COVID-19 Literature Review
11/2/2021
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1. Interferon beta-1a plus Remdesivir was not superior to Remdesivir alone in hospitalized patients with COVID-19 pneumonia
2. Vaccine effectiveness of 2 doses of Pfizer-BioNTech vaccine against COVID-19 hospitalization was 93%
3. Study published in Science demonstrate robust cellular immune memory to SARS-CoV-2 and variants for at least 6 months after mRNA vaccination
4. Overall estimated vaccine efficacy was 74.0% after 2 doses of AstraZeneca. 83.5% in participants 65 years of age or older
5. There is no evidence of an increased risk for early pregnancy loss after Covid-19 vaccination
6. Colchicine was not associated with reductions in 28-day mortality, duration of hospital stay, or risk of progressing to invasive mechanical ventilation or death
7. Compared with 6 mg of dexamethasone, 12 mg of dexamethasone did not have a statistically significantly effect in mortality
8. Pfizer's 3rd jab (booster) demonstrates 96% efficacy
9. There is no increased risk for mortality among COVID-19 vaccine recipients compared to unvaccinated individuals.
10. There is substantial new-onset post COVID-19 morbidity (malaise/fatigue/exhaustion, cough, chest pain, dysguesia, fever, dyspnea) in pediatric and adult populations
11. Self-reported history of high-risk allergy was associated with an increased risk of self-reported allergic reactions within 3 days of mRNA COVID-19 vaccination
12. Most patients with hematologic cancer remained without serological protection after 2 dose mRNA vaccination, despite delayed second vaccination dosage.
13. Treatment with fluvoxamine (100 mg twice daily for 10 days) among high-risk outpatients with early diagnosed COVID-19 reduced the need for hospitalization from 16% to 11%
14. A third dose of the BNT162b2 mRNA vaccine is 93% effective in protecting individuals against severe COVID-19-and 84% effective in preventing death from COVID, compared with receiving only two doses at least 5 months prior
15. Among high-risk patients with mild-to-moderate Covid-19, Sotrovimab (mAb) reduced the risk of disease progression - relative risk reduction of 85%
16. immunity against the delta variant of SARS-CoV-2 waned in ALL age groups a few months after receipt of the second dose of mRNA vaccine

The Lancet - 10/18/2021 - INF-Beta1a + Remdesivir vs Remdesivir Alone	• Between Aug 5, 2020, and Nov 11, 2020, 969 patients were enrolled and randomly assigned to the interferon beta-1a plus Remdesivir group (n=487) or to the placebo plus Remdesivir group (n=482). • The mean duration of symptoms before enrolment was 8·7 days (SD 4·4) in the interferon beta-1a plus Remdesivir group and 8·5 days (SD 4·3) days in the placebo plus Remdesivir group. • Patients in both groups had a time to recovery of 5 days (95% CI not estimable) (rate ratio of interferon beta-1a plus Remdesivir group *vs* placebo plus Remdesivir 0·99 [95% CI 0·87–1·13]; p=0·88). • The Kaplan-Meier estimate of mortality at 28 days was 5% (95% CI 3–7%) in the interferon beta-1a plus Remdesivir group and 3% (2–6%) in the placebo plus Remdesivir group (hazard ratio 1·33 [95% CI 0·69–2·55]; p=0·39). • Patients who did not require high-flow oxygen at baseline were more likely to have at least one related adverse event in the interferon beta-1a plus Remdesivir group (33 [7%] of 442 patients) than in the placebo plus Remdesivir group (15 [3%] of 435). • In patients who required high-flow oxygen at baseline, 24 (69%) of 35 had an adverse event and 21 (60%) had a serious adverse event in the interferon beta-1a plus Remdesivir group compared with 13 (39%) of 33 who had an adverse event and eight (24%) who had a serious adverse event in the placebo plus Remdesivir group • Interferon beta-1a plus Remdesivir was not superior to Remdesivir alone in hospitalized patients with COVID-19 pneumonia.

