06/08/2022 - COVID-19 Literature Review
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1. Videoconference hampers idea generation and comes with a cognitive cost.
2. In a cohort of HIV positive pts in Africa, in hospital mortality from COVID was 24% with a hospitalization rate of 38%. regardless or ART adherence or viral load suppression, HIV infection HIV infection was associated with higher COVID severity and mortality.
3. Vaccine effectiveness of Moderna vaccine in children 6 - 11 was 88%
4. Healthy lifestyle choices and adoption at middle age results in life expectancy gains even beyond 80 years of age.
5. Plant-based COVID vaccine is 78% effective against COVID
6. 55% of patients with impaired exercise capacity in Long COVID had a raised VWF(Ag):ADAMTS13 ratio ≥1.5 (OR 4) demonstrating a relationship between a hypercoagulable state and Long COVID symptomatology.
7. COVID PCR can be detected in stool after 4 months of clinical pulmonary illness.
8. Paxlovid, but not Molnupiravir was associated with a reduced risk of hospitalization in real-world non-hospitalized COVID-19 patients
9. In people with COVID, sotrovimab use led to lower rates of progression to severe COVID compared to those Molnupiravir use.
10. dexamethasone/Remdesivir was associated with significantly more adverse events (37%), treatment-related adverse events (10%), and severe or life-threatening adverse events (36%) compared to baricitinib/remdeisivir with 30%, 4%, 28% respectively.
11. Pts with COVID and neurologic symptoms had viral antigen in CSF, and evidence of neuroaxonal injury and more marked inflammatory profile in CSF compared to controls.

Nature - 4/27/2022 - Virtual communications curbs creative idea generation	• COVID-19 accelerated a decade-long shift to remote work by normalizing working from home on a large scale. Indeed, 75% of US employees in a 2021 survey reported a personal preference for working remotely at least one day per week[1], and studies estimate that 20% of US workdays will take place at home after the pandemic ends[2]. • Here we examine how this shift away from in-person interaction affects innovation, which relies on collaborative idea generation as the foundation of commercial and scientific progress[3]. In a laboratory study and a field experiment across five countries (in Europe, the Middle East and South Asia), • We show that videoconferencing inhibits the production of creative ideas. • By contrast, when it comes to selecting which idea to pursue, we find no evidence that videoconferencing groups are less effective (and preliminary evidence that they may be more effective) than in-person groups. Departing from previous theories that focus on how oral and written technologies limit the synchronicity and extent of information exchanged[4,5,6], we find that our effects are driven by differences in the physical nature of videoconferencing and in-person interactions.

	Specifically, using eye-gaze and recall measures, as well as latent semantic analysis, we demonstrate that • Videoconferencing hampers idea generation because it focuses communicators on a screen, which prompts a narrower cognitive focus. • Our results suggest that virtual interaction comes with a cognitive cost for creative idea generation • https://www.nature.com/articles/s41586-022-04643-y
Lancet - 5/10/2022 - COVID and severity of illness in pts living with HIV.	• Of 197 479 patients reporting HIV status, 16 955 (8·6%) were people living with HIV. 16 283 (96.0%) of the 16 955 people living with HIV were from Africa; 10 603 (62·9%) were female and 6271 (37·1%) were male; the mean age was 45·5 years (SD 13·7); • 6339 (38·3%) were admitted to hospital with severe illness; and 3913 • (24·3%) died in hospital. Of the 10 166 people living with HIV with known antiretroviral therapy (ART) status, • 9302 (91·5%) were on ART. • Compared with individuals without HIV, people living with HIV had 15% increased odds of severe presentation with COVID-19 (aOR 1·15, 95% CI 1·10–1·20) and were 38% more likely to die in hospital (aHR 1·38, 1·34–1·41). Among people living with HIV, male sex, age 45–75 years, and having chronic cardiac disease or hypertension increased the odds of severe COVID-19; male sex, age older than 18 years, having diabetes, hypertension, malignancy, tuberculosis, or chronic kidney disease increased the risk of in-hospital mortality. • The use of ART or viral load suppression were associated with a reduced risk of poor outcomes; however, HIV infection remained a risk factor for severity and mortality regardless of ART and viral load suppression status • https://www.thelancet.com/journals/lanhiv/article/PIIS2352-3018(22)00097-2/fulltext
Nature - 5/2020 - EBV as trigger and driver of Multiple sclerosis	• Described link and potential causal role of EBV in the development of multiple sclerosis • https://www.nature.com/articles/s41591-022-01823-1
NEJM - 5/11/2022 - Moderna efficacy and safety in children	• ***In part 1*** of the trial, 751 children received 50-μg or 100-μg injections of the mRNA-1273 vaccine, and on the basis of safety and immunogenicity results, the 50-μg dose level was selected for ***part 2.*** In part 2 of the trial, 4016 children were randomly assigned to receive two injections of mRNA-1273 (50 μg each) or placebo and were followed for a median of 82 days (interquartile range, 14 to 94) after the first injection. This dose level was

