

The Daily COVID-19 Literature Surveillance Summary

June 4th 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	Non-randomized controlled cohort/follow-up study**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning
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

Climate:

- [Delayed presentation for stroke](#) may prohibit time-sensitive treatment with tissue plasminogen activator (tPA).
- Theories attempting to explain the relatively [low case fatality rate \(CFR\) in Africa](#) (3%) compared to the Americas (6%) and Europe (9%) include:
 - Minimal early transmission from Asia and Europe
 - Younger population and warm, dry climate
 - Underestimation of the CFR due to limited resources and testing

Epidemiology:

- Data from the [Korean Centers for Disease Control and Prevention](#) estimates the burden of disease from the pandemic to be 4.930 Disability-Adjusted Life Years (DALYs) per 100,000 population.
- Belgian authors studying [anosmia in COVID-19](#) found:
 - 87% of those reporting anosmia for less than 12 days were RT-PCR positive for COVID-19 (vs 23% >12d).
 - However, olfactory performance testing found 25% patients were actually normosmic.

Understanding the Pathology:

- Data from the [University of Washington hospital system](#) found <1% of asymptomatic patients without known exposure tested positive for COVID-19, compared to 10.3% in symptomatic patients.
- A [retrospective study of the first 1000 COVID-19 patients at New York-Presbyterian Hospital](#) found a bimodal distribution in time-to-intubation after symptom onset (3-4 days & 9 days), suggesting careful monitoring for patients who are 5-8 days post-symptom onset to anticipate disease progression.

Transmission:

- Scant evidence of detectable SARS-CoV-2 in [semen](#) and [breastmilk](#) has researchers calling for more robust research to understand implications of potential sexual and vertical transmission.
- Serologic and RT-PCR testing of [an entire otolaryngology unit staff](#) (n=58) in a high-prevalence region of Italy found 9% positivity; however, survey results showed out-of-hospital COVID-19 exposure was associated with a higher risk of infection ($p=0.008$).

Management:

- An international interdisciplinary group of physicians review the literature, and outline a [multidisciplinary approach for managing COVID-19 patients](#), emphasizing the importance of early identification and proper timing of interventions.
- Authors argue against using [two consecutive negative PCR tests](#) as a guide for discontinuation of isolation precautions, especially considering nearly 1/5 patients test positive after two negatives and the substantial amount of PPE and resources required.

Adjusting the Practice:

- European pathologists release guidelines for [maintaining safe and effective laboratory procedures](#) during the COVID-19 pandemic.
- A case series from the University of Washington Medical Center describes a [successful and timely organ transplantation procedure](#).

R&D Diagnosis and Treatment:

- Brazilian authors [comparing lung ultrasonographic findings to histopathological analysis](#) of 10 fatal COVID-19 cases found full agreement between the two diagnostic modalities. This adds to growing evidence of the utility of ultrasound in screening and monitoring disease progression in COVID-19 patients.
- A systematic review and meta-analysis of 9 studies (n=200) evaluating efficacy of [mesenchymal stem cells \(MSCs\)](#) in treating COVID-19 acute respiratory distress syndrome (ARDS) displayed a trend towards reduced mortality that was not statistically significant. However, given the lack of adverse events associated with MSC, authors posit that further research is warranted.

Mental Health and Resilience:

- Authors from Brown University discuss [combating misinformation during the COVID-19 pandemic](#).
- A [cross-sectional study of 339 psychotherapists](#) found 62.7% experienced moderate levels of vicarious trauma and 15% experienced high levels. Higher levels were seen in younger and inexperienced clinicians, highlighting the importance of managing countertransference.

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CLIMATE

UNDERUTILIZATION OF HEALTHCARE FOR STROKES DURING THE COVID-19 OUTBREAK

Onteddu SR, Nalleballe K, Sharma R, Brown AT.. Int J Stroke. 2020 Jun 1:1747493020934362. doi: 10.1177/1747493020934362. Online ahead of print.

Level of Evidence: 3

BLUF

Physicians affiliated with the University of Arkansas for Medical Sciences report lower rates of stroke presentation and intravenous tissue plasminogen activator (tPA) administration in TriNetX hospitals during the COVID-19 outbreak (January 20 to May 16, 2020) compared with two date ranges from the previous year (Figure 1). Similar results from an Italian study on acute coronary syndrome support the authors' conclusions that COVID-19 may reduce willingness to seek medical care, and they posit that reduced use rates for time-sensitive procedures (like tPA administration) may reflect delayed help-seeking behavior in patients; health care workers and leaders should encourage people to get medical care, if needed.

FIGURES

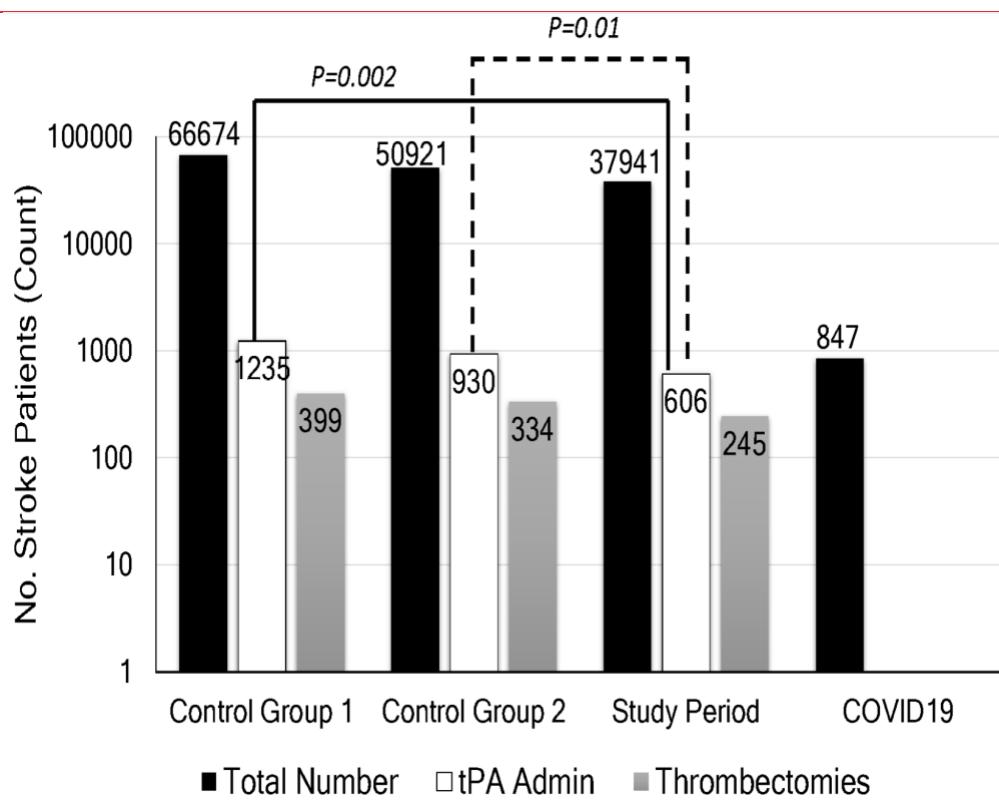


Figure 1. Rates of hospital admission and administration of tPA and thrombectomies during and prior to COVID-19.

