The Daily COVID-19 Literature Surveillance Summary

November 17, 2020

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COVID-19 Daily Literature Surveillance

COVID19LST

Bringing you real time, distilled information for guiding best practices during the COVID-19 pandemic

LEVEL OF EVIDENCE

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

Question	Step 1 (Level 1*)	Step 2 (Level 2*)	Step 3 (Level 3*)	Step 4 (Level 4*)	Step 5 (Level 5)
How common is the problem?	Local and current random sample surveys (or censuses)	Systematic review of surveys that allow matching to local circumstances**	Local non-random sample**	Case-series**	n/a
Is this diagnostic or monitoring test accurate? (Diagnosis)	Systematic review of cross sectional studies with consistently applied reference standard and blinding	Individual cross sectional studies with consistently applied reference standard and blinding	Non-consecutive studies, or studies without consistently applied reference standards**	Case-control studies, or "poor or non-independent reference standard**	Mechanism-based reasoning
What will happen if we do not add a therapy? (Prognosis)	Systematic review of inception cohort studies	Inception cohort studies	Cohort study or control arm of randomized trial*	Case-series or case-control studies, or poor quality prognostic cohort study**	n/a
Does this intervention help? (Treatment Benefits)	Systematic review of randomized trials or *n*-of-1 trials	Randomized trial or observational study with dramatic effect	Non-randomized controlled cohort/follow-up study**	Case-series, case-control studies, or historically controlled studies**	Mechanism-based reasoning
What are the COMMON harms? (Treatment Harms)	Systematic review of randomized trials, systematic review of nested case-control studies, *n*-of-1 trial with the patient you are raising the question about, or observational study with dramatic effect	Individual randomized trial or (exceptionally) observational study with dramatic effect	Non-randomized controlled cohort/follow-up study (post-marketing surveillance) provided there are sufficient numbers to rule out a common harm. (For long-term harms the duration of follow-up must be sufficient.)**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning
What are the RARE harms? (Treatment Harms)	Systematic review of randomized trials or *n*-of-1 trial	Randomized trial or (exceptionally) observational study with dramatic effect			
Is this (early detection) test worthwhile? (Screening)	Systematic review of randomized trials	Randomized trial	Non -randomized controlled cohort/follow-up study**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning

*** Level may be graded down on the basis of study quality, imprecision, indirectness (study PICO does not match questions PICO), because of inconsistency between studies, or because the absolute effect size is very small; Level may be graded up if there is a large or very large effect size.**

**** As always, a systematic review is generally better than an individual study.**

How to cite the Levels of Evidence Table

OCEBM Levels of Evidence Working Group*. "The Oxford 2011 Levels of Evidence".

Oxford Centre for Evidence-Based Medicine. http://www.cebm.net/index.aspx?o=5653

** OCEBM Table of Evidence Working Group = Jeremy Howick, Iain Chalmers (James Lind Library), Paul Glasziou, Trish Greenhalgh, Carl Heneghan, Alessandro Liberati, Ivan Moschetti, Bob Phillips, Hazel Thornton, Olive Goddard and Mary Hodgkinson*

EXECUTIVE SUMMARY

Epidemiology

- Persistent fatigue following SARS-CoV-2 infection is common and independent of severity of initial infection according to one study. Immunologists and infectious disease specialists at St. James's Hospital in Dublin, Ireland examined prevalence of post-COVID-19 fatigue in 128 patients who had recovered from COVID-19 using the Chalder Fatigue Score (CFQ-11). They found 52.3% (67/128) of participants met the criteria for fatigue at a median of 10 weeks following initial symptoms and fatigue was associated with female gender and preexisting depression/anxiety, but data showed no association between total CFQ-11 score and age, disease course, or laboratory measures of inflammation. These results suggest post-COVID-19 fatigue may be more prevalent than previously understood, and authors advocate for further research among those with previous SARS-CoV-2 infection.

- An Outbreak of COVID-19 on an Aircraft Carrier Spreads Fast. Public Health experts affiliated with the U.S. Navy conducted an epidemiologic investigation of the COVID-19 outbreak on the U.S.S. Theodore Roosevelt. Results showed that of the 26.6% of crew (1271) who tested positive for SARS-CoV-2 via RT-PCR, nearly half were asymptomatic, more than 30% of symptomatic cases initially reported having cough and headache, and among 1331 suspected or confirmed cases, 23 were hospitalized, 4 received intensive care, and 1 died. The authors suggest that the confined and densely populated areas, as well as the relatively high number of asymptomatic cases, may have contributed to the fast spread of the COVID-19 cases on the Aircraft Carrier.

- Ultrasound Imaging Findings of Acute Testicular Infection in Patients With COVID-19 were explored by a team from the Department of Ultrasound Imaging at Wuhan University Renmin Hospital. It was a retrospective study of 142 male patients hospitalized with COVID-19 who underwent bedside scrotal ultrasound. They found 32 patients (22.5%) presented with findings of acute testicular inflammation: 10 with acute orchitis, 7 with acute epididymitis, 15 with epididymo-orchitis. There was a higher frequency in men >80 years-old (p=0.003) and in the severe COVID-19 group (p=0.002). Authors suggest SARS-CoV-2 may infect the testicles and/or epididymis and recommend clinicians be aware of these genitourinary manifestations.

Transmission & Prevention

- United Kingdom's definitions of vitamin D sufficiency and recommended supplement dose are set too low. UK physicians in Infectious Disease, Endocrinology, Respiratory, and Gerontology conclude that the original threshold goal for vitamin D sufficiency, 25nmol/L, is too low and not evidence-based, suggesting that it should instead be set at 50 nmol/L and recommend supplementation with 800 IU per day. They speculate vitamin D deficiency as a risk factor for COVID-19 and advocate for an increase in the recommended Vitamin D supplement dose.

Silver Linings

- What was the impact of non-COVID-19 deaths after social distancing in Norway? American public health experts analyzed the effect of social distancing in Norway on non-COVID-19 deaths during March 16-May 18, 2020 using the Human Mortality Database's Short-term Mortality Fluctuations data series. They compared non-COVID-19 deaths in Norway during the nine-week period to expected deaths, based on historical Norwegian data and non-COVID-19 deaths in Sweden, by using the Box-Jenkins time series method and found 430 fewer non-COVID-19 deaths in Norway than expected. Authors suggest social distancing carries mortality benefits beyond COVID-19 prevention and recommend in-depth analysis of such measures on health indicators when considering risks and benefits of public health policies.

TABLE OF CONTENTS

PERSISTENT FATIGUE FOLLOWING SARS-COV-2 INFECTION IS COMMON AND INDEPENDENT OF SEVERITY OF INITIAL INFECTION

Townsend L, Dyer AH, Jones K, Dunne J, Mooney A, Gaffney F, O'Connor L, Leavy D, O'Brien K, Dowds J, Sugrue JA, Hopkins D, Martin-Loeches I, Ni Cheallaigh C, Nadarajan P, McLaughlin AM, Bourke NM, Bergin C, O'Farrelly C, Bannan C, Conlon N.. PLoS One. 2020 Nov 9;15(11):e0240784. doi: 10.1371/journal.pone.0240784. eCollection 2020.
Level of Evidence: 3 - Local non-random sample

BLUF

This prospective survey study by immunologists and infectious disease specialists at St. James's Hospital in Dublin, Ireland examined prevalence of post-COVID-19 fatigue in patients who had recovered from COVID-19 (n=128) using the Chalder Fatigue Score (CFQ-11). They found 52.3% (67/128) of participants met the criteria for fatigue at a median of 10 weeks following initial symptoms (Table 1) and fatigue was associated with female gender and preexisting depression/anxiety, but data showed no association between total CFQ-11 score and age, disease course, or laboratory measures of inflammation. These results suggest post-COVID-19 fatigue may be more prevalent than previously understood, and authors advocate for further research among those with previous SARS-CoV-2 infection.

ABSTRACT

Fatigue is a common symptom in those presenting with symptomatic COVID-19 infection. However, it is unknown if COVID-19 results in persistent fatigue in those recovered from acute infection. We examined the prevalence of fatigue in individuals recovered from the acute phase of COVID-19 illness using the Chalder Fatigue Score (CFQ-11). We further examined potential predictors of fatigue following COVID-19 infection, evaluating indicators of COVID-19 severity, markers of peripheral immune activation and circulating pro-inflammatory cytokines. Of 128 participants (49.5 +- 15 years; 54% female), more than half reported persistent fatigue (67/128; 52.3%) at median of 10 weeks after initial COVID-19 symptoms. There was no association between COVID-19 severity (need for inpatient admission, supplemental oxygen or critical care) and fatigue following COVID-19. Additionally, there was no association between routine laboratory markers of inflammation and cell turnover (leukocyte, neutrophil or lymphocyte counts, neutrophil-to-lymphocyte ratio, lactate dehydrogenase, C-reactive protein) or pro-inflammatory molecules (IL-6 or sCD25) and fatigue post COVID-19. Female gender and those with a pre-existing diagnosis of depression/anxiety were over-represented in those with fatigue. Our findings demonstrate a significant burden of post-viral fatigue in individuals with previous SARS-CoV-2 infection after the acute phase of COVID-19 illness. This study highlights the importance of assessing those recovering from COVID-19 for symptoms of severe fatigue, irrespective of severity of initial illness, and may identify a group worthy of further study and early intervention.