6 - 11 years old	• associated with mainly low-grade, transient adverse events, most commonly injection-site pain, headache, and fatigue. ○ No vaccine-related serious adverse events, multisystem inflammatory syndrome in children, myocarditis, or pericarditis were reported as of the data-cutoff date. • One month after the second injection (day 57), the neutralizing antibody titer in children who received mRNA-1273 at a 50-μg level was 1610 (95% confidence interval [CI], 1457 to 1780), as compared with 1300 (95% CI, 1171 to 1443) at the 100-μg level in young adults, with serologic responses in at least 99.0% of the participants in both age groups, findings that met the prespecified noninferiority success criterion. • Estimated vaccine efficacy was 88.0% (95% CI, 70.0 to 95.8) against Covid-19 occurring 14 days or more after the first injection, at a time when B.1.617.2 **(delta) was the dominant circulating variant**. • Two 50-μg doses of the mRNA-1273 vaccine were found to be safe and effective in inducing immune responses and preventing Covid-19 in children 6 to 11 years of age • https://www.nejm.org/doi/full/10.1056/NEJMoa2203315
NEJM - 5/4/2022 - Plant-based COVID vaccine anyone ?	• Coronavirus-like particles (CoVLP) that are produced in plants and display the prefusion spike glycoprotein of the original strain of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are combined with an adjuvant (Adjuvant System 03 [AS03]) to form the candidate vaccine • A total of 24,141 volunteers participated in the trial; the median age of the participants was 29 years. Covid-19 was confirmed by polymerase-chain-reaction assay in 165 participants in the intention-to-treat population; all viral samples that could be sequenced contained variants of the original strain. • ***Vaccine efficacy was 69.5%*** (95% confidence interval [CI], 56.7 to 78.8) against any symptomatic Covid-19 caused by five variants that were identified by sequencing. • In a post hoc analysis, vaccine efficacy was 78.8% (95% CI, 55.8 to 90.8) against moderate-to-severe disease and 74.0% (95% CI, 62.1 to 82.5) among the participants who were seronegative at baseline. • No severe cases of Covid-19 occurred in the vaccine group, in which the median viral load for breakthrough cases was lower than that in the placebo group by a factor of more than 100. • Solicited adverse events were mostly mild or moderate and transient and were more frequent in the vaccine group than in the placebo group; local adverse events occurred in 92.3% and 45.5% of participants, respectively, and systemic adverse events in 87.3% and 65.0%. The incidence of unsolicited adverse events was similar in the two groups up to 21 days after each dose (22.7% and 20.4%) and from day 43 through day 201 (4.2% and 4.0%)