	• Patients who required high-flow oxygen at baseline had worse outcomes after treatment with interferon beta-1a compared with those given placebo • https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00384-2/fulltext
CDC - Effectiveness of Pfizer in Children 12-18	• Among hospitalized U.S. patients aged 12–18 years, vaccine effectiveness of 2 doses of Pfizer-BioNTech vaccine against COVID-19 hospitalization during June–September 2021, was 93% (95% confidence interval = 83%–97%). • https://www.cdc.gov/mmwr/volumes/70/wr/mm7042e1.htm?s_cid=mm7042e1_w
Science - 10/14/2021 - mRNA vaccines induced durable immune memory SARS-CoV2 and variants	• The durability of immune memory after SARS-CoV-2 mRNA vaccination remains unclear. Here, we longitudinally profiled vaccine responses in SARS-CoV-2 naïve and recovered individuals for 6 months after vaccination. • Antibodies declined from peak levels but remained detectable in most subjects at 6 months. • We found mRNA vaccines generated functional memory B cells that increased from 3-6 months post-vaccination, with the majority of these cells cross-binding the Alpha, Beta, and Delta variants. • mRNA vaccination further induced antigen-specific CD4+ and CD8+ T cells, and early CD4+ T cell responses correlated with long-term humoral immunity. Recall responses to vaccination in individuals with pre-existing immunity primarily increased antibody levels without substantially altering antibody decay rates. • Together, these findings demonstrate robust cellular immune memory to SARS-CoV-2 and variants for at least 6 months after mRNA vaccination. • https://www.science.org/doi/10.1126/science.abm0829
NEJM - 9/29/2021 - phase 3 results for 2 doses of AstraZeneca vaccine	• A total of 32,451 participants underwent randomization, in a 2:1 ratio, to receive AZD1222 (21,635 participants) or placebo (10,816 participants). AZD1222 was safe, with low incidences of serious and medically attended adverse events and adverse events of special interest; the incidences were similar to those observed in the placebo group. • Solicited local and systemic reactions were generally mild or moderate in both groups. • **Overall estimated vaccine efficacy was 74.0% (**95% confidence interval [CI], 65.3 to 80.5; P<0.001) and estimated • **vaccine efficacy was 83.5%** (95% CI, 54.2 to 94.1) **in participants 65 years of age or older**. • High vaccine efficacy was consistent across a range of demographic subgroups. • In the fully vaccinated analysis subgroup, no severe or critical symptomatic Covid-19 cases were observed among the 17,662 participants in the AZD1222 group; 8 cases were noted among the 8550 participants in the placebo group (<0.1%). The estimated vaccine efficacy for preventing SARS-CoV-2 infection (nucleocapsid antibody seroconversion) was 64.3% (95% CI, 56.1 to 71.0; P<0.001). SARS-CoV-2 spike protein binding and neutralizing antibodies increased after the first dose and increased further when measured 28 days after the second dose. • https://www.nejm.org/doi/full/10.1056/NEJMoa2105290?query=featured_coronavirus
NEJM - 10/20/2021 - COVID Vaccine, Pregnancy, and Miscarriage	• Among 13,956 women with ongoing pregnancies (of whom 5.5% were vaccinated) and 4521 women with miscarriages (of whom 5.1% were vaccinated), the median number of days between vaccination and miscarriage or confirmation of ongoing pregnancy was 19 (Fig. S2). • Among women with miscarriages, the adjusted odds ratios for Covid-19 vaccination were 0.91 (95% confidence interval [CI], 0.75 to 1.10) for vaccination in the previous 3 weeks and 0.81 (95% CI, 0.69 to 0.95) for vaccination in the previous 5 weeks (Table 1). The results

	were similar in an analysis that included all available vaccine types (Table S5), in an analysis stratified according to the number of doses received (one or two) (Table S6), and in sensitivity analyses limited to health care personnel (for whom vaccination was routinely recommended other than in the first trimester) or women with at least 8 weeks of follow-up after confirmed pregnancy (to exclude subsequent pregnancy loss) (Table S7) • Our study found no evidence of an increased risk for early pregnancy loss after Covid-19 vaccination and adds to the findings from other reports supporting Covid-19 vaccination during pregnancy. • https://www.nejm.org/doi/full/10.1056/NEJMc2114466?query=featured_home