FIGURES

Characteristic	Overall (N = 128)	Non-Fatigued (N = 61)	Fatigued (N = 67)	Statistic
Age (mean ± SD)	49.5 ± 15	49.7 ± 16	49.3 ± 14.3	t = 0.16, p = 0.44
Gender, female (N, %)	69 (53.9%)	24 (39.3%)	45 (67.2%)	χ^2 = 9.95, p = 0.002
Body Mass Index, kg/m^2, (mean ± SD)	28.7 ± 5.3	28.6 ± 4.9	28.8 ± 5.8	t = -0.09, p = 0.54
Clinical Frailty Scale (median, IQR)	2 (1–2)	2 (1–2)	1 (1–2)	z = -0.15, p = 0.88
Total Number of Medical Comorbidities (median, IQR)	1 (0–2)	1 (0–3)	1 (0–2)	z = -1.40, p = 0.16
Total Number of Regular Medications (median, IQR)	1 (0–4)	1 (0–4)	0 (0–4)	z = -1.35, p = 0.18
History of Anxiety/Depression	10 (7.8%)	1 (1.6%)	9 (13.4%)	χ^2 = 5.18, p = 0.02
Interval from COVID-19 Symptoms to Fatigue Assessment				
<56 days (<8 weeks)	26 (20.3%)	9 (14.8%)	17 (25.4%)	
56–69 days (8–10 weeks)	31 (24.2%)	20 (32.8%)	11 (16.4%)	
69–83 days (10–12 weeks)	33 (25.8%)	16 (26.2%)	17 (25.4%)	
>84 days (12 weeks)	38 (29.7%)	16 (26.2%)	22 (32.8%)	χ^2 = 5.8, p = 0.12
Total CFQ-11 Score (mean ± SD) [Liekert Scoring]	15.8 ± 5.9	11.2 ± 3.2	20.0 ± 4.4	t = -12.8, p<0.001
Physical Fatigue (mean ± SD) [CFQ-11 items 1–7]	11.38 ± 4.22	7.72 ± 1.87	14.54± 2.94	z = -9.52, p<0.001
Psychological Fatigue (mean ± SD) [CFQ-11 items 8–11]	4.72 ± 1.99	3.79 ± 0.97	5.52 ± 2.29	z = -5.91, p<0.001
Total CFQ-11 Score (mean ± SD) [Bimodal Scoring]	4.2 ± 3.5	1 ± 1.2	7 ± 2.2	t = -18.6, p<0.001

SD: Standard Deviation, N: Number; IQR: Interquartile Range. CFQ-11: Chalder Fatigue Scale. Data are presented as means with standard deviations or medians with interquartile ranges as appropriate. Proportions are expressed both as numbers and percentages. Statistical analysis was carried out using t-tests, Wilcoxon rank sum tests and chi-square tests as appropriate in order to compare differences in those without fatigue and those non-fatigued/with non-severe fatigue as per the CFQ-11 "caseness" definition for severe fatigue.

Table 1. Baseline characteristics of study participants by fatigue case status ("caseness").

AN OUTBREAK OF COVID-19 ON AN AIRCRAFT CARRIER

Kasper MR, Geibe JR, Sears CL, Riegodedios AJ, Luse T, Von Thun AM, McGinnis MB, Olson N, Houskamp D, Fenequito R, Burgess TH, Armstrong AW, DeLong G, Hawkins RJ, Gillingham BL.. N Engl J Med. 2020 Nov 11. doi: 10.1056/NEJMoa2019375. Online ahead of print.
Level of Evidence: 4 - Local non-random sample

BLUF

Public Health experts affiliated with the U.S. Navy conducted an epidemiologic investigation of the COVID-19 outbreak on the U.S.S. Theodore Roosevelt. Results showed that of the 26.6% of crew (n= 1271) who tested positive for SARS-CoV-2 via RT-PCR nearly half were asymptomatic, more than 30% of symptomatic cases initially reported having cough and headache, and among 1331 suspected or confirmed cases, 23 were hospitalized, 4 received intensive care, and 1 died. The authors suggest that the confined and densely populated areas, as well as the relatively high number of asymptomatic cases, may have contributed to the fast spread of the COVID-19 cases on the Aircraft Carrier.

ABSTRACT

BACKGROUND: An outbreak of coronavirus disease 2019 (Covid-19) occurred on the U.S.S. Theodore Roosevelt, a nuclear-powered aircraft carrier with a crew of 4779 personnel. METHODS: We obtained clinical and demographic data for all crew members, including results of testing by real-time reverse-transcriptase polymerase chain reaction (rRT-PCR). All crew members were followed up for a minimum of 10 weeks, regardless of test results or the absence of symptoms. RESULTS: The crew was predominantly young (mean age, 27 years) and was in general good health, meeting U.S. Navy standards for sea duty. Over the course of the outbreak, 1271 crew members (26.6% of the crew) tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection by rRT-PCR testing, and more than 1000 infections were identified within 5 weeks after the first laboratory-confirmed infection. An additional 60 crew members had suspected Covid-19 (i.e., illness that met Council of State and Territorial Epidemiologists clinical criteria for Covid-19 without a positive test result). Among the crew members with laboratory-confirmed infection, 76.9% (978 of 1271) had no symptoms at the time that they tested positive and 55.0% had symptoms develop at any time during the clinical course. Among the 1331 crew members with suspected or confirmed Covid-19, 23 (1.7%) were hospitalized, 4 (0.3%) received intensive care, and 1 died. Crew members who worked in confined spaces appeared more likely to become infected. CONCLUSIONS: SARS-CoV-2 spread quickly among the crew of the U.S.S. Theodore Roosevelt. Transmission was facilitated by close-quarters conditions and by asymptomatic and presymptomatic infected crew members. Nearly half of those who tested positive for the virus never had symptoms.

FIGURES

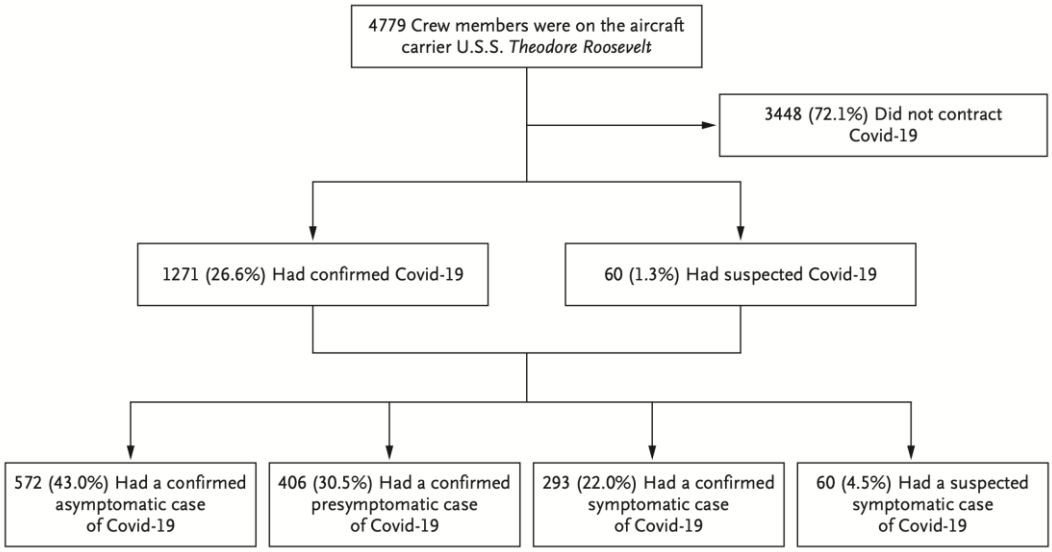

Figure 1. Distribution of Personnel According to Case Status.
A confirmed case of coronavirus disease 2019 (Covid-19) was defined as one in which a nasopharyngeal swab specimen was positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by real-time reverse-transcriptase polymerase chain reaction. A suspected case was defined as one that met Council of State and Territorial Epidemiologists clinical criteria for Covid-19 without a positive test result. Confirmed cases were further classified as symptomatic (with symptom onset before the first positive laboratory test), presymptomatic (with the first positive laboratory test before subsequent symptom onset), and asymptomatic (positive laboratory test but clinical criteria never met).