GLOBAL

WHY IS THERE LOW MORBIDITY AND MORTALITY OF COVID-19 IN AFRICA?

Njenga MK, Dawa J, Nanyangi M, Gachohi J, Ngere I, Letko M, Otieno CF, Gunn BM, Osoro E.. Am J Trop Med Hyg. 2020 Jun 1. doi: 10.4269/ajtmh.20-0474. Online ahead of print.

Level of Evidence: Other

BLUF

In this perspective article, authors hypothesize reasons why Africa has relatively low case fatality rate (CFR) of COVID-19 cases compared to other highly populated areas (Figures 1, 2). Possible causes include low seeding of SARS-CoV-2, the possibility of preexisting immunity from prior exposure to other coronaviruses, low median age of the continent (<20 years

old), warmer and drier weather, and effective travel restrictions. Additionally, low CFR could be attributed to artifact, given poor surveillance and low testing numbers due to limited resources, and some are anticipating a surge in cases and deaths yet to come.

ABSTRACT

Three months since the detection of the first COVID-19 case in Africa, almost all countries of the continent continued to report lower morbidity and mortality than the global trend, including Europe and North America. We reviewed the merits of various hypotheses advanced to explain this phenomenon, including low seeding rate, effective mitigation measures, population that is more youthful, favorable weather, and possible prior exposure to a cross-reactive virus. Having a youthful population and favorable weather appears compelling, particularly their combined effect; however, progression of the pandemic in the region and globally may dispel these in the coming months.

FIGURES

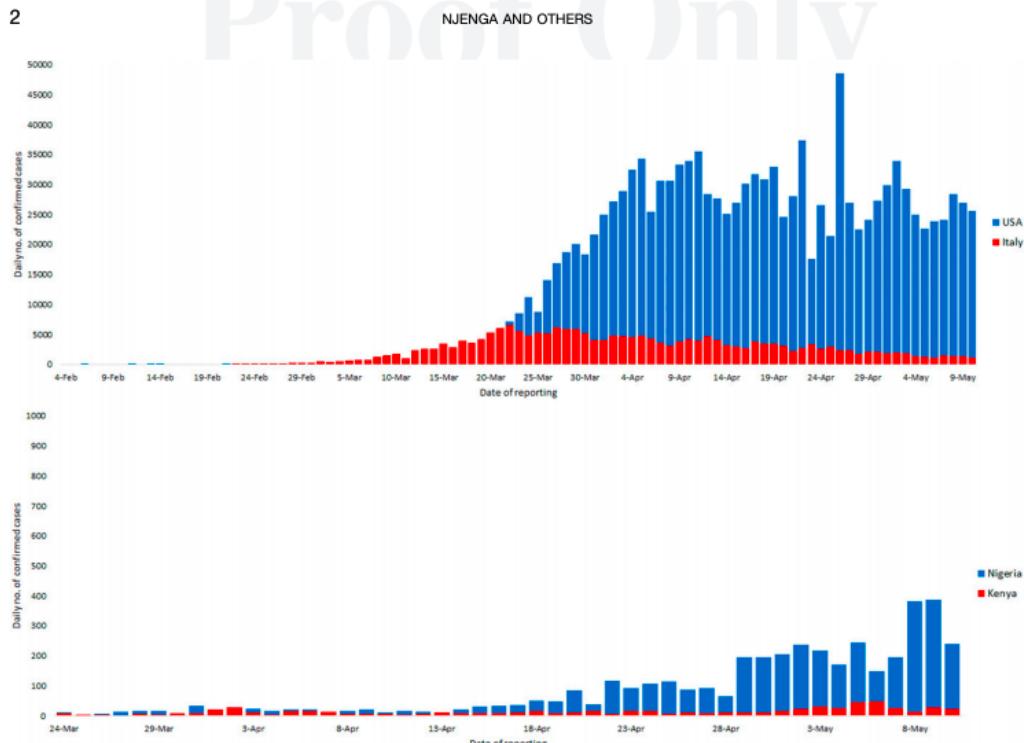


FIGURE 1. COVID-19 epi curves for the United States and Italy (top) and Nigeria and Kenya (bottom). The x axis starts from 2 weeks after the first reported case in the United States (top) and Nigeria (bottom). The different y axis scales were used to allow visibility of the low number of cases in Nigeria and Kenya when compared with the United States and Italy. Data used to develop these curves were obtained from publicly available repositories and national health ministries as described in the Data Sources section.

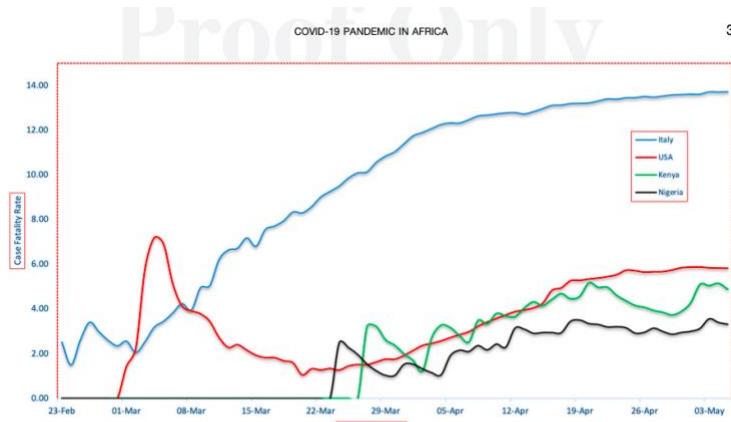


FIGURE 2. COVID-19 case fatality rate (CFR) for the United States, Italy, Nigeria, and Kenya. Data used to calculate the CFR were downloaded from publicly available repositories and national health ministries as described in the Data Sources section. The limitations to the CFR provided here include the fact that the number of cases (denominator) from each country is dependent on the strength of each country's surveillance system and may underestimate the actual number of cases because of limitations in testing or those that do not seek medical care due to asymptomatic or mild infections.

DISPARITIES

COVID-19: THE ETHICS OF CLINICAL RESEARCH IN QUARANTINE

Evans NG.. BMJ. 2020 May 29;369:m2060. doi: 10.1136/bmj.m2060.

Level of Evidence: Other

BLUF

A philosopher weighs the ethics of clinical research and quarantine, noting that while meaningful scientific insight is important, the research comes from a public health-imposed restriction of human rights (quarantine). The author further discusses the ethical implications of quarantine, citing the Princess Diamond cruise ship as an example of how quarantine might exacerbate illness. The author concludes with an emphasis on the need to prioritize research benefits that outweigh the risks of forced quarantine and the infringement of liberties and to consider acknowledging the ethical dilemmas present in the research when publishing.