Lancet - 10/18/2021 - Colchicine and COVID	• Between Nov 27, 2020, and March 4, 2021, • 11 340 (58%) of 19 423 patients enrolled into the RECOVERY trial were eligible to receive colchicine; 5610 (49%) patients were randomly assigned to the colchicine group and 5730 (51%) to the usual care group. • Overall, 1173 (21%) patients in the colchicine group and 1190 (21%) patients in the usual care group died within 28 days (rate ratio 1·01 [95% CI 0·93 to 1·10]; **p=0·77).** Consistent results were seen in all prespecified subgroups of patients. • Median time to discharge alive (10 days [IQR 5 to >28]) was the same in both groups, and there was no significant difference in the proportion of patients discharged from hospital alive within 28 days (3901 [70%] patients in the colchicine group and 4032 [70%] usual care group; rate ratio 0·98 [95% CI 0·94 to 1·03]; p=0·44). • In those not on invasive mechanical ventilation at baseline, there was no significant difference in the proportion meeting the composite endpoint of invasive mechanical ventilation or death (1344 [25%] in the colchicine group *vs* 1343 [25%] patients in the usual care group; risk ratio 1·02 [95% CI 0·96 to 1·09]; p=0·47) • In adults hospitalized with COVID-19, colchicine was not associated with reductions in 28-day mortality, duration of hospital stay, or risk of progressing to invasive mechanical ventilation or death • https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00435-5/fulltext
JAMA - 10/21/2021 - 12mg vs 6mg dexamethasone for COVID	• In this randomized trial that included 1000 patients with COVID-19 and severe hypoxemia, treatment with 12 mg/d of dexamethasone resulted in 22.0 days alive without life support at 28 days compared with 20.5 days in those receiving 6 mg/d of dexamethasone. This difference was not statistically significant • Among patients with COVID-19 and severe hypoxemia, 12 mg/d of dexamethasone compared with 6 mg/d of dexamethasone did not result in statistically significantly more days alive without life support at 28 days • https://jamanetwork.com/journals/jama/fullarticle/2785529
Financial Times - 10/21/2021 - efficacy of booster jab	• In a trial with 10,000 participants who had all completed a two-shot Pfizer regimen, half were randomized to receive a further equal-strength dose of the shot, and half a placebo. Five cases of COVID were registered in patients receiving the booster compared with 109 who were given a placebo • 95.6% efficacy • https://www.ft.com/content/d4e58d38-37d6-40cd-9d72-6b9bfd0a3683
CDC - 10/22/2021 - COVID vaccine and mortality	• During December 2020–July 2021, COVID-19 vaccine recipients had lower rates of non–COVID-19 mortality than did unvaccinated persons after adjusting for age, sex, race and ethnicity, and study site • There is no increased risk for mortality among COVID-19 vaccine recipients. This finding reinforces the safety profile of currently approved COVID-19 vaccines in the United States

	• https://www.cdc.gov/mmwr/volumes/70/wr/mm7043e2.htm?s_cid=mm7043e2_x
MedRxIV - 10/2021 - Post-COVID	• The study population included 157,134 individuals (11,950 children/adolescents and 145,184 adults) with confirmed COVID-19. COVID-19 and control cohort were well-balanced regarding covariates. • For all health outcomes combined, incidence rates (IRs) in the COVID-19 cohort were significantly higher than those in the control cohort in both children/adolescents (IRR=1.30, 95%-CI=[1.25-1.35], IR COVID-19=436.91, IR Control=335.98) and adults (IRR=1.33, 95%-CI=[1.31-1.34], IR COVID-19=615.82, IR Control=464.15). The relative magnitude of increased documented morbidity was similar for the physical, mental, and physical/mental overlap domain. • In the COVID-19 cohort, incidence rates were significantly higher in all 13 diagnosis/symptom complexes in adults and in ten diagnosis/symptom complexes in children/adolescents. IRR estimates were similar for the age groups 0-11 and 12-17. Incidence rates in children/adolescents were consistently lower than those in adults. • Among the specific outcomes with the highest IRR and an incidence rate of at least **1/100 person-years** in the COVID-19 cohort in children and adolescents were o malaise/fatigue/exhaustion (IRR=2.28, 95%-CI=[1.71-3.06], IR COVID-19=12.58, IR Control=5.51), o cough (IRR=1.74, 95%-CI=[1.48-2.04], IR COVID-19=36.56, IR Control=21.06), and o throat/chest pain (IRR=1.72, 95%-CI=[1.39-2.12], IR COVID-19=20.01, IR Control=11.66). o In adults, these included dysguesia (IRR=6.69, 95%-CI=[5.88-7.60], IR COVID-19=12.42, IR Control=1.86), o fever (IRR=3.33, 95%-CI=[3.01-3.68], IR COVID-19=11.53, IR Control=3.46), and o dyspnea (IRR=2.88, 95%-CI=[2.74-3.02], IR COVID-19=43.91, IR Control=15.27). • There is substantial new-onset post COVID-19 morbidity in pediatric and adult populations based on routine health care documentation • https://www.medrxiv.org/content/10.1101/2021.10.21.21265133v1
JAMA - 10/26/2021 - High risk allergy history and COVID vaccine allergic reactions	• A total of 52 998 health care employees (mean [SD] age, 42 [14] years; 38 167 women [72.0%]) were included in the cohort, of whom 51 706 (97.6%) received 2 doses of an mRNA COVID-19 vaccine and • 474 (0.9%) reported a history of high-risk allergy. • Individuals with vs without a history of high-risk allergy reported more allergic reactions after receiving dose 1 or 2 of the vaccine (**11.6%** [n = 55] vs **4.7%** [n = 2461]). In the adjusted model, a • history of high-risk allergy was associated with an increased risk of allergic reactions (adjusted relative risk [aRR], 2.46; 95% CI, 1.92-3.16), with risk being highest for **hives** (aRR, 3.81; 95% CI, 2.33-6.22) and **angioedema** (aRR, 4.36; 95% CI, 2.52-7.54) • self-reported history of high-risk allergy was associated with an increased risk of self-reported allergic reactions within 3 days of mRNA COVID-19 vaccination, however, it did not impede the completion of the 2-dose vaccine protocol • https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2785466
Cancer Cell - 10/11/2021 - Immunogenicity in pts with hematologic malignancies.	• ..our study re-emphasizes the vulnerabilities of patients with cancer, especially those with hematologic malignancies, *vis-à-vis* the COVID-19 pandemic. • Whereas the second vaccination significantly increased seroconversion rates in patients with cancer, most patients with hematologic cancer remained without serological protection. Moreover, • delayed second vaccination showed no obvious advantage, highlighting the importance of early (and possibly repeated) boosting of cancer patients as an attempt to rescue their very

	poor single-dose vaccine immunogenicity. Likewise, the data compose a strong case for continued transmission mitigation measures in community and healthcare settings, e.g., protective measures in crowded areas, such as public transport, and the inclusion of young persons in ring vaccinations of patients' contact groups • https://www.cell.com/cancer-cell/fulltext/S1535-6108(21)00545-6#secsectitle0010
Lancet - 10/27/2021 - Fluvoxamine and COVID	• Fluvoxamine is a selective serotonin reuptake inhibitor (SSRI) and a σ-1 receptor (S1R) agonist. There are several potential mechanisms for fluvoxamine in treatment of COVID-19 illness, including anti-inflammatory and possible antiviral effects. • 9803 potential participants for this trial. The trial was initiated on June 2, 2020, with the current protocol reporting randomization to fluvoxamine from Jan 20 to Aug 5, 2021, when the trial arms were stopped for superiority. 741 patients were allocated to fluvoxamine and 756 to placebo. The average age of participants was 50 years (range 18–102 years); 58% were female. • The proportion of patients observed in a COVID-19 emergency setting for more than 6 h or transferred to a tertiary hospital due to COVID-19 was lower for the fluvoxamine group compared with placebo (79 [**11**%] of 741 vs 119 [**16**%] of 756); relative risk [RR] 0·68; 95% Bayesian credible interval [95% BCI]: 0·52–0·88), with a probability of superiority of 99·8% surpassing the prespecified superiority threshold of 97·6% (risk difference 5·0%). • Of the composite primary outcome events, 87% were hospitalizations. Findings for the primary outcome were similar for the modified intention-to-treat analysis (RR 0·69, 95% BCI 0·53–0·90) and larger in the per-protocol analysis (RR 0·34, 95% BCI, 0·21–0·54). • There were 17 deaths in the fluvoxamine group and 25 deaths in the placebo group in the primary intention-to-treat