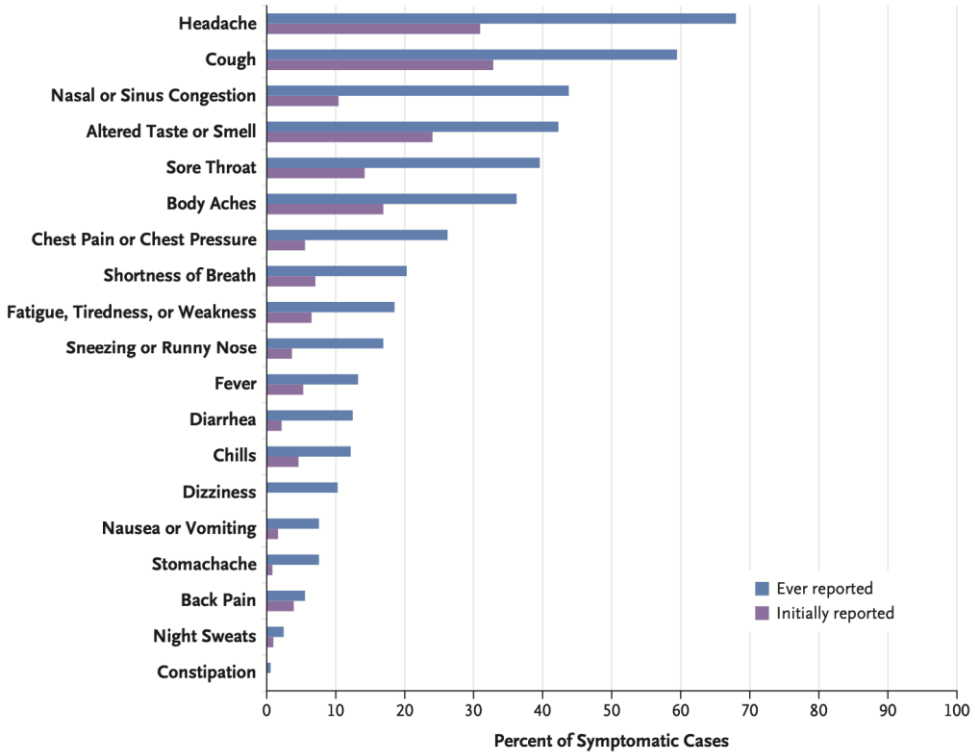

Figure 3. Distribution of Symptomatic Confirmed or Suspected Covid-19 Cases According to Symptoms.

SYMPTOMS AND CLINICAL PRESENTATION

ADULTS

RISK FACTORS OF LIVER INJURY IN PATIENTS WITH CORONAVIRUS DISEASE 2019 IN JIANGSU, CHINA: A RETROSPECTIVE, MULTI-CENTER STUDY

Wang J, Zhu L, Xue L, Liu L, Yan X, Yan X, Huang S, Zhang B, Xu T, Li C, Ji F, Ming F, Zhao Y, Cheng J, Shao H, Chen K, Zhao XA, Sang D, Zhao H, Guan X, Chen X, Chen Y, Liu J, Huang R, Zhu C, Wu C.. J Med Virol. 2020 Nov 11. doi: 10.1002/jmv.26663. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

This retrospective multi-center study conducted by Infectious disease physicians in Jiangsu, China found that patients without prior history of chronic hepatic disease (n=228) who contracted COVID-19 developed mild to moderate liver injury. Findings show that the populations most at risk of developing hepatic disease with COVID-19 were those above the age of 50 (p=0.041), the male sex (p=0.003), and those who were using the drug Lopinavir-Ritonavir (p=0.016). The authors suggest further studies explore the development of hepatic disease in patients with COVID-19.

ABSTRACT

We aimed to describe liver injury and identify the risk factors of liver injury in COVID-19 patients without chronic liver diseases (CLD). The clinical data of 228 confirmed COVID-19 patients without CLD were retrospectively collected from ten hospitals in Jiangsu, China. Sixty-seven (29.4%) of 228 patients without CLD showed abnormal liver function on admission, including increased alanine aminotransferase (ALT, 25 [11.0%]) U/L, aspartate aminotransferase (AST, 30 [13.2%]) U/L, gamma-glutamyl transferase (GGT, 28 [12.4%]) U/L, total bilirubin (Tbil, 16 [7.0%]) mumol/L, and alkaline phosphatase (ALP, 10 [4.5%]) U/L. During hospitalization, 129 (56.3%) of 228 patients showed abnormal liver function, including elevated ALT (84 [36.8%]), AST (58 [25.4%]), GGT (67 [29.5%]) and Tbil (59 [25.9%]). Age over 50 years (odds ratio [OR] 2.086, 95% confidence interval [CI] 1.030-4.225, P=0.041), male sex (OR 2.737, 95%CI 1.418-5.284, P=0.003), and lopinavir-ritonavir (OR

2.504, 95%CI 1.187-5.283, P=0.016) were associated with higher risk of liver function abnormality, while the atomized inhalation of interferon alpha-2b (OR 0.256, 95%CI 0.126-0.520, P<0.001) was associated with reduced risk of liver function abnormality during hospitalization. Mild to moderate liver injury was common in COVID-19 patients in Jiangsu, China. Age over 50 years, male sex, and lopinavir-ritonavir were the independent risk factors of liver impairment in COVID-19 patients during hospitalization.

DELAYED CATASTROPHIC THROMBOTIC EVENTS IN YOUNG AND ASYMPTOMATIC POST COVID-19 PATIENTS

Fan BE, Umapathi T, Chua K, Chia YW, Wong SW, Tan GWL, Chandrasekar S, Lum YH, Vasoo S, Dalan R.. J Thromb Thrombolysis. 2020 Nov 7. doi: 10.1007/s11239-020-02332-z. Online ahead of print.
Level of Evidence: 4 - Case-series

BLUF

A case series conducted in Singapore from July 2020 to September 2020 found that four patients who had all recovered from active COVID-19 infection developed large arterial thromboses at a median of 78 days from IgG anti-SARS-Cov-2 seroconversion (Figure 1, 2, 3). Authors suggest that long-term complications in recovered COVID-19 patients can include delayed large vessel thrombotic events, and recommend clinicians to monitor for post-infective thrombotic sequelae in clinically convalescent patients.

FIGURES

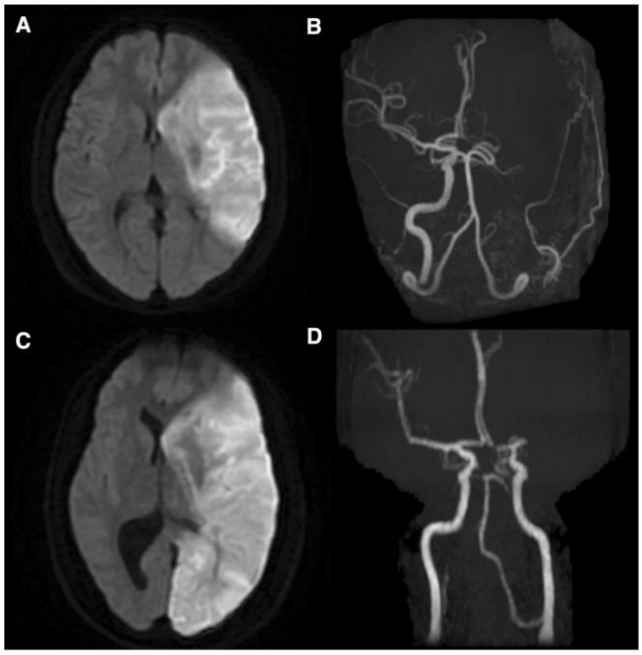

Fig. 1 **a-d** Acute magnetic resonance brain images of the 2 patients with large vessel ischaemic stroke. They show large areas of restricted diffusion in left middle cerebral, and middle cerebral, posterior cerebral artery territories, respectively. Adjoining intracranial magnetic resonance angiograms show loss of normal flow void in the left internal carotid and middle cerebral arteries in the first patient (**a**, **b**), and M1 segment of left middle cerebral artery in the second patient (**c**, **d**)

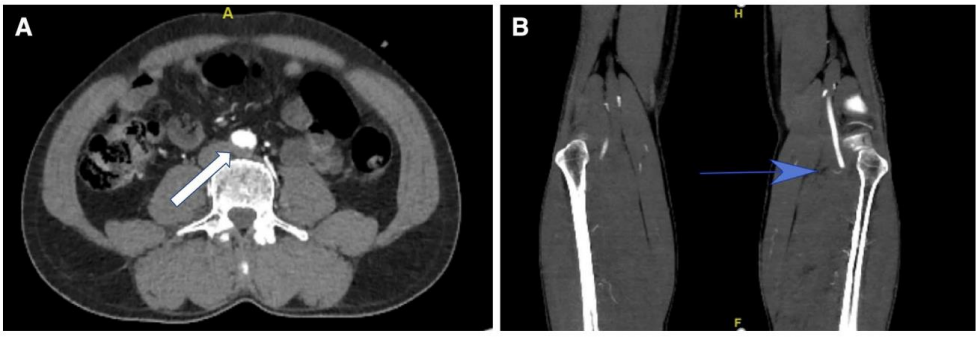

Fig. 2 **a** An eccentric thrombus (white arrow) is present in the distal aorta just before its bifurcation. **b** An abrupt cut off of the left popliteal artery (blue arrow)

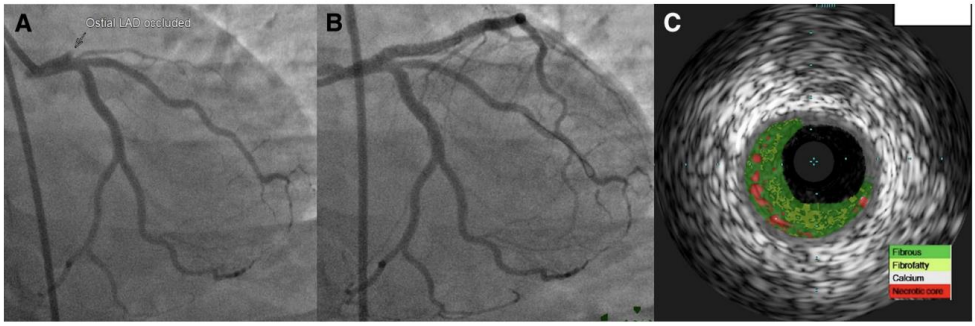

Fig. 3 **a** Coronary angiogram showed complete occlusion of ostial left anterior descending artery (LAD). Left circumflex artery and ramus intermedius branch are normal. **b** Restoration of flow in the LAD after implantation of drug eluting stent. **c** Intravascular ultrasound (virtual histology) showed predominantly fibrotic plaque with minimal necrotic core in the ostial LAD

