Dr. Leo's COVID Corner – February 2022

1. A 3rd injection(booster) of mRNA vaccine is 94% effective at preventing ER visits and 82% effective at preventing urgent care visits. Also 94% effective at preventing hospitalization
2. A 3rd injection(booster) of mRNA vaccine decreased risk of symptomatic COVID by 50%
3. Unvaccinated individuals had 68x greater risk of dying from COVID than individuals with full series (3 doses) of mRNA vaccine.
4. 1-year out from ICU treatment for COVID, pts described residual physical (74%), mental 26%, and cognitive (16%) symptoms
5. During Omicron wave, total cases, ED visits and hospitalization were much higher than Delta wave..... Duh! See figure 1 of link
6. AKI with COVID-19 was closely related to decline status of kidney function at one-year after symptom onset
7. Homologous and heterologous booster vaccines had an acceptable safety profile and were immunogenic in adults after a primary series
8. Risk of myocarditis after receipt of the 2nd vaccine dose in adolescents 12 to 15 years of age was estimated to be 1 case per 12,361 (male) and 1 case per 144,439 (female)
9. 7% of all Lung transplantations between 8/2020 and 9/2021 were due to COVID. Most were bilateral lung transplants
10. COVID-19 causes a prolonged change to the airway immune landscape in those with persistent lung disease, with evidence of cell death and tissue repair linked to ongoing activation of cytotoxic T cells
11. COVID-related environmental contamination is uncommon with 5.5% of surfaces samples (PCR testing) noted to be contaminated and only 0.3% of surfaces samples via viral culture.
12. 4 main risk factors noted to be associated with Long COVID: DMT2, high level viremia, EBV reactivation viremia and Auto-Antibodies.
13. List of NNT (number needed to treat) outpatient therapies for COVID

CDC - 1/21/2022 - Vaccine Effectiveness - especially third dose of mRNA vaccine.	• Vaccine effectiveness was significantly higher among patients who received their second mRNA COVID-19 vaccine dose <180 days before medical encounters compared with those vaccinated ≥180 days earlier. During both Delta- and Omicron-predominant periods,
	• receipt of a third vaccine dose was highly effective at preventing
	  ○ COVID-19–associated emergency department (94%)
	  ○ and urgent care encounters (82%)
	  ○ and preventing COVID-19–associated hospitalizations (94%).
	  ○ https://www.cdc.gov/mmwr/volumes/71/wr/mm7104e3.htm?s_cid=mm7104e3_x

MedRxiv - 1/2022 - mRNA vaccine effectiveness against symptomatic infection	• For BNT162b2, cumulative symptomatic infection incidence was
	  ○ 2.9% (95% CI: 2.8-3.1%) in the booster-dose cohort
	  ○ and 5.5% (95% CI: 5.3-5.7%) in the primary-series cohort, after 49 days of follow-up.
	  ○ Adjusted hazard ratio for symptomatic infection was 0.50 (95% CI: 0.47-0.53).
	• Booster effectiveness relative to primary series was 50.1% (95% CI: 47.3-52.8%). For mRNA-1273, cumulative symptomatic infection incidence was 1.9% (95% CI: 1.7-2.2%) in the booster-dose cohort and 3.5% (95% CI: 3.2-3.9%) in the primary-series cohort, after 35 days of follow-up. The adjusted hazard ratio for symptomatic infection was 0.49 (95% CI: 0.43-0.57). Booster effectiveness relative

	to primary series was 50.8% (95% CI: 43.4-57.3%). There were fewer cases of severe COVID-19 in booster-dose cohorts than in primary-series cohorts, but cases of severe COVID-19 were rare in all cohorts • https://www.medrxiv.org/content/10.1101/2022.01.18.22269452v1 • Also demonstrated in this JAMA article ○ https://jamanetwork.com/journals/jama/fullarticle/2788485
CDC - 1/2022 - COVID-related cases and deaths by vaccination status.	• People who were unvaccinated had a greater risk (13x greater) of testing positive for COVID-19 and a greater risk (68X greater)of dying from COVID-19 than people who were fully vaccinated (3 doses of mRNA vaccine).https://covid.cdc.gov/covid-data-tracker/#rates-by-vaccine-status