analysis (odds ratio [OR] 0·68, 95% CI: 0·36–1·27). There was one death in the fluvoxamine group and 12 in the placebo group for the per-protocol population (OR 0·09; 95% CI 0·01–0·47). We found no significant differences in number of treatment emergent adverse events among patients in the fluvoxamine and placebo groups • Treatment with fluvoxamine (100 mg twice daily for 10 days) among high-risk outpatients with early diagnosed COVID-19 reduced the need for hospitalization defined as retention in a COVID-19 emergency setting or transfer to a tertiary hospital • https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(21)00448-4/fulltext
Lancet - 10/29/2021 - effectiveness of 3rd dose of mRNA vaccine	• 1 158 269 individuals were eligible to be included in the third dose group. Following matching, the third dose and control groups each included 728 321 individuals. Participants had a median age of 52 years (IQR 37–68) and 51% were female. The median follow-up time was 13 days (IQR 6–21) in both groups. • Vaccine effectiveness evaluated at least 7 days after receipt of the third dose, compared with receiving only two doses at least 5 months ago, was estimated to be 93% (231 events for two doses *vs* 29 events for three doses; 95% CI 88–97) for admission to hospital, 92% (157 *vs* 17 events; 82–97) for severe disease, and 81% (44 *vs* seven events; 59–97) for COVID-19-related death • Our findings suggest that a third dose of the BNT162b2 mRNA vaccine is effective in protecting individuals against severe COVID-19-related outcomes, compared with receiving only two doses at least 5 months ago • https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)02249-2/fulltext
NEJM - 10/27/2021 - Sotrovimab (mAb) and COVID	• Sotrovimab is a pan-sarbecovirus monoclonal antibody that was designed to prevent progression of Covid-19 • In this prespecified interim analysis, which included an intention-to-treat population of 583 patients (291 in the sotrovimab group and 292 in the placebo group),

	• 3 patients (1%) in the sotrovimab group, as compared with 21 patients (7%) in the placebo group, had disease progression leading to hospitalization or death (relative risk reduction, 85%; 97.24% confidence interval, 44 to 96; P=0.002). In the placebo group, 5 patients were admitted to the intensive care unit, including 1 who died by day 29. Safety was assessed in 868 patients (430 in the sotrovimab group and 438 in the placebo group). • Adverse events were reported by 17% of the patients in the sotrovimab group and 19% of those in the placebo group; serious adverse events were less common with sotrovimab than with placebo (in 2% and 6% of the patients, respectively) • Among high-risk patients with mild-to-moderate Covid-19, sotrovimab reduced the risk of disease progression • https://www.nejm.org/doi/full/10.1056/NEJMoa2107934?query=featured_coronavirus
NEJM - 10/27/2021 - waning Immunity to COVID after mRNA vaccine in Israel	• Among persons 60 years of age or older, the rate of infection in the July 11–31 period was higher among persons who became fully vaccinated in January 2021 (when they were first eligible) than among those fully vaccinated 2 months later, in March (rate ratio, 1.6; 95% confidence interval [CI], 1.3 to 2.0). • Among persons 40 to 59 years of age, the rate ratio for infection among those fully vaccinated in February (when they were first eligible), as compared with 2 months later, in April, was 1.7 (95% CI, 1.4 to 2.1). Among persons 16 to 39 years of age, the rate ratio for infection among those fully vaccinated in March (when they were first eligible), as compared with 2 months later, in May, was 1.6 (95% CI, 1.3 to 2.0). The rate ratio for severe disease among persons fully vaccinated in the month when they were first eligible, as compared with those fully vaccinated in March, was 1.8 (95% CI, 1.1 to 2.9) among persons 60 years of age or older and 2.2 (95% CI, 0.6 to 7.7) among those 40 to 59 years of age; owing to small numbers, the rate ratio could not be calculated among persons 16 to 39 years of age • These findings indicate that immunity against the delta variant of SARS-CoV-2 waned in all age groups a few months after receipt of the second dose of vaccine • https://www.nejm.org/doi/full/10.1056/NEJMoa2114228?query=featured_coronavirus