ADVANCED AGE

ULTRASOUND IMAGING FINDINGS OF ACUTE TESTICULAR INFECTION IN PATIENTS WITH CORONAVIRUS DISEASE 2019: A SINGLE-CENTER-BASED STUDY IN WUHAN, CHINA

Chen L, Huang X, Yi Z, Deng Q, Jiang N, Feng C, Zhou Q, Sun B, Chen W, Guo R.. J Ultrasound Med. 2020 Nov 11. doi: 10.1002/jum.15558. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

A team from the Department of Ultrasound Imaging at Wuhan University Renmin Hospital conducted a retrospective study of 142 male patients hospitalized with COVID-19 between February 15 and March 31, 2020 who underwent bedside scrotal ultrasound. They found 32 patients (22.5%) presented with findings of acute testicular inflammation (10 with acute orchitis, 7 with acute epididymitis, 15 with epididymo-orchitis)(Figure 1), with higher frequency in men >80 years-old (Tables 2, 3; p=0.003) and in the severe COVID-19 group (p=0.002). Authors suggest SARS-CoV-2 may infect the testicles and/or epididymis and recommend clinicians be aware of these genitourinary manifestations.

ABSTRACT

OBJECTIVES: Coronavirus disease 2019 (COVID-19), caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has become a global pandemic, raising widespread public health concerns. Our team treated hospitalized patients with COVID-19 in Wuhan, where the outbreak first began, and we suspected that SARS-CoV-2 may cause testicular infection in male patients. We conducted this study to explore that observation. METHODS: We enrolled male patients with a confirmed diagnosis of COVID-19 and performed a bedside ultrasound (US) examination of the scrotum, focused on findings of acute inflammation such as tunica albuginea thickening, enlargement and heterogeneous echogenicity of the testis, epididymis, or both, an abscess, scrotal wall edema, and hydrocele. Then we compared the proportions of observed epididymo-orchitis in patients from different age groups and COVID-19 severity groups. RESULTS: A total of 142 patients with COVID-19 were enrolled in our study, and 32 (22.5%) patients had acute orchitis, epididymitis, or epididymo-orchitis on scrotal US imaging, according to the diagnosis criteria. The observed risk of acute scrotal infection increased with age, with the incidence reaching 53.3% in men older than 80 years. We also observed that men with severe COVID-19 had a significantly higher possibility of epididymo-orchitis compared to the nonsevere COVID-19 group (P = .037). CONCLUSIONS: This study shows US imaging evidence that SARS-CoV-2 may cause infection of the testis or epididymis, and the risk is worthy of the attention of clinicians.

US Finding	All Patients (n = 142)	Disease Severity Groups		P
		1 (Nonsevere) (n = 83)	2 (Severe) (n = 59)	
Unilateral onset	17 (12.0)	7 (8.4)	10 (16.9)	.188
Bilateral onset	22 (15.5)	10 (12.0)	12 (20.3)	.178
Inflammatory characteristics				
Thickened tunica albuginea	36 (25.4)	11 (13.3)	25 (42.2)	<.001
Enlargement of testis	10 (7.0)	4 (4.8)	6 (10.2)	.319
Heterogeneous echogenicity of testis	14 (9.9)	4 (4.8)	10 (16.9)	.017
Increased vascular flow on CDFI of testis	29 (20.4)	9 (10.8)	20 (33.9)	.001
Enlargement of epididymis	11 (7.7)	5 (6.0)	6 (10.2)	.526
Heterogeneous echogenicity of epididymis	8 (5.6)	3 (3.6)	5 (8.5)	.277
Increased vascular flow on CDFI of epididymis	24 (16.9)	9 (10.8)	15 (25.4)	.022
Abscess in epididymis	4 (2.8)	0 (0)	4 (6.8)	.028
Hydrocele	11 (7.7)	3 (3.6)	8 (13.6)	.052
Scrotal swelling	5 (8.5)	1 (3.6)	4 (6.8)	.160
Subcategorized by infection type				
Acute orchitis	10 (7.0)	3 (3.6)	7 (11.9)	.093
Acute epididymitis	7 (4.9)	3 (3.6)	4 (6.8)	.450
Acute epididymo-orchitis	15 (10.6)	5 (6.0)	10 (16.9)	.037
Total	32 (22.5)	11 (13.3)	21 (35.6)	.002

Data are presented as number (percent).

Table 2: "Ultrasound Findings of Acute Scrotal Infections in Patients With COVID-19".

Characteristic	All Patients (n = 142)	Acute Scrotal Infection		P
		Positive (n = 32)	Negative (n = 110)	
Age, y	58.3 (43.0–73.0)	70.3 (60.0–82.0)	54.8 (39.0–71.0)	<.001
<40	32 (22.5)	2 (6.3)	30 (27.3)	.012
40–59	39 (27.5)	6 (18.8)	33 (30.0)	.210
60–79	56 (39.4)	16 (50.0)	40 (36.4)	.093
>80	15 (10.6)	8 (25.0)	7 (6.4)	.003
Interval, d	15.4 (7–28)	14.6 (9–27)	15.6 (7–28)	.304
Acute scrotal symptoms	13 (9.2)	10 (31.3)	3 (2.7)	<.001
Comorbid diseases				
Chronic kidney disease	22 (15.5)	8 (25.0)	14 (12.7)	.102
Diabetes	19 (13.4)	5 (15.6)	14 (12.7)	.768
Coronary heart disease	17 (12.0)	6 (18.8)	11 (10.0)	.216
Hepatic cirrhosis	9 (6.3)	3 (9.4)	6 (5.5)	.421

Data are presented as median (IQR), number (percent), and median (range) where applicable.

Table 3: "Comparison of Acute Scrotum Infection With Clinical Characteristics".

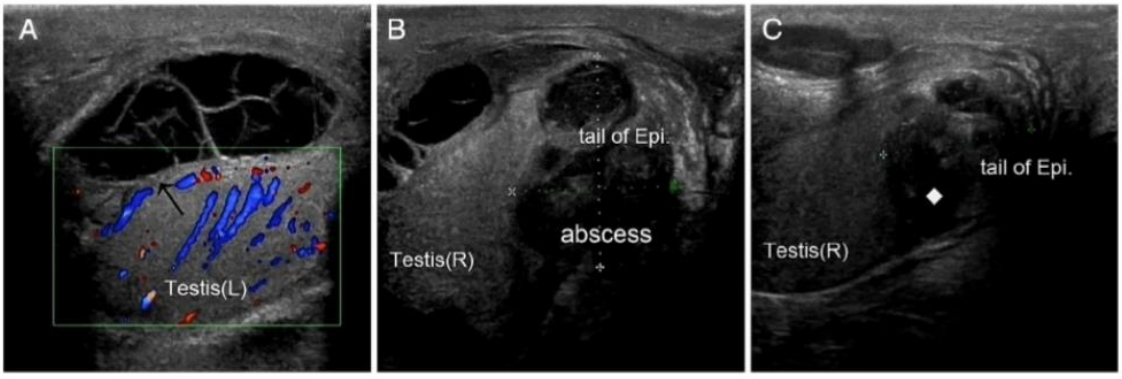

Figure 1:"Scrotal US imaging of a 57-year-old patient with COVID-19 and acute infection findings.A, Sagittal Color Doppler image of the left testicle showing enlargement and increased low signals of the left testicle and tunica albuginea (arrow) thickening. The testicle is sur-rounded by hydrocele containing some septal echoes.B, Sagittal grayscale image of the right testicle. The tail of the epididymis is remark-ably enlarged and contains multiple abscesses.C, Ultrasound image of the right testicle acquired at the second examination 6 days later showing that the tissue enlargement is in remission; the abscess in the tail of epididymis is almost fully absorbed; and only a small necrotic zone (diamond) remains".

VITAMIN D DEFICIENCY AGGRAVATES COVID-19: SYSTEMATIC REVIEW AND META-ANALYSIS

Pereira M, Dantas Damascena A, Galvão Azevedo LM, de Almeida Oliveira T, da Mota Santana J.. Crit Rev Food Sci Nutr. 2020 Nov 4:1-9. doi: 10.1080/10408398.2020.1841090. Online ahead of print.
Level of Evidence: 2 - Systematic review of surveys that allow matching to local circumstances

BLUF

This systemic review of 27 articles, conducted by researchers mainly from the Collective Health Institute and Universidade Federal do Oeste da Bahia (Brazil), found that vitamin D deficiency (25-hydroxy vitamin D level below 50 nmol/l) was not associated with increased risk of COVID-19 infection (OR=1.35, 95% CI 0.80 to 1.88, I^2=83%; Figure 3). However, those with severe cases of COVID-19 had 64% more vitamin D deficiency than mild cases (Figure 4), and those with vitamin D insufficiency had increased SARS-CoV-2-associated mortality (OR=1.82, 95%CI=1.06-2.58, I^2=59%; Figure 5). These findings suggest that vitamin D levels may play a role in the overall survival rate from COVID-19, and treatment for vitamin D deficiency may improve outcomes.

