Dr. Leo's COVID Corner
October 2022

Please see Dr. Leo's most recent literature research. **In addition, Dr. Leo will be expanding his literature research to include other clinically related topics. Please feel free to send him any articles that you would like to see included to lgiriohe@umm.edu**

1. Cardiovascular screening led to no significant between-group differences in safety outcomes
2. Some metabolic disorders and higher fatigue scores were noted in young adults with long COVID
3. Among patients 65 years of age or older, the rates of hospitalization and death due to Covid-19 were significantly lower after Paxlovid use
4. Possible hypothesis about long COVID being caused by small clots after acute illness.
5. Regular physical activity seems to be related to a lower likelihood of adverse COVID-19 outcomes.
6. SARS-CoV-2 has evolved and mutated continuously leading to lower incubation periods with each sub variant; down to 3.4 days of incubation period for omicron
7. Bloodstream infections occur at an elevated rate among PWH (patients with HIV) with high reoccurrence rates and associated morbidity and mortality
8. An entirely oral, highly bioavailable treatment, including rifampin, may be as effective as parenteral treatment in selected patients with vertebral osteo.
9. A prospective MRI study of 346 people with mild COVID, and controls, demonstrated myocardial inflammation at 3 months, worse with symptoms, and edema at ~1 year on 57% of participants
10. Cure rates for pulmonary MAC range from 39% - 84% after an average of 13 months of therapy.
11. Tele ID vs in-person ID consults had similar outcomes for length of hospital stay, transfers, readmission, and mortality

NEJM - 8/27/22 - 5 year outcomes of the Danish CARDIOVASCULAR SCREENING TRIAL	• A total of 46,611 participants underwent randomization. After exclusion of 85 men who had died or emigrated before being invited to undergo screening, there were 16,736 men in the invited group and 29,790 men in the control group; 10,471 of the men in the invited group underwent screening (62.6%). In intention-to-treat analyses, after a median follow-up of 5.6 years, 2106 men (12.6%) in the invited group and 3915 men (13.1%) in the control group had died (hazard ratio, 0.95; 95% confidence interval [CI], 0.90 to 1.00; **P=0.06).** The hazard ratio for stroke in the invited group, as compared with the control group, was 0.93 (95% CI, 0.86 to 0.99); for myocardial infarction, 0.91 (95% CI, 0.81 to 1.03); for

	aortic dissection, 0.95 (95% CI, 0.61 to 1.49); and for aortic rupture, 0.81 (95% CI, 0.49 to 1.35). • There were no significant between-group differences in safety outcomes • https://www.nejm.org/doi/full/10.1056/NEJMoa2208681

Lancet - 8/25/2021 - long COVID in young adults	• Between May 20, 2021, and Nov 26, 2021, we enrolled 501 participants. 29 (6%) of 501 were female and 464 (93%) were male, and the median age was 21 years (IQR 21–23). Eight (2%) of 501 had incomplete data and were not included into the study groups. 177 participants had previous COVID-19 that was more than 180 days (mean 340 days) since diagnosis (ie, the non-recent COVID-19 group) compared with 251 serologically negative individuals (ie, the control group). We included 19 participants in the recent COVID-19 group and 46 in the asymptomatic infection group.
	• We found a significant trend towards metabolic disorders in participants of the non-recent COVID-19 group compared with those in the control group:
	  ○ higher BMI (median 24·0 kg/m^2 [IQR 22·0–25·8] *vs* 23·2 kg/m^2 [27·1–25·0]; p=0·035),
	  ○ lower aerobic threshold (39% [36–43] *vs* 41% [37–46]; p=0·012), and
	  ○ higher blood cholesterol (4·2 µM [3·7–4·7] *vs* 3·9 µM [3·5–4·5]; p<0·0001) and LDL concentrations (2·4 µM [1·9–2·9] *vs* 2·2 µM [1·7–2·7]; p=0·001).
	• The only significant psychosocial difference was found in the results of the Chalder Fatigue scale with the non-recent COVID-19 group reporting higher fatigue scores than the control group (median 12 points [IQR 11–15] *vs* 11 [9–14]; p=0·027). No significant differences in other psychosocial questionnaire scores, ophthalmological outcomes, and sperm quality or motility were reported between the control group and non-recent COVID-19 group
	• https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00449-2/fulltext