	• https://www.nejm.org/doi/full/10.1056/NEJMoa2201300

Age and aging - 5/2022 - Impact of modifiable healthy lifestyle adoption on lifetime gain from middle to older age.	• We examined a prospective cohort of 20,373 men and 26,247 women aged 40–80 years.
	• Eight modifiable lifestyle factors were assessed:
	  ○ consumption of fruit,
	  ○ fish and milk,
	  ○ walking and/or sports participation,
	  ○ body-mass index,
	  ○ smoking status,
	  ○ alcohol consumption and
	  ○ sleep duration.
	• Modifiable healthy lifestyle factors scored one point each, for a maximum of eight points. The impact of modifiable healthy lifestyle adoption on lifetime gain during the ages of 40–102 years was analyzed
	• during the median 21 years of follow-up, 8,966 individuals (3,683 men and 5,283 women) died.
	• Life expectancy at 40 years (95% confidence intervals) for 7–8 health lifestyle points was 46.8 (45.6–48.1) and 51.3 (50.0–52.6) years for men and women, respectively.
	• The potential impact of modifiable healthy lifestyle adoption on lifetime gain persisted over the age of 80 years or more, in individuals with ≥5 factors ($P < 0.001$), particularly older men. The benefits were more pronounced among patients with major comorbidities, such as cardiovascular disease, cancer, hypertension, diabetes, kidney disease and those with multimorbidity throughout all age categories
	• https://academic.oup.com/ageing/article/51/5/afac080/6572254?login=false

Blood advances - 5/11/2022 - Impaired exercise capacity in post-COVID syndrome	• Post-COVID syndrome (PCS) or Long-COVID is an increasingly recognized complication of acute SARS-CoV-2 infection, characterized by persistent fatigue, reduced exercise tolerance chest pain, shortness of breath and cognitive slowing. • Acute COVID-19 is strongly linked with increased risk of thrombosis; a prothrombotic state, quantified by elevated Von Willebrand Factor (VWF) Antigen (Ag):ADAMTS13 ratio, and is associated with severity of acute COVID-19 infection. • We investigated if patients with PCS also had evidence of a pro-thrombotic state associating with symptom severity. In a large cohort of patients referred to a dedicated post-COVID-19 clinic, thrombotic risk including VWF(Ag):ADAMTS13 ratio, was investigated. • An elevated VWF(Ag):ADAMTS13 ratio (≥1.5) was raised in nearly one-third of the cohort and four times more likely in patients with impaired exercise capacity as evidenced by desaturation ≥3% and/or rise in lactate level more than 1 from baseline on 1-minute sit to stand test and/or 6-minute walk test (p<0.0001). 20% (56/276) had impaired

	exercise capacity, of which 55% (31/56) had a raised VWF(Ag):ADAMTS13 ratio ≥1.5 (p<0.0001). • FVIII and VWF(Ag) were elevated in 26% and 18% respectively and support a hypercoagulable state in some patients with PCS. These findings suggest possible ongoing microvascular/endothelial dysfunction in the pathogenesis of PCS and highlight a potential role for antithrombotic therapy in the management of these patients • 55% of patients with impaired exercise capacity had a raised VWF(Ag):ADAMTS13 ratio ≥1.5 (OR 4) • https://ashpublications.org/bloodadvances/article/doi/10.1182/bloodadvances.2021006944/485206/Impaired-exercise-capacity-in-post-COVID-syndrome
JAMA - 5/11/2022 - COVID PCR can persist in stool for months	• In her new study, fecal SARS-CoV-2 RNA was detected in about half of the participants within the first week after a polymerase chain reaction–confirmed diagnosis of COVID-19. • At 4 months, no participants were still shedding viral particles from the respiratory tract, but 12.7% continued to shed SARS-CoV-2 RNA in feces. • At 7 months, 3.8% were still shedding SARS-CoV-2 in feces • https://jamanetwork.com/journals/jama/fullarticle/2792688