ABSTRACT

There is still limited evidence regarding the influence of vitamin D in people with COVID-19. In this systematic review and meta-analysis, we analyze the association between vitamin D deficiency and COVID-19 severity, via an analysis of the prevalence of vitamin D deficiency and insufficiency in people with the disease. Five online databases -Embase, PubMed, Scopus, Web of Science, ScienceDirect and pre-print Medrevix were searched. The inclusion criteria were observational studies measuring serum vitamin D in adult and elderly subjects with COVID-19. The main outcome was the prevalence of vitamin D deficiency in severe cases of COVID-19. We carried out a meta-analysis with random effect measures. We identified 1542 articles and selected 27. Vitamin D deficiency was not associated with a higher chance of infection by COVID-19 (OR = 1.35; 95% CI = 0.80-1.88), but we identified that severe cases of COVID-19 present 64% (OR = 1.64; 95% CI = 1.30-2.09) more vitamin D deficiency compared with mild cases. A vitamin D concentration insufficiency increased hospitalization (OR = 1.81, 95% CI = 1.41-2.21) and mortality from COVID-19 (OR = 1.82, 95% CI = 1.06-2.58). We observed a positive association between vitamin D deficiency and the severity of the disease.

FIGURES

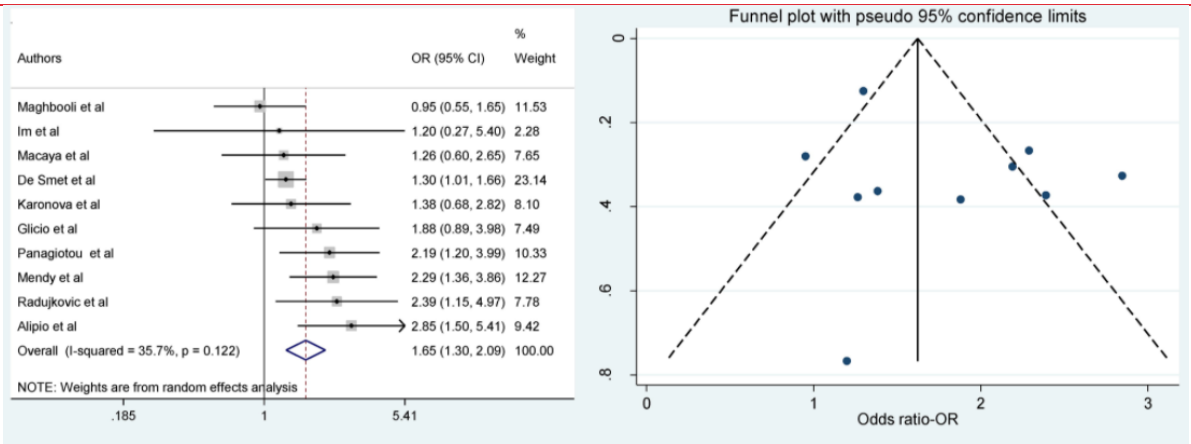

Figure 4. Forest plot and funnel plot of the association between vitamin D deficiency and occurrence of several COVID-19.

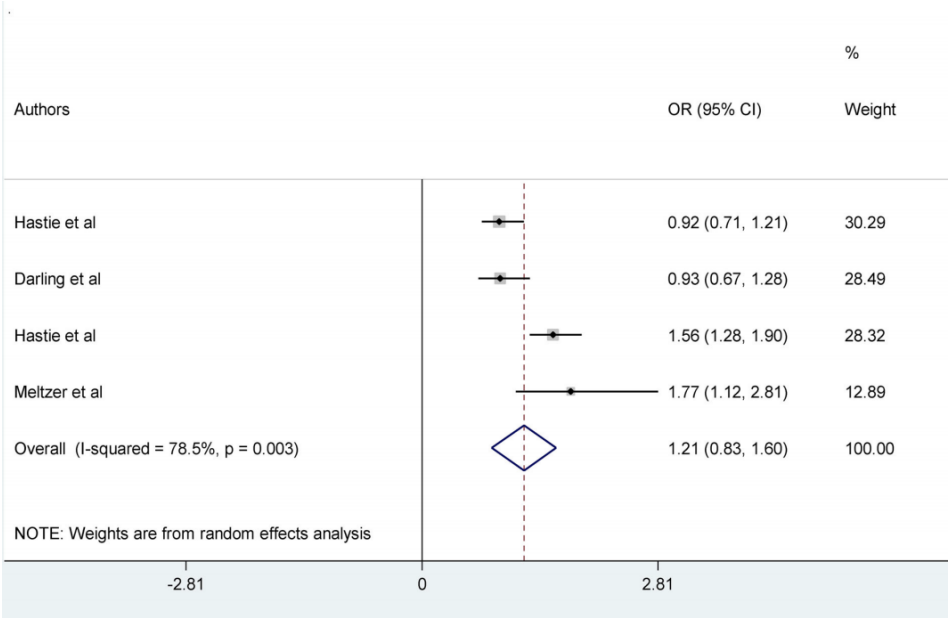

Figure 3. Vitamin D deficiency (less than 50 nmol/L) and chance of infection for COVID-19.

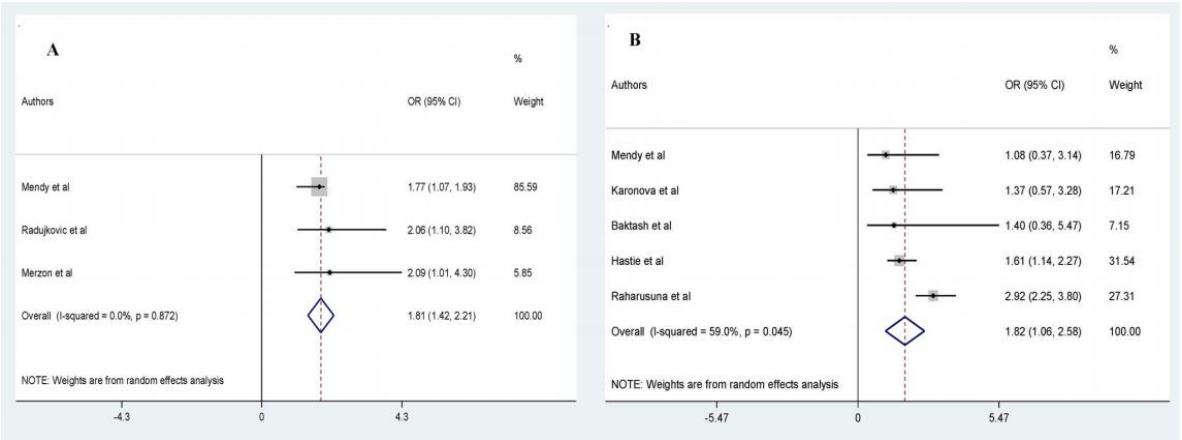

Figure 5. Vitamin D deficiency and chance of hospitalization (A) and death (B) in patients with COVID-19 infection

PREVENTING VITAMIN D DEFICIENCY DURING THE COVID-19 PANDEMIC: UK DEFINITIONS OF VITAMIN D SUFFICIENCY AND RECOMMENDED SUPPLEMENT DOSE ARE SET TOO LOW

Griffin G, Hewison M, Hopkin J, Kenny RA, Quinton R, Rhodes J, Thickett D.. Clin Med (Lond). 2020 Nov 6:clinmed.2020-0858. doi: 10.7861/clinmed.2020-0858. Online ahead of print.
Level of Evidence: 1 - Expert Opinion

BLUF

United Kingdom physicians in Infectious Disease, Endocrinology, Respiratory, and Gerontology conclude that the original threshold goal for vitamin D sufficiency (25nmol/L) is too low and not evidence-based, suggesting that it should instead be set at 50 nmol/L and recommend supplementation with 800 IU per day (Figure 1, Table 1). They speculate vitamin D deficiency as a risk factor for COVID-19 and advocate for an increase in the recommended Vitamin D supplement dose.

ABSTRACT

There is growing evidence linking vitamin D deficiency with risk of COVID-19. It is therefore distressing that there is major disagreement about the optimal serum level for 25-hydroxyvitamin D (25(OH)D) and appropriate supplement dose. The UK Scientific Advisory Committee for Nutrition has set the lowest level for defining sufficiency (10 ng/ml or 25 nmol/L) of any national advisory body or scientific society and consequently recommends supplementation with 10 micrograms (400 IU) per day. We have searched for published evidence to support this but not found it. There is considerable evidence to support the higher level for sufficiency (20 ng/ml or 50 nmol/L) recommended by the European Food Safety Authority and the American Institute of Medicine and hence greater supplementation (20 micrograms or 800 IU per day). Serum 25(OH)D concentrations in the UK typically fall by around 50% through winter. We believe that governments should urgently recommend supplementation with 20-25 micrograms (800-1,000 IU) per day.