NEJM - 8/25/2022 - Paxlovid use outcomes during omicron surge	• A total of 109,254 patients met the eligibility criteria, of whom 3902 (4%) received nirmatrelvir during the study period. Among patients 65 years of age or older, the rate of hospitalization due to Covid-19 was 14.7 cases per 100,000 person-days among treated patients as compared with 58.9 cases per 100,000 person-days among untreated patients (adjusted hazard ratio, 0.27; 95% confidence interval [CI], 0.15 to 0.49). The adjusted hazard ratio for death due to Covid-19 was 0.21 (95% CI, 0.05 to 0.82). Among patients 40 to

	64 years of age, the rate of hospitalization due to Covid-19 was 15.2 cases per 100,000 person-days among treated patients and 15.8 cases per 100,000 person-days among untreated patients (adjusted hazard ratio, 0.74; 95% CI, 0.35 to 1.58). The adjusted hazard ratio for death due to Covid-19 was 1.32 (95% CI, 0.16 to 10.75). • https://www.nejm.org/doi/full/10.1056/NEJMoa2204919?query=featured_home
Nature - 8/24/2022 - could tiny blood clots be causing long COVID?	• "...Researchers are baffled by long COVID: hundreds of studies have tried to unpick its mechanism, without much success. Now some scientists, and an increasing number of people with the condition, have been lining up behind the as-yet-unproven hypothesis that tiny, persistent clots might be constricting blood flow to vital organs, resulting in the bizarre constellation of symptoms that people experience...But many hematologists and COVID-19 researchers worry that enthusiasm for the clot hypothesis has outpaced the data.." • https://www.nature.com/articles/d41586-022-02286-7
BMJ - 8/2022 - physical activity and risk of infection and mortality from COVID	• Sixteen studies were included (n=1 853 610). • Overall, those who engaged in regular physical activity had a lower risk of infection (RR=0.89; 95% CI 0.84 to 0.95; I^2=0%), hospitalization (RR=0.64; 95% CI 0.54 to 0.76; I^2=48.01%), severe COVID-19 illness (RR=0.66; 95% CI 0.58 to 0.77; I^2=50.93%) and COVID-19-related death (RR=0.57; 95% CI 0.46 to 0.71; I^2=26.63%) as compared with their inactive peers. The results indicated a non-linear dose–response relationship between physical activity presented in metabolic equivalent of task (MET)-min per week and severe COVID-19 illness and death (p for non-linearity <0.001) with a flattening of the dose–response curve at around 500 MET-min per week. • https://bjsm.bmj.com/content/early/2022/07/07/bjsports-2022-105733

JAMA - 8/22/2022 - incubation period of different COVID strains	• A total of 142 studies with 8112 patients were included. The
	• pooled incubation period was 6.57 days (95% CI, 6.26-6.88) and ranged from 1.80 to 18.87 days. The incubation period of COVID-19 caused by the Alpha, Beta, Delta, and Omicron variants were reported in 1 study (with 6374 patients), 1 study (10 patients), 6 studies (2368 patients) and 5 studies (829 patients), respectively.
	  ○ The mean incubation period of COVID-19 was 5.00 days (95% CI, 4.94-5.06 days) for cases caused by the Alpha variant,
	  ○ 4.50 days (95% CI, 1.83-7.17 days) for the Beta variant,