EPIDEMIOLOGY

THE BURDEN OF DISEASE DUE TO COVID-19 IN KOREA USING DISABILITY-ADJUSTED LIFE YEARS

Jo MW, Go DS, Kim R, Lee SW, Ock M, Kim YE, Oh IH, Yoon SJ, Park H.. J Korean Med Sci. 2020 Jun 1;35(21):e199. doi: 10.3346/jkms.2020.35.e199.

Level of Evidence: 4

BLUF

Researchers studied the burden of COVID-19 using Korea Centers for Disease Control and Prevention data from January 20-April 24, 2020 to determine Disability-Adjusted Life Years (DALYs), years of life lived with disability (YLDs), and years of life lost (YLLs) by sex and age for 10,708 COVID-19 positive patients in Korea. The majority of DALYs were derived from YLLs, indicating that to decrease the disease burden of COVID-19 in Korea, decision-makers should focus on reducing mortality in preparing for a second wave of COVID-19.

SUMMARY

Researchers discovered:

- Estimated COVID-19 disease burden was 2,531.0 total DALYs, and 4.930 DALYs per 100,000 population
- YLLs represented 89.7% of the total DALYs
- YLDs comprised 10.3% of the total DALYs
- YLDs were higher in females (155.2) than in males (105.1)
- Conversely, YLLs were higher in males (1,274.3) than in females (996.4)
- DALYs per 100,000 population were highest in people aged ≥ 80 years, followed by those aged 70-79, 60-69, and 50-59 years
- However, incidence of DALYs per 100,000 population was the highest in individuals aged 20-29 years

ABSTRACT

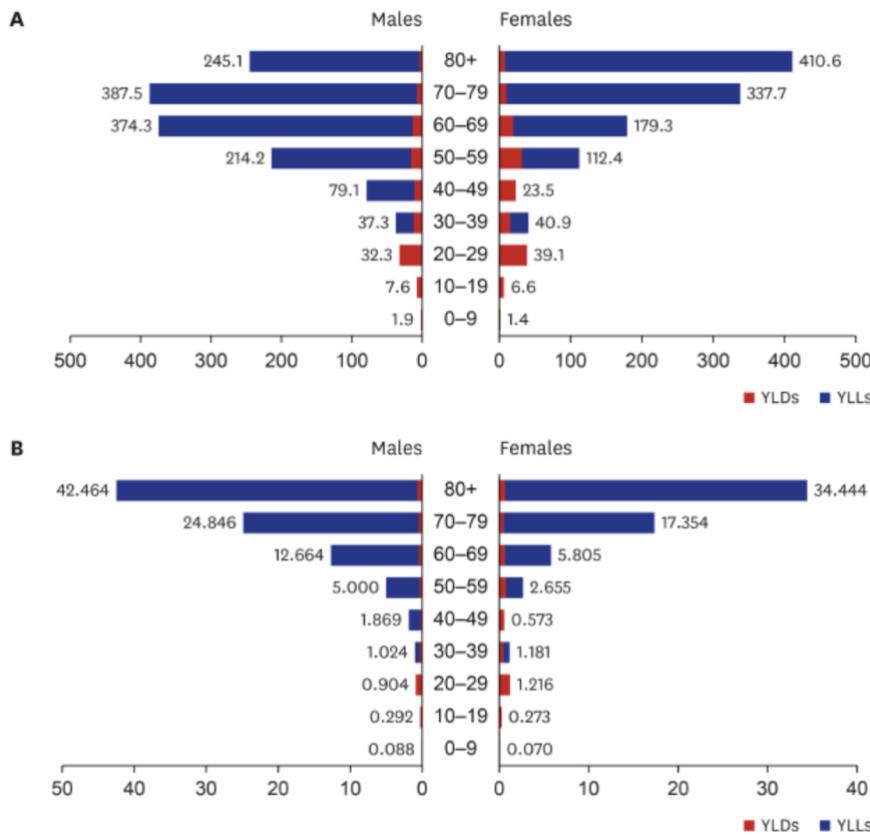
BACKGROUND: The world is currently experiencing a pandemic of coronavirus disease 2019 (COVID-19). In Korea, as in other countries, the number of confirmed cases and deaths due to COVID-19 have been rising. This study aimed to calculate the burden of disease due to COVID-19 in Korea.

METHODS: We used data on confirmed cases and deaths due to COVID-19 between January 20 and April 24, 2020 provided by the Korea Centers for Disease Control and Prevention, the local governments and the public media to determine disability-adjusted life years (DALYs) by sex and age. Morbidity was estimated directly among the confirmed, cured, and fatal cases. Disability weights were adopted from previous similar causes on the severity of COVID-19 for the years of life lived with disability (YLDs). The years of life lost (YLLs) were calculated using the standard life expectancy from the 2018 life tables for each sex and age.

RESULTS: The YLDs were higher in females (155.2) than in males (105.1), but the YLLs were higher in males (1,274.3) than in females (996.4). The total disease burden attributable to COVID-19 in Korea during the study period, was estimated to be 2,531.0 DALYs, and 4.930 DALYs per 100,000 population. The YLDs and the YLLs constituted 10.3% and 89.7% of the total DALYs, respectively. The DALYs per 100,000 population were highest in people aged ≥ 80 years, followed by those aged 70-79, 60-69, and 50-59 years, but the incidence was the highest in individuals aged 20-29 years.

CONCLUSION: This study provided the estimates of DALYs due to COVID-19 in Korea. Most of the disease burden from COVID-19 was derived from YLL; this indicates that decision-makers should focus and make an effort on reducing fatality for preparing the second wave of COVID-19.

FIGURES



Graphical abstract indicating total YLDs and YLLs (A) and YLDs and YLLs per 100,000 population (B) between males and females within stratified age groups.

MODELING

STATISTICAL ANALYSIS OF THE IMPACT OF ENVIRONMENTAL TEMPERATURE ON THE EXPONENTIAL GROWTH RATE OF CASES INFECTED BY COVID-19

Livadiotis G.. PLoS One. 2020 May 29;15(5):e0233875. doi: 10.1371/journal.pone.0233875. eCollection 2020.

Level of Evidence: Other

BLUF

Using temperature and growth-rate datasets from Italy and the U.S., statistical models were created at the Southwest Research Institute in San Antonio, Texas. Using this model the authors found a statistically significant negative correlation between temperature and exponential growth rate (no p-value given). 86.1°F ($\pm 4.3^{\circ}\text{F}$) was determined to be the temperature necessary to eliminate exponential growth of the SARS-CoV-2 virus. These findings may suggest that the virus transmits less effectively in warmer temperatures. See included figures for additional details on the case rate and temperature relationship examined.