FIGURES

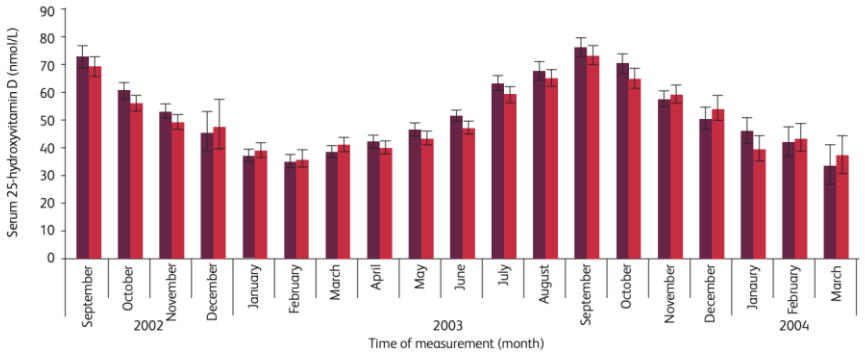

Fig 1. Seasonal variation in serum vitamin D concentrations (mean (95% confidence interval)) among 7,437 white British (1958 British birth cohort) at age 45. Dark red bar = male, red bar = female. Adapted with permission from Hypponen and Power 2007.[4]

Table 1. Calculated daily vitamin D3 dose for achieving in vitamin D-deficient individuals target 25-hydroxyvitamin D levels of 50 nmol/L and 75 nmol/L, respectively

	30-year-old person	70-year-old person
Target 25(OH)D level 50 nmol/L		
50 kg body weight	9 micrograms (360 IU)	5 micrograms (200IU)
75 kg body weight	13.5 micrograms (540 IU)	7.7 micrograms (308 IU)
100 kg body weight	18 micrograms (720 IU)	10 micrograms (400 IU)
Target 25(OH)D level 75 nmol/L		
50 kg body weight	42 micrograms (1680 IU)	24 micrograms (960 IU)
75 kg body weight	63 micrograms (2520 IU)	36.5 micrograms (1460 IU)
100 kg body weight	84 micrograms (3360 IU)	49 micrograms (1960 IU)

Based on a systematic review of 94 cohort studies that included 11,566 supplemented individuals (Zittermann *et al*[21]).
Baseline 25(OH)D level 25 nmol/L.

MONITOR FOR COVID-19 VACCINE RESISTANCE EVOLUTION DURING CLINICAL TRIALS

Kennedy DA, Read AF.. PLoS Biol. 2020 Nov 9;18(11):e3001000. doi: 10.1371/journal.pbio.3001000. Online ahead of print.
Level of Evidence: Other - Guidelines and Recommendations

BLUF

This publication by academicians affiliated with Center for Infectious Disease Dynamics and Department of Entomology at The Pennsylvania State University discusses the possibility of vaccine resistance while proposing a schematic to repurpose ongoing clinical trials to enable risk assessment for resistance evolution (Figure 1). They highlight vaccine features that minimize risk of resistance including immune response induction targeting multiple viral epitopes, stopping transmission via pathogen growth suppression from vaccine-protected hosts, and prompting an immune response against all circulating serotypes. Authors suggest a vaccine lacking any of these features may lead to viral evolution and recommend vaccine resistance risk assessment be incorporated into the development process.

ABSTRACT

Although less common than the evolution of antimicrobial drug resistance, vaccine resistance can and has evolved. How likely is it that COVID-19 vaccines currently in development will be undermined by viral evolution? We argue that this can be determined by repurposing samples that are already being collected as part of clinical trials. Such information would be useful for prioritizing investment among candidate vaccines and maximizing the potential long-term impact of COVID-19 vaccines.

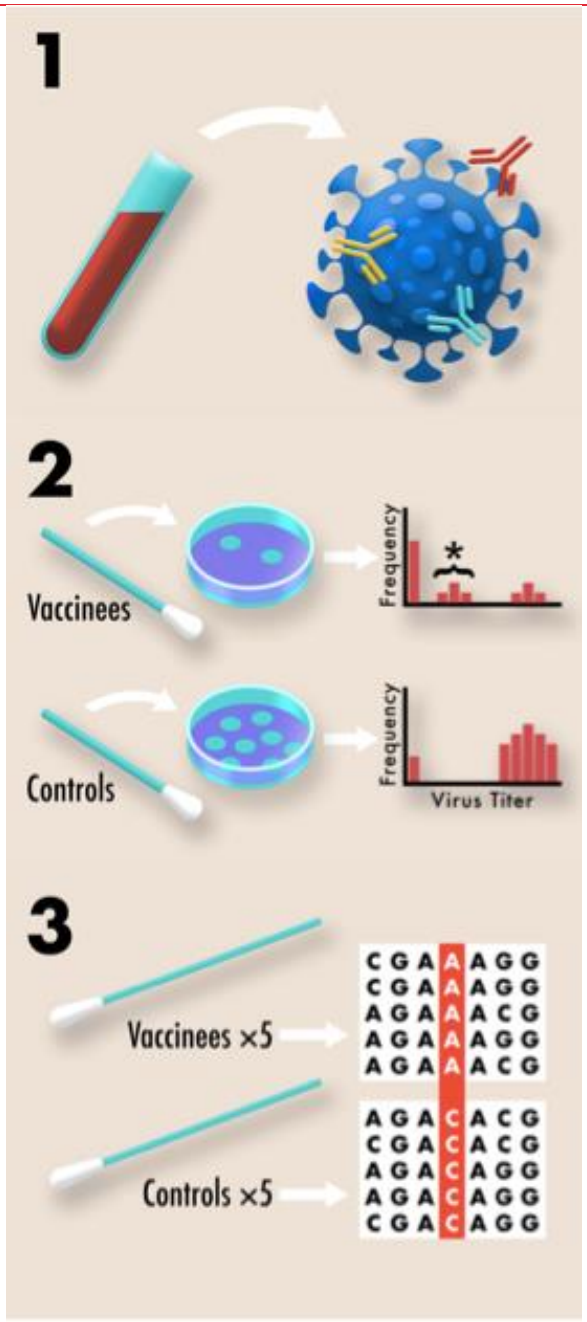

Fig 1. Schematic illustrating three ways that standard samples from COVID-19 clinical trials can be repurposed to assess the risk that vaccine resistance will evolve. 1. The complexity of B-cell and T-cell responses can be measured using blood samples [10,11]. Different neutralizing antibodies are depicted above in different colors. More complex responses indicate more evolutionarily robust immunity. 2. The effect of vaccination on transmission potential can be assessed by collecting viral titer data using routine nasal swabs. Plaque assays from multiple vaccinated and control individuals are compiled into a histogram. Undetectable viral titers suggest little or no transmission potential, due to either complete immune protection or the absence of exposure. High viral titers suggest high transmission potential due to the absence of a protective immune response. Intermediate viral titers, marked above with an asterisk, suggest moderate transmission potential due to partial vaccine protection. Intermediate titers indicate an increased risk for resistance evolution since pathogen diversity can be generated within hosts and selection can act during transmission between hosts. 3. Pre-existing variation for vaccine resistance can be assessed by recovering genome sequences from nasopharyngeal swabs of symptomatic COVID-19 cases included in the study. In a placebo controlled, double blind study, any significant differences in the genome sequences of samples from vaccinated and control individuals would suggest at least partial vaccine resistance.

SURGICAL MASKS VS RESPIRATORS FOR THE PROTECTION AGAINST CORONAVIRUS INFECTION: STATE OF THE ART

Violante T, Violante FS.. Med Lav. 2020 Oct 31;111(5):365-371. doi: 10.23749/mdl.v111i5.9692.
Level of Evidence: Other - Review / Literature Review

BLUF

Italian physicians analyzed seven systematic reviews (via PubMed search) on the effectiveness of surgical masks and filtering facepiece respirators (FFP) in conferring protection against SARS-CoV-2. These data suggested both surgical masks and FFP2 (see summary) were equally efficient in protecting against airborne viruses, while the more cost-effective and easy-to-use surgical masks adequately protect healthcare workers in most settings. Authors encourage continued research to confirm these findings and better describe relative protection of different mask types.

SUMMARY

In Europe, surgical masks are classified into 3 types:
- Type I: Minimum bacterial filtration efficiency of 95%. Used by the patients and the public.
- Type II and IIR: Used by health-care workers with a minimum bacterial filtration efficiency of 98%. The breathability index of Type II and IIR are 40 Pa/4.9 cm^2 and 60 Pa/4.9 cm^2 respectively.

There are 3 types of filtering facepiece respirators (FFP) per EN standards (viral filtration efficiency assessed using NaCl and paraffin oil aerosols):
- FFP1: filtration capacity of 80%
- FFP2: filtration capacity of 94%
- FFP3: filtration capacity of 99%

N95/N100 are the masks used in the US. N95 has a filtration capacity of 94%.
These ratings do not take bacterial filtration efficiency into consideration.

ABSTRACT

BACKGROUND: During the Covid-19 outbreak, a recurrent subject in scientific literature has been brought back into discussion: whether surgical masks provide a sufficient protection against airborne SARS-CoV-2 infections. OBJECTIVES: The objective of this review is to summarize the available studies which have compared the respective effectiveness of surgical masks and filtering facepiece respirators for the prevention of infections caused by viruses that are transmitted by the respiratory tract. METHODS: The relevant scientific literature was identified by querying the PubMed database with a combination of search strings. The narrower search string "(surgical mask *) AND (respirator OR respirators)" included all the relevant articles retrieved using broader search strategies. Of all the relevant articles found, seven systematic reviews were selected and examined. RESULTS: The currently available scientific evidence seems to suggest that surgical masks and N95 respirators/FFP2 confer an equivalent degree of protection against airborne viral infections. DISCUSSION: Since surgical masks are less expensive than N95 respirators but seem to be as effective in protecting against airborne infection and they are also more comfortable for the user, requiring less respiratory work, they should be the standard protective device for health care workers and especially for workers who carry out non-medical jobs. Filtering facepiece respirators, whose extended use is less comfortable for the wearer, may be preferred for procedures which require greater protection for a shorter time.