Lancet Preprint - 5/17/2022. - Paxlovid and Molnupiravir in prevention of hospitalization from COVID	• 93,883 patients,
	  ○ 83,154 (88·6%), 5,808 (6·2%), and 4,921 (5·2%) were oral antiviral non-users, Molnupiravir users, and nirmatrelvir/ritonavir users respectively.
	• Compared to non-users,
	  ○ oral antiviral users were older and had more comorbidities, lower complete vaccination rate, and more hospitalizations in the previous year.
	• Molnupiravir users were older, and had more comorbidities, lower complete vaccination rate, and more hospitalizations in the previous year than nirmatrelvir/ritonavir users.
	• At a median follow-up of 30 days, 1,931 (2·1%) patients were admitted to hospital and 225 (0·2%) patients developed the secondary endpoint.
	• After propensity score weighting, nirmatrelvir/ritonavir use (weighted hazard ratio 0·79, 95% CI 0·65-0·95, P =0·011) but not Molnupiravir use (weighted hazard ratio 1·17, 95% CI 0·99-1·39, P =0·062) was associated with a reduced risk of hospitalization than non-users. The use of Molnupiravir or nirmatrelvir/ritonavir was not associated with a lower risk of the secondary endpoint as compared to non-users.
	• In the subgroup of patients aged ≥60 years or aged <60 years with comorbidities, nirmatrelvir/ritonavir use but not Molnupiravir use was associated with a reduced risk of hospitalization than non-users
	• https://papers.ssrn.com/sol3/papers.cfm?abstract_id=4112160

	• https://www.medrxiv.org/content/10.1101/2022.05.19.22275291v1
MedRxIV - 5/23/2022 - Sotrovimab vs molnupiravir for prevention of severe COVID	• Patients treated with sotrovimab (n=3288) and Molnupiravir (n=2663) were similar with respect to most baseline characteristics. The mean age of all 5951 patients was 52 (SD=16) years; 59% were female, 89% White and 87% had three or more COVID-19 vaccinations. • Within 28 days after treatment initiation, 84 (1.4%) COVID-19 related hospitalizations/deaths were observed (31 treated with sotrovimab and 53 with Molnupiravir). Cox proportional hazards models stratified by area showed that after adjusting for demographics, high-risk cohort categories, vaccination status, calendar time, body mass index and other comorbidities, treatment with sotrovimab was associated with a substantially lower risk than treatment with Molnupiravir (hazard ratio, HR=0.53, 95% CI: 0.32-0.88; P=0.014). Consistent results were obtained from propensity score weighted Cox models (HR=0.51, 95% CI: 0.31-0.83; P=0.007) and when restricted to fully vaccinated people (HR=0.52, 95% CI: 0.30-0.90; P=0.020). No substantial effect modifications by other characteristics were detected (all P values for interaction>0.10) • In routine care of non-hospitalized high-risk adult patients with COVID-19 in England, those who received sotrovimab were at lower risk of severe COVID-19 outcomes than those receiving Molnupiravir • https://www.medrxiv.org/content/10.1101/2022.05.22.22275417v1
CDC - 5/24/2022 - Post-COVID conditions among adult COVID survivors	• COVID-19 survivors have twice the risk for developing pulmonary embolism or respiratory conditions; • one in five COVID-19 survivors aged 18–64 years and one in four survivors aged ≥65 years experienced at least one incident condition that might be attributable to previous COVID-19 • https://www.cdc.gov/mmwr/volumes/71/wr/mm7121e1.htm?s_cid=mm7121e1_x
Lancet - Baricitinib vs Dexamethasone for hospitalized COVID pts.	• Between Dec 1, 2020, and April 13, 2021, 1047 patients were assessed for eligibility. 1010 patients were enrolled and • randomly assigned, 516 (51%) to Baricitinib plus Remdesivir plus placebo and • 494 (49%) to dexamethasone plus Remdesivir plus placebo. The mean age of the patients was 58·3 years (SD 14·0) and 590 (58%) of 1010 patients were male. 588 (58%) of 1010 patients were White, 188 (19%) were Black, 70 (7%) were Asian, and 18 (2%) were American Indian or Alaska Native. 347 (34%) of 1010 patients were Hispanic or Latino. • Mechanical ventilation-free survival by day 29 was similar between the study groups (Kaplan-Meier estimates of 87·0% [95% CI 83·7 to 89·6] in the Baricitinib plus Remdesivir plus placebo group and 87·6% [84·2 to