ABSTRACT

We perform a statistical analysis for understanding the effect of the environmental temperature on the exponential growth rate of the cases infected by COVID-19 for US and Italian regions. In particular, we analyze the datasets of regional infected cases, derive the growth rates for regions characterized by a readable exponential growth phase in their evolution spread curve and plot them against the environmental temperatures averaged within the same regions, derive the relationship between temperature and growth rate, and evaluate its statistical confidence. The results clearly support the first reported statistically significant relationship of negative correlation between the average environmental temperature and exponential growth rates of the infected cases. The critical temperature, which eliminates the exponential growth, and thus the COVID-19 spread in US regions, is estimated to be $\text{TC} = 86.1 \pm 4.3 \text{ F}^{\circ}$.

FIGURES

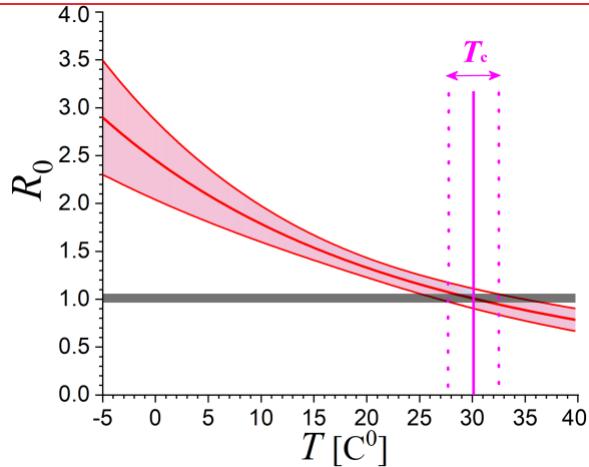


Figure 8. Relationship of the reproduction number R_0 and its uncertainty with environmental temperature T . According to this, new affected cases cease ($R_0 = 1$) when temperature climbs to $T_C \sim 30$ C° or (~86 F°).

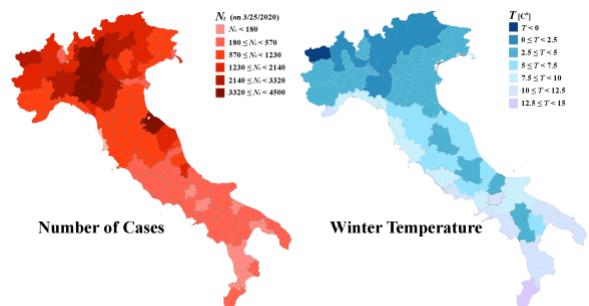


Figure 2. Regional distribution of infected cases N_t by 3/25/2020 (left), and average winter temperature T in mainland Italy (right).

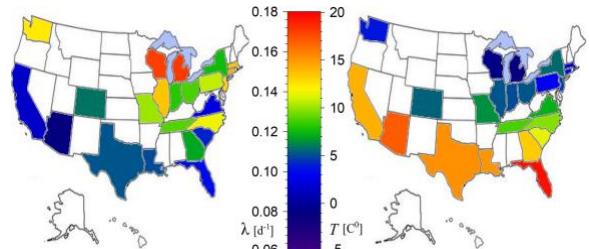


Figure 2. Regional distribution of infected cases N_t by 3/25/2020 (left), and average winter temperature T in mainland Italy (right).

SYMPTOMS AND CLINICAL PRESENTATION

PSYCHOPHYSICAL OLFACTORY TESTS AND DETECTION OF COVID-19 IN PATIENTS WITH SUDDEN ONSET OLFACTORY DYSFUNCTION: A PROSPECTIVE STUDY

Lechien JR, Cabaraux P, Chiesa-Estomba CM, Khalife M, Plzak J, Hans S, Martiny D, Calvo-Henriquez C, Barillari MR, Hopkins C, Saussez S.. Ear Nose Throat J. 2020 May 29:145561320929169. doi: 10.1177/0145561320929169. Online ahead of print.

Level of Evidence: 3

BLUF

This study assessed patients presenting with self reported sudden onset anosmia without other initial symptoms between April 6 - 10, 2020 in Mons, Belgium, to both determine if anosmia correlated with COVID-19 disease and to test olfactory

function among self reported anosmic patients with a "Sniffin Sticks" test. They found 87.5% of those reporting anosmia for less than 12 days were COVID-19 positive by RT-PCR, with positivity dropping to 23% in patients whose anosmia began over 12 days ago. Among those evaluated with a Sniffin Sticks test roughly 1 in 4 demonstrated normosmia, despite self reported anosmia. Their results suggest that COVID-19 should be considered in patients presenting with olfactory dysfunction.

ABSTRACT

OBJECTIVE: To investigate the coronavirus disease 2019 (COVID-19) status of patients with initial sudden olfactory anosmia (ISOA) through nasopharyngeal swabs for reverse transcription-polymerase chain reaction (RT-PCR) analysis and to explore their olfactory dysfunctions with psychophysical olfactory evaluation.

METHODS: A total of 78 ISOA patients were recruited from April 6, 2020, to April 10, 2020, through a public call of University of Mons (Mons, Belgium). Patients benefited from nasopharyngeal swabs and fulfilled the patient-reported outcome questionnaire. Among them, 46 patients performed psychophysical olfactory evaluation using olfactory identification testing. Based on the duration of the ISOA, 2 groups of patients were compared: patients with olfactory dysfunction duration ≤ 12 days (group 1) and those with duration > 12 days (group 2).

RESULTS: In group 1, 42 patients (87.5%) had a positive viral load determined by RT-PCR and 6 patients (12.5%) were negative. In group 2, 7 patients (23%) had a positive viral load and 23 patients (77%) were negative. The psychophysical olfactory evaluation reported that anosmia and hyposmia occurred in 24 (52%) and 11 (24%) patients, respectively. Eleven patients were normosmic. The viral load was significantly higher in patients of group 1 compared with those of group 2.

CONCLUSIONS: Coronavirus disease 2019 was detected in a high proportion of ISOA patients, especially over the first 12 days of olfactory dysfunction. Anosmia is an important symptom to consider in the detection of COVID-19 infection.

MAGNETIC RESONANCE IMAGING ALTERATION OF THE BRAIN IN A PATIENT WITH CORONAVIRUS DISEASE 2019 (COVID-19) AND ANOSMIA

Politi LS, Salsano E, Grimaldi M.. JAMA Neurol. 2020 May 29. doi: 10.1001/jamaneurol.2020.2125. Online ahead of print.
Level of Evidence: Other

BLUF

In this case report, researchers share magnetic resonance imaging (MRI) evidence of brain changes in the right gyrus rectus presumably due to SARS-CoV-2 infection in a 25 year old female patient with COVID-19 presenting predominantly with anosmia (Figure 1). A follow-up MRI performed 28 days later showed complete resolution of the previously seen changes (Figure 2). The timeline and patient's symptom status on day 28 is unclear, however, the authors do report she eventually recovered from the anosmia. These researchers speculate that SARS-CoV-2 may lead to neuroinvasion via the olfactory pathway, however additional studies are warranted to better understand this hypothesis.