	○ 4.41 days (95% CI, 3.76-5.05 days) for the Delta variant, and ○ 3.42 days (95% CI, 2.88-3.96 days) for the Omicron variant. The mean incubation was 7.43 days (95% CI, 5.75-9.11 days) among older patients (ie, aged over 60 years old), 8.82 days (95% CI, 8.19-9.45 days) among infected children (ages 18 years or younger), 6.99 days (95% CI, 6.07-7.92 days) among patients with non-severe illness, and 6.69 days (95% CI, 4.53-8.85 days) among patients with severe illness. ○ https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2795489
OFID - 8/2022 - risk factors and outcomes of BSI in PWH	• Among 2895 PWH, 396 BSI episodes occurred in 228 (8%) PWH. There were 278 (72%) Gram-positive and 109 (28%) Gram-negative BSI. • People with human immunodeficiency virus with lower CD4 nadirs, higher Charlson comorbidity indices, and hepatitis C virus were at highest risk for BSI. • Long-term all-cause mortality was greater in those experiencing BSI (HR, 5.25; 95% CI, 4.21–6.55). • CD4 count <200 cells/mm^3 measured closest to the time of BSI was associated with 1-year mortality after BSI (aOR, 3.88; 95% CI, 1.78–8.46). Repeat episodes (42%) and polymicrobial BSI (19%) were common • Bloodstream infections continue to occur at an elevated rate among PWH with high reoccurrence rates and associated morbidity and mortality. • https://doi.org/10.1093/ofid/ofac318
OFID - Oral vs standard antimicrobial treatment for native vertebral osteomyelitis	• The study population included 249 patients, and 33 (13.3%) experienced clinical failure; the OT group consisted of 54 patients (21.7%). Multivariate regression analysis of the whole population selected Charlson comorbidity index (adjusted odds ratio [aOR], 1.291; 95% confidence interval [CI], 1.114–1.497; *P* = .001) and MDRO etiology (aOR, 3.301; 95% CI, 1.368–7.964; *P* = .008) as independent factors for clinical failure. • Among patients affected by a non-MDRO NVO, OT was not associated with an increased risk of clinical failure (aOR, 0.487; 95% CI, .133–1.782; *P* = .271), even after adjustment for the propensity score of receiving OT. • In the subgroup of patients with staphylococcal or unknown etiology, NVO rifampin was independently associated with favorable outcome (aOR, 0.315; 95% CI, .105–.949; *P* = .040). • https://doi.org/10.1093/ofid/ofac366

Nature Medicine - 9/5/22 - Long-term cardiac pathology after mild COVID	• Cardiac symptoms are increasingly recognized as late complications of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in previously well individuals with mild initial illness, but the underlying pathophysiology leading to long-term cardiac symptoms remains unclear. In this study, we conducted serial cardiac assessments in a selected population of individuals with Coronavirus Disease 2019 (COVID-19) with no previous cardiac disease or notable comorbidities by measuring blood biomarkers of heart injury or dysfunction and by performing magnetic resonance imaging. Baseline measurements from 346 individuals with COVID-19 (52% females) were obtained at a median of 109 days (interquartile range (IQR), 77–177 days) after infection, when 73% of participants reported cardiac symptoms, such as exertional dyspnea (62%), palpitations (28%), atypical chest pain (27%) and syncope (3%). Symptomatic individuals had higher heart rates and higher imaging values or contrast agent accumulation, denoting inflammatory cardiac involvement, compared to asymptomatic individuals. Structural heart disease or high levels of biomarkers of cardiac injury or dysfunction were rare in symptomatic individuals.
	• At follow-up (329 days (IQR, 274–383 days) after infection),
	  ○ 57% of participants had persistent cardiac symptoms.
	  ○ Diffuse myocardial edema was more pronounced in participants who remained symptomatic at follow-up as compared to those who improved. Female gender and diffuse myocardial involvement on baseline imaging independently predicted the presence of cardiac symptoms at follow-up. Ongoing inflammatory cardiac involvement may, at least in part, explain the lingering cardiac symptoms in previously well individuals with mild initial COVID-19 illness
	• https://www.nature.com/articles/s41591-022-02000-0

OFID - 8/2022 0 clinical features and treatment outcomes for pulmonary MAC	• Organisms belonging to the *Mycobacterium avium* complex (MAC) are the most common cause of PNTM [6, 7]. The diagnostic criteria for pulmonary MAC (PMAC) include a combination of clinical, radiologic, and microbiologic criteria [3, 8]. Treatment of patients with PMAC requires the use of multiple antibiotics for several months • curates ranged from 39% to 84% with 13 month of treatment (+/- 10 months) • https://doi.org/10.1093/ofid/ofac375
OFID - 8/2022 - in-person vs	• We compared outcomes at 3 community hospitals before and after switching from in-person to a Tele-ID group from an academic

Tele ID outcomes	medical center. Compared to in-person, Tele-ID received significantly more consultations with similar outcomes for length of hospital stay, transfers, readmission, and mortality. Tele-ID is a suitable alternative for community settings. • https://doi.org/10.1093/ofid/ofac410