between 2/1-7/23 were identified; of those, patients admitted 5 days before – 30 days after a positive test with no history of end stage kidney disease (ESKD) and measurements of outpatient serum creatinine in the 7-365 days prior to hospitalization were included in the study (n=5,216). 32% of participants (n=1655) had AKI, with 12% (n=201) receiving kidney replacement therapy (KRT). 80% of participants experienced AKI within 1 day of hospitalization, and almost half (47%) had not returned to baseline serum creatinine levels at discharge. Significant predictors of AKI during hospitalization included older age, male sex, Black race, co-morbidities (obesity, diabetes, and hospitalization), and lower estimated glomerular filtration rate (eGFR; indicates level of kidney function). AKI was associated with longer hospital stay (5.56 additional days), higher use of

mechanical ventilation (odds ratio, 6.46), and higher risk of death (odds ratio, 6.71) compared to patients without AKI, the latter of which had a stronger association in Black patients. There was considerable variation in AKI rates by hospital (range: 10-56%) and over time (from 40% in March to 27% in July); this variation was predominantly explained by the shifting proportion of Black patients, and to a lesser degree, age and comorbidity burden of patients hospitalized with COVID-19. Differences in outcomes by race are the result of exposure to societal, economic, environmental, and other inequities.

Key Takeaways:

- Almost half of patients hospitalized with COVID-19 who developed AKI in this study experienced partial or incomplete recovery, necessitating close monitoring and post-AKI care to reduce reoccurrence and alleviate long-term adverse consequences.
- Findings regarding mechanical ventilation use, length of hospital stays, and risk of death associated with AKI among patients hospitalized with COVID-19 should be incorporated into pandemic management and planning for future waves.
- Disparate outcomes by race within an integrated health care system designed to provide equitable access and reduce variation in care reflect differences in exposure to social, economic, and environmental factors that may increase risk of AKI and its adverse effects.

*Denotes a study that has received considerable media attention