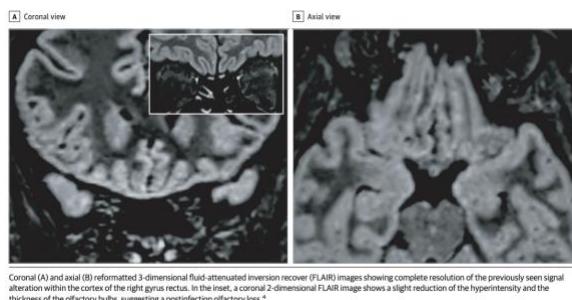
SUMMARY

Summarizing excerpt: "This is the first report of in vivo human brain involvement in a patient with COVID-19 showing a signal alteration compatible with viral brain invasion in a cortical region (ie, posterior gyrus rectus) that is associated with olfaction. Alternative diagnoses...are unlikely given the clinical context. Based on the MRI findings, including the slight olfactory bulb changes, we can speculate that SARS-CoV-2 might invade the brain through the olfactory pathway and cause an olfactory dysfunction of sensorineural origin; cerebrospinal fluid and pathology studies are required to confirm this hypothesis. Ours and others' observations of normal brain imaging in other patients with COVID-19-associated olfactory dysfunctions and the disappearance of the cortical MRI abnormalities in the follow-up study of this patient suggest that imaging changes are not always present in COVID-19 or might be limited to the very early phase of the infection. Further, anosmia can be the predominant COVID-19 manifestation, and this should be considered for the identification and isolation of patients with infection to avoid disease spread."

FIGURES



Figure 1. Brain Magnetic Resonance Imaging Alterations in a Patient With Coronavirus Disease 2019 (COVID-19) Presenting With Anosmia 4 Days From Symptom Onset



Coronal (A) and axial (B) reformatted 3-dimensional fluid-attenuated inversion recovery (FLAIR) images showing complete resolution of the previously seen signal alteration within the cortex of the right gyrus rectus. In the inset, a coronal 2-dimensional FLAIR image shows a slight reduction of the hyperintensity and the thickness of the olfactory bulbs, suggesting a postinfection olfactory loss.*

Figure 2. Follow-up Magnetic Resonance Imaging Study in the Same Patient 28 Days From Symptom Onset

ADULTS

CHARACTERIZATION AND CLINICAL COURSE OF 1000 PATIENTS WITH CORONAVIRUS DISEASE 2019 IN NEW YORK: RETROSPECTIVE CASE SERIES

Argenziano MG, Bruce SL, Slater CL, Tiao JR, Baldwin MR, Barr RG, Chang BP, Chau KH, Choi JJ, Gavin N, Goyal P, Mills AM, Patel AA, Romney MS, Safford MM, Schluger NW, Sengupta S, Sobieszczyk ME, Zucker JE, Asadourian PA, Bell FM, Boyd R, Cohen MF, Colquhoun MI, Colville LA, de Jonge JH, Dershowitz LB, Dey SA, Eiseman KA, Girvin ZP, Goni DT, Harb AA, Herzik N, Householder S, Karaaslan LE, Lee H, Lieberman E, Ling A, Lu R, Shou AY, Sisti AC, Snow ZE, Sperring CP, Xiong Y, Zhou HW, Natarajan K, Hripcsak G, Chen R.. BMJ. 2020 May 29;369:m1996. doi: 10.1136/bmj.m1996.

Level of Evidence: 3

BLUF

A retrospective study characterizing the first 1000 patients diagnosed with COVID-19 by RT-PCR at the New York-Presbyterian/Columbia University Irving Medical Center found a bimodal distribution in length of time to intubation (modes of 3-4 days & 9 days after symptom onset) and prolonged intubation time for patients still hospitalized (median time: 28.5 days). There were also high percentages of acute kidney injury (78%) and patients requiring dialysis (35.2%). Their findings suggest that careful clinical monitoring may be warranted for patients who are 5-8 days post-symptom onset and can help inform clinicians to anticipate disease progression (figure 1 & 2).

ABSTRACT

OBJECTIVE: To characterize patients with coronavirus disease 2019 (covid-19) in a large New York City medical center and describe their clinical course across the emergency department, hospital wards, and intensive care units. **DESIGN:**

Retrospective manual medical record review.

SETTING: New York-Presbyterian/Columbia University Irving Medical Center, a quaternary care academic medical center in New York City.

PARTICIPANTS: The first 1000 consecutive patients with a positive result on the reverse transcriptase polymerase chain reaction assay for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) who presented to the emergency department or were admitted to hospital between 1 March and 5 April 2020. Patient data were manually abstracted from electronic medical records.

MAIN OUTCOME MEASURES: Characterization of patients, including demographics, presenting symptoms, comorbidities on presentation, hospital course, time to intubation, complications, mortality, and disposition.

RESULTS: Of the first 1000 patients, 150 presented to the emergency department, 614 were admitted to hospital (not intensive care units), and 236 were admitted or transferred to intensive care units. The most common presenting symptoms were cough (732/1000), fever (728/1000), and dyspnea (631/1000). Patients in hospital, particularly those treated in intensive care units, often had baseline comorbidities including hypertension, diabetes, and obesity. Patients admitted to intensive care units were older, predominantly male (158/236, 66.9%), and had long lengths of stay (median 23 days, interquartile range 12-32 days); 78.0% (184/236) developed acute kidney injury and 35.2% (83/236) needed dialysis. Only 4.4% (6/136) of patients who required mechanical ventilation were first intubated more than 14 days after symptom onset. Time to intubation from symptom onset had a bimodal distribution, with modes at three to four days, and at nine days. As of 30 April, 90 patients remained in hospital and 211 had died in hospital.

CONCLUSIONS: Patients admitted to hospital with covid-19 at this medical center faced major morbidity and mortality, with high rates of acute kidney injury and inpatient dialysis, prolonged intubations, and a bimodal distribution of time to intubation from symptom onset.