ENDOCRINOLOGY

A CASE OF POSTPARTUM THYROIDITIS FOLLOWING SARS-COV-2 INFECTION

Mizuno S, Inaba H, Kobayashi KI, Kubo K, Ito S, Hirobata T, Inoue G, Akamizu T, Komiya N.. Endocr J. 2020 Nov 12. doi: 10.1507/endocrj.EJ20-0553. Online ahead of print.
Level of Evidence: Other - Case Report

BLUF

Investigators from Japanese Red Cross Wakayama Medical Center and Wakayama Medical University (Japan) present a case of a 29-year-old female who developed painless postpartum thyroiditis (PPT) following a COVID-19 infection and 4.5 months after childbirth. Laboratory findings included a positive anti-thyroglobulin antibody of 167.4IU/mL (normal is less than 28) and normal serum thyroglobulin, and ultrasound revealed a normal thyroid size. The condition was self limited and she had a complete recovery after 1 month (Table 1). This is one of the first documented cases of PPT following COVID-19 infection and could indicate that there might be a relationship between the inflammation in COVID-19 and thyroid conditions.

ABSTRACT

Postpartum thyroiditis (PPT) is characterized by mild thyrotoxicosis occurring within one year of parturition commonly followed by transient hypothyroidism. Having genetic background of autoimmune thyroid disorders is a risk factor for it because the immune reactivation during postpartum period is a trigger for PPT. Pandemic of COVID-19: caused by SARS-CoV-2 infection is a global health problem, and occurrence of Graves' disease and Hashimoto's thyroiditis after the viral infection have been reported but occurrence of PPT with COVID-19 has never been reported. A 29-year-old woman developed general fatigue four and a half months after parturition, and was diagnosed as having PPT: one month before, she had COVID-19. Hereafter, we define the date of delivery as Day 0 to make timeline clear. SARS-CoV-2 infection was diagnosed by PCR on Day 103, its disappearance from the upper airway confirmed on Day 124, and the thyroiditis diagnosed on Day 136. She had been euthyroid on Day 0 and 95, but thyrotoxic on Day 136. Serum thyroglobulin (Tg) concentration was normal in the presence of anti-Tg antibody, other thyroid-related autoantibodies were negative, and by ultrasonography, the thyroid gland was normal in size and no evidence of increased vascularity. Thyroid function returned to normal by Day 172 without any specific drug therapy. In conclusion, although a clear causal relationship could not be found, we documented the world's first case of PPT developed following COVID-19.

FIGURES

Measurement	*Day*										Ref. Range
	0	*95*	*103*	*104*	*124*	*126*	*127*	*136*	*172*	*205*	
WBC/μL	N.D.	N.D.	N.D.	6,100	N.D.	N.D.	N.D.	4,800	4,140	5,300	4,000–9,500
Neu (%)	N.D.	N.D.	N.D.	82.5	N.D.	N.D.	N.D.	51.1	55.6	50.8	35–75
Lym (%)	N.D.	N.D.	N.D.	10.0	N.D.	N.D.	N.D.	35.6	35.5	39.2	25–50
Lymphocytes (/μL)	N.D.	N.D.	N.D.	610	N.D.	N.D.	N.D.	1,708	1,469	2,077	1,000–3,000
FT4, ng/dL	0.91	1.09	N.D.	N.D.	N.D.	N.D.	N.D.	2.00	1.23	0.88	0.9–1.7
FT3, pg/mL	N.D.	3.04	N.D.	N.D.	N.D.	N.D.	N.D.	5.44	3.61	2.76	2.3–4.0
TSH, μIU/mL	0.818	1.37	N.D.	N.D.	N.D.	N.D.	N.D.	0.020	0.043	2.01	0.5–5.0
Tg, ng/mL	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	5.26	5.20	1.23	<33.7
TgAb, IU/mL	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	12.24	N.D.	35.1	<5
TPOAb, IU/mL	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	<3	<3	<3	<3
TRAb, IU/mL	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	<0.9	<0.9	<0.9	<2.0
SARS-CoV-2 PCR	N.D.	N.D.	(+)	N.D.	(–)	(–)	N.D.	N.D.	N.D.	N.D.	N.A.
Events			↑ Delivery		Admission High fever (39.0°C)			Hospital Discharge	Onset of PPT	Recovery from PPT	

Footnotes: WBC, white blood cell; Neu, proportion of neutrophils; Lym, proportion of lymphocytes. The day of delivery was defined as Day *0* in this communication, so that the clinical onset of postpartum thyroiditis (PPT) is *Day 136*. Tg, thyroglobulin; TgAb, Anti-Tg autoantibody; TPOAb, anti-thyroperoxidase autoantibody; TRAb, anti-TSH receptor autoantibody (3rd generation assay); N.D., not determined; N.A., not applicable.

Table 1. Key events and laboratory data along the timeline

ADJUSTING PRACTICE DURING COVID-19

ACUTE CARE

STRONG SECOND COVID-19 WAVE CALLS FOR A SECOND LOOK AT ICU TRIAGE GUIDELINES

Suter P, Pargger H.. Swiss Med Wkly. 2020 Nov 12;150:w20407. doi: 10.4414/smw.2020.20407. eCollection 2020 Nov 2.
Level of Evidence: Other - Guidelines and Recommendations

BLUF

A professional opinion piece, written by Swiss Intensive Care professionals, calls for a re-examination of Intensive Care Unit (ICU) triaging guidelines given the second wave of the COVID-19 pandemic in Europe. As the second wave of infections has posed the threat of a scarcity of beds available, the authors believe that a new set of triaging protocols are required due to new information on transmission patterns of the virus and improved knowledge on management of the disease. The authors propose using the newly revised Swiss ICU triage guidelines (illustrated below) as a framework for other ICU triage guidelines and for decision-making for ICU patients to mitigate the second wave of COVID-19.

SUMMARY

The authors relate the key changes of the revised Swiss guidelines for triaging ICU patients, which are summarized below:
1) The short-term prognosis criteria became more stringent in the case of a bed shortage
2) Removal of age, disability, and dementia from being acceptable criteria, except in the case of quantifying risk for severe disease
3) Addition of Frailty as a prognostic factor used in evaluation
4) A revision of triage criteria, now including Frailty and the Charleson Comorbidition Index
5) Addition of a national, centralized system organizing patient transfer in times of low ICU bed availability

EMERGENCY MEDICINE

FALLING METHAMPHETAMINE-RELATED PRESENTATIONS TO A CLINICAL TOXICOLOGY UNIT DURING THE COVID-19 PANDEMIC

Fry M, Harris K, Isoardi KZ.. Emerg Med Australas. 2020 Nov 6. doi: 10.1111/1742-6723.13677. Online ahead of print.
Level of Evidence: 4 - Case-series, case-control, or historically controlled studies

BLUF

Investigators affiliated with The University of Queensland compared the toxicological cases at Princess Alexandra Hospital's emergency department (ED; western Australia) from March 12, 2020 to September 12, 2020 to those of the same 6-month time period in 2019 (Figure 1). They observed a decrease in methamphetamine-related ED presentations by 15% during the pandemic, which may be due to travel restrictions, increased boarder patrol, increased cost, and decreased availability. Additionally, gamma-hydroxybutyrate (GBH) related presentations have increased from 4% to 9% during the pandemic, as well as marijuana related presentations from 8% to 12%. Although restrictions in Australia are starting to ease, there may continue to be a shortage of methamphetamine access, drawing those with substance use disorders to alternative drugs, such as GHB, during the pandemic.

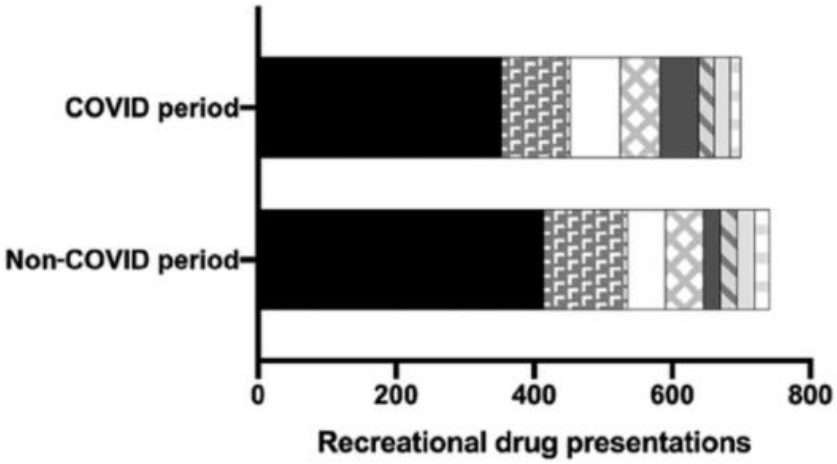

Figure 1. Recreational drug presentations to a tertiary hospital during the 6-month period following the declaration of the COVID-19 pandemic compared to the same period 1 year earlier. From left to right, GBH, Methamphetamine, opioid, marijuana, benzodiazepines, GHB, cocaine, pregabalin, methylenedioxymethamphetamine.