JAMA - 1/24/2022 - clinical outcomes of Patients 1-year survival after ICU treatment for COVID	• Of the 452 eligible patients, 301 (66.8%) patients could be included, and 246 (81.5%) patients (mean [SD] age, 61.2 [9.3] years; 176 men [71.5%]; median ICU stay, 18 days [IQR, 11 to 32]) completed the 1-year follow-up questionnaires. At 1 year after ICU treatment for COVID-19,
	  ○ physical symptoms (described in table 4) were reported by 182 of 245 patients (74.3% [95% CI, 68.3% to 79.6%]),
	  ○ mental symptoms (anxiety/depression) were reported by 64 of 244 patients (26.2% [95% CI, 20.8% to 32.2%]), and
	  ○ cognitive symptoms were reported by 39 of 241 patients (16.2% [95% CI, 11.8% to 21.5%]).
	• The most frequently reported new physical problems were weakened condition (95/244 patients [38.9%]), joint stiffness (64/243 patients [26.3%]) joint pain (62/243 patients [25.5%]), muscle weakness (60/242 patients [24.8%]) and myalgia (52/244 patients [21.3%])
	• https://jamanetwork.com/journals/jama/fullarticle/2788504

CDC - 1/25/2022 - Trends in Disease Severity during Omicron	• Despite Omicron seeing the highest reported numbers of COVID-19 cases and hospitalizations during the pandemic, disease severity indicators, including length of stay, ICU admission, and death, were lower than during previous pandemic peaks • see figure 1 • https://www.cdc.gov/mmwr/volumes/71/wr/mm7104e4.htm?s_cid=mm7104e4_x
Lancet - 1/25/2022 - Association of AKI with 1-year outcome of	• In total, 1,734 study participants were included in this study. Median follow-up duration was 342.0 days (IQR, 223.0-358.0) after symptom onset. After multivariable adjustment, • percentage of eGFR decreased from acute phase to follow-up was 8.30% (95% CI, 5.99-10.61) higher among AKI participants than those without AKI at acute phase. • Participants with AKI had an odds ratio (OR) of 4.60 (95% CI, 2.10-10.08) for reduced renal function at follow-up. The percentage of eGFR decreased for