FIGURES

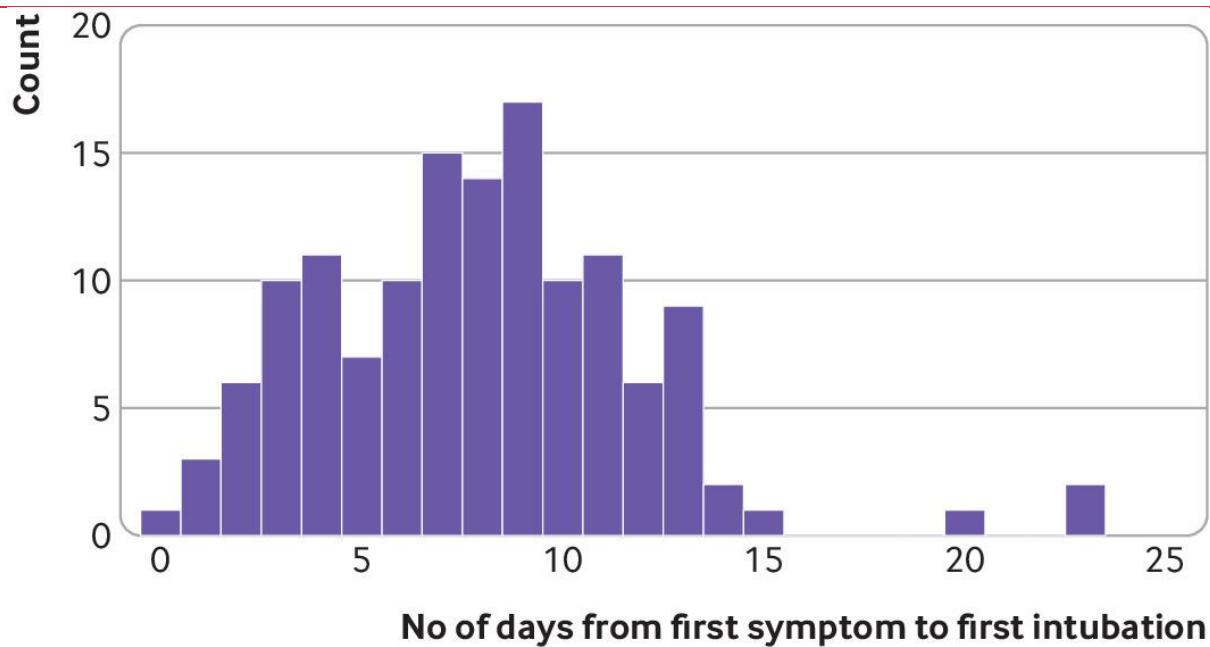


Figure 1: Bimodal distribution (3-4 days, 9 days) of time to intubation from COVID-19 symptom onset.

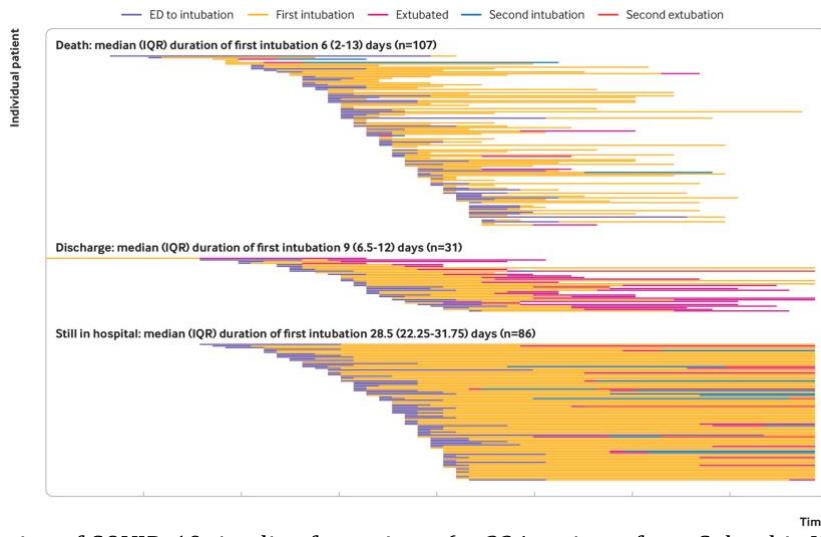


Figure 2: Pictorial depiction of COVID-19 timeline for patients (n=224 patients from Columbia University Irving Medical Center).

COVID-19 PATIENTS WITH HYPERTENSION HAVE MORE SEVERE DISEASE: A MULTICENTER RETROSPECTIVE OBSERVATIONAL STUDY

Huang S, Wang J, Liu F, Liu J, Cao G, Yang C, Liu W, Tu C, Zhu M, Xiong B.. Hypertens Res. 2020 Jun 1. doi: 10.1038/s41440-020-0485-2. Online ahead of print.

Level of Evidence: 4

BLUF

The authors performed a retrospective observational study at two hospitals in Wuhan, China (n=310 patients with COVID-19) and found that patients with hypertension were more likely to be older and have more severe progression of COVID-19 based on ICU admission, elevated D-dimer, and higher mortality (Table 3). However, a multivariate regression analysis adjusting for

age and sex did not show hypertension as a statistically significant risk factor for greater COVID-19 disease severity or mortality (Table 5). These findings suggest hypertension may be a risk factor worth monitoring for severe COVID-19 disease progression, but more studies with larger sample sizes are needed.

ABSTRACT

This study aims to explore the effect of hypertension on disease progression and prognosis in patients with coronavirus disease 2019 (COVID-19). A total of 310 patients diagnosed with COVID-19 were studied. A comparison was made between two groups of patients, those with hypertension and those without hypertension. Their demographic data, clinical manifestations, laboratory indicators, and treatment methods were collected and analyzed. A total of 310 patients, including 113 patients with hypertension and 197 patients without hypertension, were included in the analysis. Compared with patients without hypertension, patients with hypertension were older, were more likely to have diabetes and cerebrovascular disease, and were more likely to be transferred to the intensive care unit. The neutrophil count and lactate dehydrogenase, fibrinogen, and D-dimer levels in hypertensive patients were significantly higher than those in nonhypertensive patients ($P < 0.05$). However, multivariate analysis (adjusted for age and sex) failed to show that hypertension was an independent risk factor for COVID-19 mortality or severity. COVID-19 patients with hypertension were more likely than patients without hypertension to have severe pneumonia, excessive inflammatory reactions, organ and tissue damage, and deterioration of the disease. Patients with hypertension should be given additional attention to prevent worsening of their condition.