EFFICACY AND SAFETY OF EARLY TREATMENT WITH SARILUMAB IN HOSPITALISED ADULTS WITH COVID-19 PRESENTING CYTOKINE RELEASE SYNDROME (SARICOR STUDY): PROTOCOL OF A PHASE II, OPEN-LABEL, RANDOMISED, MULTICENTRE, CONTROLLED CLINICAL TRIAL

León López R, Fernández SC, Limia Pérez L, Romero Palacios A, Fernández-Roldán MC, Aguilar Alonso E, Pérez Camacho I, Rodriguez-Baño J, Merchante N, Olalla J, Esteban-Moreno MÁ, Santos M, Luque-Pineda A, Torre-Cisneros J.. BMJ Open. 2020 Nov 14;10(11):e039951. doi: 10.1136/bmjopen-2020-039951.
Level of Evidence: 5 - Mechanism-based reasoning

BLUF

Infectious disease researchers from Spain summarize the protocol for their Phase II, open-label, randomized, multicenter, controlled clinical trial investigating the efficacy, safety, and limitation of administering sarilumab (200 mg vs 400 mg) together with the best available therapy (BAT) to patients with "COVID-19 presenting cytokine release syndrome" (Figure 1, 2). While awaiting the results, the authors hypothesize that early use of sarilumab, in addition to standard therapy, may potentially reduce COVID-19 severity and mortality.

ABSTRACT

INTRODUCTION: About 25% of patients with COVID-19 develop acute respiratory distress syndrome (ARDS) associated with a high release of pro-inflammatory cytokines such as interleukin-6 (IL-6). The aim of the SARICOR study is to demonstrate that early administration of sarilumab (an IL-6 receptor inhibitor) in hospitalised patients with COVID-19, pulmonary infiltrates and a high IL-6 or D-dimer serum level could reduce the progression of ARDS requiring high-flow nasal oxygen or mechanical ventilation (non-invasive or invasive). METHODS AND ANALYSIS: Phase II, open-label, randomised, multicentre, controlled clinical trial to study the efficacy and safety of the administration of two doses of sarilumab (200 and 400 mg) plus best available therapy (BAT) in hospitalised adults with COVID-19 presenting cytokine release syndrome. This strategy will be compared with a BAT control group. The efficacy and safety will be monitored up to 28 days postadministration. A total of 120 patients will be recruited (40 patients in each arm). ETHICS AND DISSEMINATION: The clinical trial has been approved by the Research Ethics Committee of the coordinating centre and authorised by the Spanish Agency of Medicines and Medical Products. If the hypothesis is verified, the dissemination of the results could change clinical practice by increasing early administration of sarilumab in adult patients with COVID-19 presenting cytokine release syndrome, thus reducing intensive care unit admissions. TRIAL REGISTRATION NUMBER: NCT04357860.

FIGURES

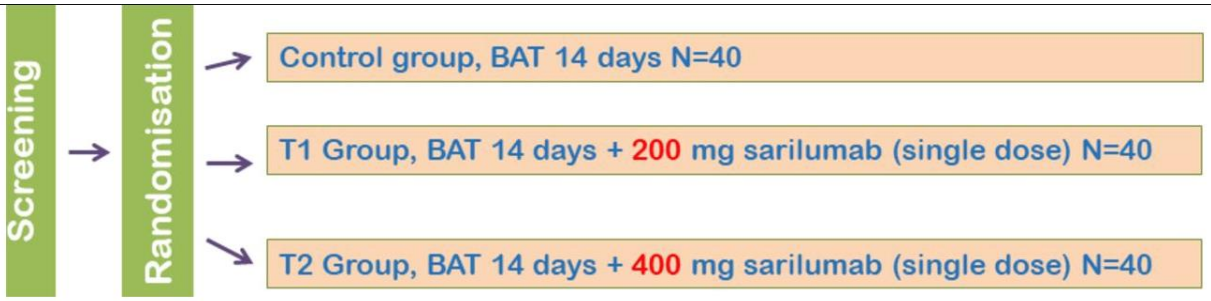

Figure 1. Flow diagram.
BAT, best available therapy.

- Early use of sarilumab can reduce the progression of respiratory failure and prevent the saturation of intensive care units.
- The trial will study two doses of the drug. One could be selected for phase III trials with a larger sample.
- Limitations include not being a blind trial and having a limited sample size.
- The stock of sarilumab is limited in Spain. The government distributes the drug to ensure the treatment of patients with rheumatoid arthritis. Pharmacies must request authorisation for dispensation of the drug on a case-by-case basis.
- The incidence of new cases is decreasing in Spain.

Figure 2. Strengths and limitations of this study

NON-COVID-19 DEATHS AFTER SOCIAL DISTANCING IN NORWAY

Catalano R, Casey JA, Bruckner TA, Gemmill A.. Eur J Epidemiol. 2020 Nov 9. doi: 10.1007/s10654-020-00691-8. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

American public health experts analyzed the effect of social distancing in Norway on non-COVID-19 deaths during March 16-May 18, 2020 using the Human Mortality Database's Short-term Mortality Fluctuations data series. They compared non-COVID-19 deaths in Norway during the nine-week period to expected deaths (based on historical Norwegian data and non-COVID-19 deaths in Sweden) using the Box-Jenkins time series method (Table 1) and found 430 fewer non-COVID-19 deaths in Norway than expected (Figure 1). Authors suggest social distancing carries mortality benefits beyond COVID-19 prevention, and recommend in-depth analysis of such measures on health indicators when considering risks and benefits of public health policies.

ABSTRACT

Lay persons and policy makers have speculated on how national differences in the imposition of social distancing to reduce SARS CoV-2 (severe acute respiratory syndrome coronavirus 2) infection has affected non-COVID-19 deaths. No rigorous estimation of the effect appears in the scholarly literature. We use time-series methods to compare non-COVID-19 deaths in Norway during its 9 weeks of mandated social distancing to those expected from history as well as from non-COVID-19 deaths in relatively less restricted Sweden. We estimate that 430 fewer Norwegians than expected died from causes other than COVID-19. We argue that failing to account for averted non-COVID-19 deaths will lead to an underestimate of the benefits of social distancing policies.

FIGURES

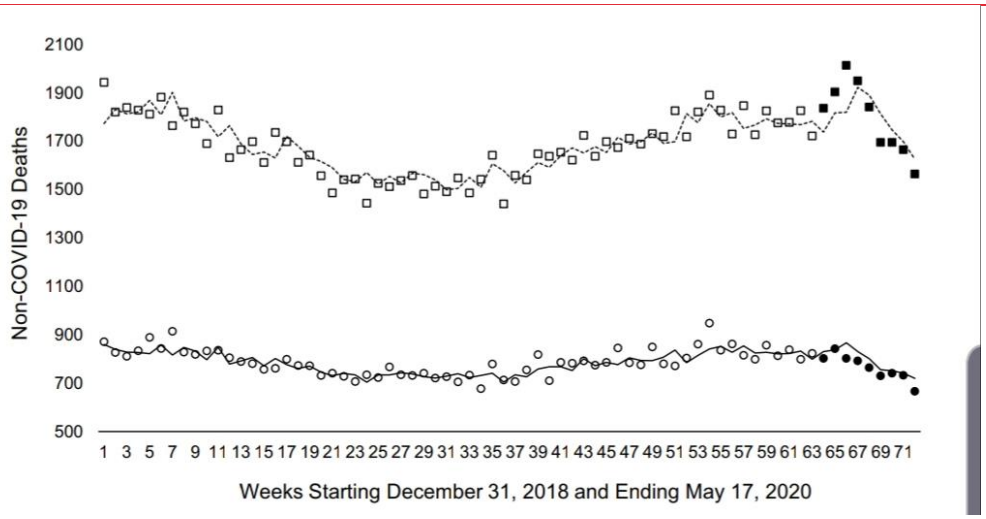

Figure 1: "Observed and expected values of Norwegian and Swedish non-Covid-19 deaths for 72 weeks from December 31, 2018 through May 17, 2020. Observed values appear as circles for Norway and boxes for Sweden. Circles and boxes during Norwegian mandated social distancing appear filled. The solid and dashed lines are expected values for Norway and Sweden respectively".

Table 1

Estimated coefficients and standard errors for transfer functions predicting non-COVID 19 deaths in Norway and Sweden for 540 weeks beginning January 3, 2010 and ending May 17, 2020

	Norway		Sweden	
	Estimate	**SE**	**Estimate**	**SE**
Constant	311.51**	36.42	1378.08**	90.80
Weekly Deaths in Comparison Country	0.28**	0.02	0.55**	0.08
Mandating Social Distancing	−47.81**	20.07	107.33*	61.82
Box Jenkins Parameters				
Moving Average at t-1	0.67**	0.07	0.38**	0.05
Autoregression at t-1	0.88**	0.05	0.89**	0.03
Autoregression at t-51	0.14**	0.04	0.15**	0.05

*p<.10; 2-tailed test

**p<.05; 2-tailed test

ACKNOWLEDGEMENTS

CONTRIBUTORS

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