kidney function in hospital survivors.	participants with AKI stage 1, stage 2, and stage 3 was 6.02% (95% CI, 3.48-8.57), 15.99% (95% CI, 10.77-21.22), and 17.79% (95% CI, 9.14-26.43) higher compared with those without AKI, respectively. • AKI at acute phase of COVID-19 was closely related to decline status of kidney function at nearly one-year after symptom onset • https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(22)00006-8/fulltext
NEJM - 1/26/2022 - homologous and heterologous COVID-19 Booster vaccinations	• Of the 458 participants who were enrolled in the trial, o 154 received mRNA-1273, o 150 received Ad26.COV2.S, and o 153 received BNT162b2 as booster vaccines; • 1 participant did not receive the assigned vaccine. • Reactogenicity was similar to that reported for the primary series. More than half the recipients reported having injection-site pain, malaise, headache, or myalgia. • For all combinations, antibody neutralizing titers against a SARS-CoV-2 D614G pseudovirus increased by a factor of 4 to 73, and binding titers increased by a factor of 5 to 55. • Homologous boosters increased neutralizing antibody titers by a factor of 4 to 20, whereas heterologous boosters increased titers by a factor of 6 to 73. Spike-specific • T-cell responses increased in all but the homologous Ad26.COV2.S-boosted subgroup. CD8+ T-cell levels were more durable in the Ad26.COV2.S-primed recipients, and heterologous boosting with the Ad26.COV2.S vaccine substantially increased spike-specific CD8+ T cells in the mRNA vaccine recipients • Homologous and heterologous booster vaccines had an acceptable safety profile and were immunogenic in adults • https://www.nejm.org/doi/full/10.1056/NEJMoa2116414?query=featured_coronavirus
NEJM - 1/26/2022 - Myocarditis in Israeli adolescents after Pfizer vaccine	• Here, we report the incidence of hospitalization for myocarditis between June 2 and October 20, 2021, among adolescents in this age group within 21 days after receipt of the first vaccine dose and within 30 days after receipt of the second dose • 404,407 adolescents (195,579 of whom were male) received the first dose of vaccine, 326,463 adolescents (157,153 of whom were male) received the second dose, and 18 cases of myocarditis leading to hospitalization were reported o Two cases of myocarditis were excluded from the study owing to reasonable alternative diagnoses. o Of the remaining 16 cases, 1 occurred in an unvaccinated adolescent and o 15 occurred in vaccinated adolescents — ▪ 1 case within 21 days after receipt of the first vaccine dose, ▪ 12 cases within 1 week after receipt of the second dose (Figure 1), and ▪ 2 later cases (1 each at 46 days and 70 days after receipt of the second dose); the 2 later cases were considered by the investigators as unlikely to be related to the vaccine • All the cases (13) were clinically mild, involving a mean duration of hospitalization of 3.1 days (range, 1 to 6) and no readmissions during 30 days of follow-up

	• The risk estimates of myocarditis among male recipients in the 21 days after the first and second doses were
	  o 0.56 cases per 100,000 after the first dose and
	  o 8.09 cases per 100,000 after the second dose
	• the risk estimates among female recipients were
	  o 0 cases per 100,000 after the first dose and
	  o 0.69 cases per 100,000 after the second dose
	• In conclusion, the incidence of myocarditis leading to hospitalization among adolescents who received the second dose of the BNT162b2 vaccine was low but was higher than among recipients of the first vaccine dose and proportionately numerically higher than in recent estimates of incidence among unvaccinated persons
	• https://www.nejm.org/doi/full/10.1056/NEJMc2116999?query=featured_coronavirus

NEJM - 1/26/2022 - Lung transplant and COVID	• We therefore analyzed lung transplantations performed between August 1, 2020, and September 30, 2021, and reported in the United Network for Organ Sharing (UNOS) registry, which collates transplantation data from all patients in participating regions in the United States
	• Of 3039 lung transplantations,
	  o 214 (7.0%) were performed for Covid-19–related respiratory failure,
	  ▪ including 140 (4.6%) for acute respiratory distress syndrome and
	  ▪ 74 (2.4%) for pulmonary fibrosis.
	• The median number of lung transplantations performed for Covid-19–related respiratory failure per center was 2.5 (range, 1 to 25).
	• Of the 214 lung transplantations, 197 (92.1%) were bilateral lung transplantations (including 2 heart–lung transplantations and 5 lung–kidney transplantations), and
	• 17 (7.9%) were single-lung transplantations (including 1 lung–kidney transplantation)
	• the median age was 52 years (interquartile range, 43 to 58),
	  o 38 (20.8%) were female, and
	  o 67 (36.6%) were Hispanic
	• The 30-day mortality was 2.2% (4 deaths), and 3-month survival was 95.6%
	• Because the 3-month survival among these patients approached that among patients who underwent lung transplantation for reasons other than Covid-19, we believe that lung transplantation may be an acceptable treatment for selected patients with irreversible respiratory failure due to Covid-19
	• https://www.nejm.org/doi/full/10.1056/NEJMc2117024?query=featured_coronavirus