FIGURES

	Total (n = 225)	Nonhypertension (n = 160)	Hypertension (n = 65)	P value
Age, years	59 (45–68)	54 (38–67)	66 (56–71)	<0.001
Sex	–	–	–	0.728
Female	101 (44.9%)	73 (45.6%)	28 (43.1%)	
Male	124 (55.1%)	87 (54.4%)	37 (56.9%)	
Signs and symptoms				
Fever	190 (84.4%)	136 (85%)	54 (83.1%)	0.718
Cough	143 (63.6%)	108 (67.5%)	35 (53.8%)	0.054
Dyspnea	113 (50.2%)	76 (47.5%)	37 (56.9%)	0.200
Expectoration	39 (17.3%)	32 (20.0%)	7 (10.8%)	0.097
Muscle ache	19 (8.4%)	12 (7.5%)	7 (10.8%)	0.424
Diarrhea	24 (10.7%)	13 (8.1%)	11 (16.9%)	0.053
Headache	2 (0.9%)	1 (0.6%)	1 (1.5%)	0.495
Treatments and prognosis				
Noninvasive mechanical ventilation	25 (11.1%)	16 (10.0%)	9 (13.8%)	0.405
Invasive mechanical ventilation	22 (9.8%)	12 (7.5%)	10 (15.4%)	0.071
ECMO	3 (1.3%)	1 (0.6%)	2 (3.1%)	0.201
ICU admission	32 (14.2%)	18 (11.3%)	14 (21.5%)	0.045
Duration of viral shedding after COVID-19 onset, days	8.0 (6.0–12.0)	9.0 (8.0–11.5)	8.5 (5.0–14.0)	0.044
Disease severity	–	–	–	
Non-severe	122 (54.2%)	99 (61.9%)	23 (35.4%)	
Severe	103 (45.8%)	61 (38.1%)	42 (64.6%)	<0.001
Death	37 (16.4%)	23 (14.4%)	14 (21.5%)	0.189
Hospitalization time, days	18.00 (12.00–26.00)	14.00 (10.25–25.25)	13.50 (10.50–22.75)	0.409

ECMO extracorporeal membrane oxygenation, ICU intensive care unit

Table 3. Baseline characteristics and treatments of hypertensive and non-hypertensive COVID-19 patients without other comorbidities.

	OR (95%CI)	P value
Severity as dependent variable		
Hypertension	1.562 (0.929–2.625)	0.092
Age, years	1.049 (1.030–1.067)	<0.001
Female sex(vs male)	0.523 (0.319–0.856)	0.010
Mortality as dependent variable		
Hypertension	1.262 (0.683–2.332)	0.458
Age, years	1.042 (1.018–1.066)	<0.001
Female sex(vs male)	0.476 (0.254–0.893)	0.021

OR odds ratio, 95% CI 95% confidence interval.

Table 5. Outcome of multivariable logistic regression.

PREDICTORS FOR SEVERE COVID-19 INFECTION

Bhargava A, Fukushima EA, Levine M, Zhao W, Tanveer F, Szpunar SM, Saravolatz L.. Clin Infect Dis. 2020 May 30:ciaa674. doi: 10.1093/cid/ciaa674. Online ahead of print.

Level of Evidence: 4

BLUF

A retrospective case series conducted at Ascension St. John Hospital in Detroit, Michigan between March 8 and April 8, 2020 involving 197 patients (82.1% black) with reverse transcriptase (RT)-PCR-confirmed COVID-19 found that acute renal injury, pre-existing renal disease, increased oxygen requirement at time of admission, and initial C-reactive protein at time of admission are risk factors for severe COVID-19 infection, suggesting that early recognition of these risk factors may lead to quicker initiation of aggressive treatment and, ultimately, improved outcomes.

ABSTRACT

BACKGROUND: COVID-19 is a pandemic disease caused by a novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Predictors for severe COVID-19 infection have not been well defined. Determination of risk factors for severe infection would enable identifying patients who may benefit from aggressive supportive care and early intervention.

METHODS: We conducted a retrospective observational study of 197 patients with confirmed COVID-19 infection admitted to a tertiary academic medical center.

RESULTS: Of 197 hospitalized patients, the mean (SD) age of the cohort was 60.6 (16.2) years, 103 (52.3%) were male and 156 (82.1%) were black. Severe COVID-19 infection was noted in 74 (37.6%) patients, requiring intubation. Patients aged above 60 were significantly more likely to have severe infection. Patients with severe infection were significantly more likely to have diabetes, renal disease, chronic pulmonary disease and had significantly higher white blood cell counts, lower lymphocyte counts, and increased C-reactive protein (CRP) compared to patients with non-severe infection. In multivariable logistic regression analysis, risk factors for severe infection included pre-existing renal disease (odds ratio [OR], 7.4; 95% CI 2.5-22.0), oxygen requirement at hospitalization (OR, 2.9; 95% CI, 1.3-6.7), acute renal injury (OR, 2.7; 95% CI 1.3-5.6) and initial CRP (OR, 1.006; 95% CI, 1.001-1.01). Race, age and socioeconomic status were not identified as independent predictors.

CONCLUSIONS: Acute or pre-existing renal disease, supplemental oxygen at the time of hospitalization and initial CRP were independent predictors for the development of severe COVID-19 infections. Every 1 unit increase in CRP increased the risk of severe disease by 0.06%.

COVID-19 ASSOCIATED CENTRAL NERVOUS SYSTEM VASCULOPATHY

Matos AR, Quintas-Neves M, Oliveira AI, Dias L, Marques S, Carvalho R, Alves JN.. Can J Neurol Sci. 2020 Jun 2:1-6. doi: 10.1017/cjn.2020.109. Online ahead of print.

Level of Evidence: Other

BLUF

A case study conducted at the Hospital de Braga in Portugal found an associated central nervous system vasculopathy as a rare complication of COVID-19. Specific details discussed below.

SUMMARY

A 42 year old man with a history of previous positive COVID-19 titer presents with altered mental status, slowness of movement, and apathy one week after previous hospitalization. Blood work up was negative and cerebrospinal fluid showed increased protein without pleocytosis with a negative SARS-CoV-2 titer. CT showed "multiple hypodense lesions involving the white matter, basal ganglia and thalamus" suggestive of ischemic lesions affecting several arterial territories, including deep watershed zones (Figure 1). The patient was started on IV immunoglobulin and steroids to treat a possible infectious vasculopathy and patient showed no new lesions on subsequent imaging.

FIGURES

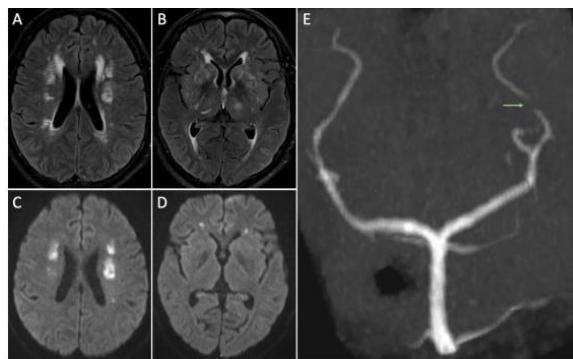


Figure 1. (A,B) Axial FLAIR sequence depicts multiple hyperintense lesions involving the deep and subcortical white matter on both hemispheres, as well as the thalamus and basal ganglia; some of the lesions showed restricted diffusion on DWI (C,D), namely on both corona radiata and bilateral deep frontal white matter. (E) 3D TOF sequence, MIP reconstruction on coronal view reveals prominent irregularity (arrow) on the P3 segment of the left posterior cerebral artery.

PEDIATRICS

FOCAL CEREBRAL ARTERIOPATHY IN A COVID-19 PEDIATRIC PATIENT

Mirzaee SMM, Gonçalves FG, Mohammadifard M, Tavakoli SM, Vossough A.. Radiology. 2020 Jun 2:202197. doi: 10.1148/radiol.2020202197. Online ahead of print.