	90·3] in the dexamethasone plus Remdesivir plus placebo group; risk difference 0·6 [95% CI −3·6 to 4·8]; p=0·91). • The odds ratio for improved status in the dexamethasone plus Remdesivir plus placebo group compared with the Baricitinib plus Remdesivir plus placebo group was 1·01 (95% CI 0·80 to 1·27). • At least one adverse event occurred in 149 **(30%)** of 503 patients in the Baricitinib plus Remdesivir plus placebo group • and 179 **(37%)** of 482 patients in the dexamethasone plus Remdesivir plus placebo group (risk difference 7·5% [1·6 to 13·3]; p=0·014). • 21 **(4%)** of 503 patients in the Baricitinib plus Remdesivir plus placebo group had at least one treatment-related adverse event versus 49 **(10%)** of 482 patients in the dexamethasone plus Remdesivir plus placebo group (risk difference 6·0% [2·8 to 9·3]; p=0·00041). • Severe or life-threatening grade 3 or 4 adverse events occurred in 143 **(28%)** of 503 patients in the Baricitinib plus Remdesivir plus placebo group and 174 **(36%)** of 482 patients in the dexamethasone plus Remdesivir plus placebo group (risk difference 7·7% [1·8 to 13·4]; p=0·012) • Baricitinib plus Remdesivir and dexamethasone plus Remdesivir resulted in similar mechanical ventilation-free survival by day 29, however, dexamethasone was associated with significantly more adverse events, treatment-related adverse events, and severe or life-threatening adverse events • https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(22)00088-1/fulltext
JAMA - 5/23/2022 - Viral antigen and inflammatory biomarkers in CSF in pts with COVID and neurologic symptoms	• Forty-four patients (median [IQR] age, 57 [48-69] years; 30 [68%] male; 26 with moderate COVID-19 and 18 with severe COVID-19 based on the World Health Organization Clinical Progression Scale), 10 healthy controls (median [IQR] age, 58 [54-60] years; 5 [50%] male), and 41 patient controls (COVID negative without evidence of CNS infection) (median [IQR] age, 59 [49-70] years; 19 [46%] male) were included in the study. • Twenty-one patients were neuroasymptomatic and 23 were neurosymptomatic (21 with encephalopathy). • In 31 of 35 patients for whom data were available (89%), CSF N-Ag was detected; viral RNA test results were negative in all. • Nucleocapsid antigen was significantly correlated with CSF neopterin ($r = 0.38$; $P = .03$) and interferon γ ($r = 0.42$; $P = .01$). No differences in CSF N-Ag concentrations were found between patient groups. • Patients had markedly increased CSF neopterin, β_2-microglobulin, interleukin (IL) 2, IL-6, IL-10, and tumor necrosis factor α compared with controls. Neurosymptomatic patients had significantly higher median (IQR) CSF interferon γ (86 [47-172] vs 21 [17-81] fg/mL; $P = .03$) and had a significantly higher inflammatory biomarker profile using principal component analysis compared with neuroasymptomatic

	patients (0.54; 95% CI, 0.03-1.05; *P* = .04). Age-adjusted median (IQR) CSF NfL concentrations were higher in patients compared with controls (960 [673-1307] vs 618 [489-786] ng/L; *P* = .002). No differences were seen in any CSF biomarkers in moderate compared with severe disease • In this study of pts with COVID and neurologic symptoms, compared with control participants, viral antigen was detectable in CSF and correlated with CNS immune activation. Patients with COVID-19 had signs of neuroaxonal injury, and neurosymptomatic patients had a more marked inflammatory profile that could not be attributed to differences in COVID-19 severity • https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2792536