Cell - 1/25/2022 - Immuno-proteomic profile in airways of pts with COVID	• Some patients hospitalized with acute COVID-19 suffer respiratory symptoms that persist for many months. We delineated the immune-proteomic landscape in the airway and peripheral blood of healthy controls and post-COVID-19 patients 3 to 6 months after hospital discharge. Post-COVID-19 patients showed abnormal airway (but not plasma) proteomes, with elevated concentration of proteins associated with apoptosis, tissue repair and epithelial injury versus healthy individuals. Increased numbers of cytotoxic lymphocytes were observed in individuals with greater airway dysfunction, while increased B cell numbers and altered monocyte subsets were associated with more widespread lung abnormalities. 1 year follow-

respiratory disease	up of some post-COVID-19 patients indicated that these abnormalities resolved over time. • In summary, COVID-19 causes a prolonged change to the airway immune landscape in those with persistent lung disease, with evidence of cell death and tissue repair linked to ongoing activation of cytotoxic T cells • https://www.cell.com/immunity/fulltext/S1074-7613(22)00046-2
CID - 1/12/2022 - SARS-CoV2 environmental contamination is uncommon	• We assessed environmental contamination of inpatient rooms housing COVID-19 patients in a dedicated COVID-19 unit. • Contamination with SARS-CoV-2 was found on 5.5% (19/347) of surfaces via RT-PCR • and 0.3% (1/347) of surfaces via cell culture. • Environmental contamination is uncommon in hospitals rooms; RNA presence is not a specific indicator of infectious virus • https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciac023/6505265

Cell - 1/24/2022 - Multiple early factors anticipate post-acute COVID (LONG COVID)	• Post-acute sequelae of COVID-19 (PASC) represent an emerging global crisis. However, quantifiable risk-factors for PASC and their biological associations are poorly resolved. We executed a deep multi-omic, longitudinal investigation of 309 COVID-19 patients from initial diagnosis to convalescence (2-3 months later), integrated with clinical data, and patient-reported symptoms.
	• We resolved four PASC-anticipating risk factors at the time of initial COVID-19 diagnosis:
	  ○ type 2 diabetes,
	  ○ SARS-CoV-2 RNAemia,
	  ○ Epstein-Barr virus viremia,
	  ○ and specific autoantibodies.
	• In patients with gastrointestinal PASC, SARS-CoV-2-specific and CMV-specific $CD8^+$ T cells exhibited unique dynamics during recovery from COVID-19. Analysis of symptom-associated immunological signatures revealed coordinated immunity polarization into four endotypes exhibiting divergent acute severity and PASC. We find that immunological associations between PASC factors diminish over time leading to distinct convalescent immune states. Detectability of most PASC factors at COVID-19 diagnosis emphasizes the importance of early disease measurements for understanding emergent chronic conditions and suggests PASC treatment strategies
	• https://www.cell.com/cell/fulltext/S0092-8674(22)00072-1

OFID - 1/19/2022 - Outpatient therapies for COVID - how do we chose?	• assuming a baseline hospitalization risk of 5% and compared the cost per hospitalization prevented with the estimate for an average Medicare COVID-19 hospitalization ($21752)
	• At a 5% risk of hospitalization the estimated NNT was
	  ○ 80 for fluvoxamine,
	  ○ 91 for colchicine,
	  ○ 72 for inhaled corticosteroids,
	  ○ 24 for nirmatrelvir/ritonavir (paxlovid)
	  ○ 50 for molnupiravir,
	  ○ 28 for remdesivir,

	○ 25 for sotrovimab, ○ 29 for casirivimab/imdevimab (before Omicron), and ○ 29 for bamlanivimab/etesevimab (before Omicron). • For drug cost per hospitalization prevented colchicine, fluvoxamine, inhaled corticosteroids, and nirmatrelvir/ritonavir were below the Medicare estimated hospitalization cost. • Given differences in efficacy, toxicity, cost and administration complexities, this assessment serves as one means to frame treatment selection • https://academic.oup.com/ofid/advance-article/doi/10.1093/ofid/ofac008/6511388?searchresult=1