Level of Evidence: 5

BLUF

A group of neurologists and radiologists from Iran report a presumptive case of focal cerebral arteriopathy resulting in ischemic stroke (Figure 1) and neurological deficits in a pediatric COVID-19 patient. The authors detected SARS-CoV-2 viral particles in both the CSF and via a nasopharyngeal swab although there were no respiratory abnormalities observed. They present this case to increase awareness of neurological susceptibility to SARS-CoV-2 as illustrated by this uncommon presentation.

FIGURES

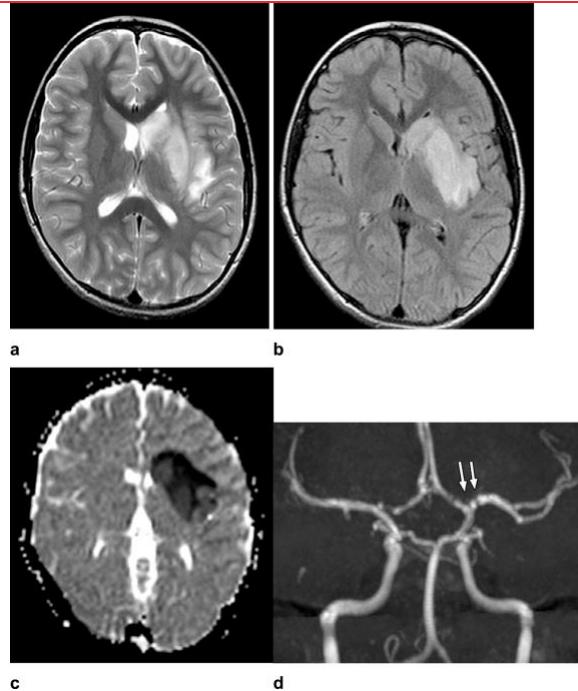


Figure 1. Axial T2-weighted (a) and FLAIR (b) Magnetic resonance imaging show diffuse hyperintense signal and edema of the caudate nucleus head, putamen, anterior limb of the internal capsule, and parts of external capsule and insula on the left side, with corresponding low values on the axial apparent diffusion coefficient map, in keeping with an acute infarct. Time-of-flight magnetic resonance angiography maximal intensity projection reformatted image demonstrates focal irregular narrowing and

banding of the proximal left M1 segment of the middle cerebral artery with a slightly reduced distal flow in the middle cerebral artery.

COVID-19 INFECTION IS A DIAGNOSTIC CHALLENGE IN INFANTS WITH ILEOCECAL INTUSSUSCEPTION

Martínez-Castaño I, Calabuig-Barbero E, González-Piñera J, López-Ayala JM.. Pediatr Emerg Care. 2020 Jun;36(6):e368. doi: 10.1097/PEC.0000000000002155.

Level of Evidence: 5

BLUF

Pediatric specialists in Spain present the case of a 6-month-old boy, positive for SARS-CoV-2 by RT-PCR, who presented with history and ultrasound findings consistent with ileocecal intussusception. This case suggests a possible association between SARS-CoV-2 infection and pediatric intussusception, however more data is needed.

ADVANCED AGE

FIRST CASE OF FOCAL EPILEPSY ASSOCIATED WITH SARS-CORONAVIRUS-2

Elgamasy S, Kamel MG, Ghozy S, Khalil A, Morra ME, Islam SMS.. J Med Virol. 2020 Jun 2. doi: 10.1002/jmv.26113. Online ahead of print.

Level of Evidence: 5

BLUF

A 73-year-old female patient admitted to a hospital in Germany for multiple episodes of focal epilepsy and subsequently developed fever/cough and tested positive for SARS-CoV-2 on hospital day 5; the patient reported no further episodes after making a full recovery (Figure 1). The authors suggest that early SARS-CoV-2 infection could present with neurological symptoms such as focal epilepsy, thus clinicians should consider COVID-19 in patients with similar presentations

ABSTRACT

A healthy patient presented to Klinikum Altmühlfranken Weissenburg Hospital, Germany, with two-morning attacks of painful muscle spasm in left upper and lower limbs, without altered consciousness. Full examinations, radiological imaging, electroencephalography, lumbar puncture, and autoimmune profile were either normal or not consistent. Subsequent epileptic episodes were observed on admission day and following days; thus, the patient was diagnosed with focal epilepsy. The patient started to develop a fever and severe cough at day 4, and SARS-Coronavirus-2 was confirmed through a nasopharyngeal swap. She received anticonvulsants and symptomatic treatments and completely recovered. This report emphasizes on potential nervous system involvement in SARS-Coronavirus-2 pathogenesis. This article is protected by copyright. All rights reserved.

FIGURES

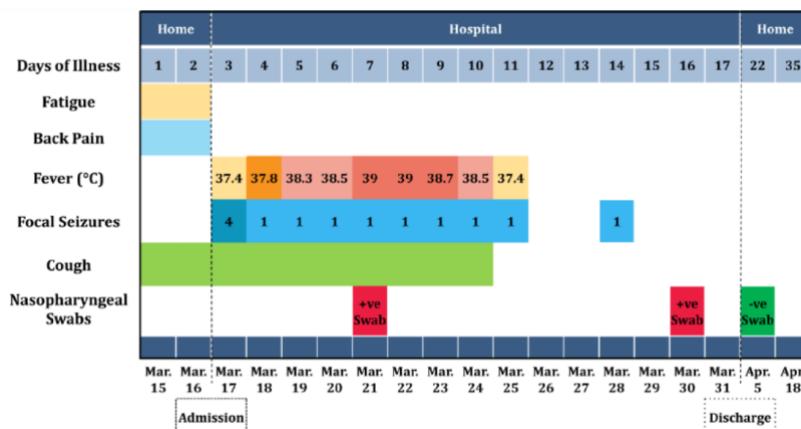


Figure 1. Symptoms and maximum body temperatures based on the day of illness and day of hospitalization, from March 15 to April 18, 2020.

UNDERSTANDING THE PATHOLOGY

IN VITRO

COVID-19: ORGANOID GO VIRAL

Clevers H.. Nat Rev Mol Cell Biol. 2020 Jun 1. doi: 10.1038/s41580-020-0258-4. Online ahead of print.

Level of Evidence: Other

BLUF

A review from the Netherlands highlights the importance of organoids, a novel in-vitro method, in the investigation of SARS-CoV-2 and virology as a whole. Utilizing both induced pluripotent stem cells and multipotent adult tissue stem cells, the method establishes an in-vitro model that more closely mimics in-vivo physiology by creating organ specific cell lines that mimic structure and function of in-vivo organs. The author suggests that this new method could change the landscape of virology research and minimize the impact of testing on animals and mammals.

TRANSMISSION & PREVENTION

SARS-COV-2 INFECTION IN HEALTH CARE WORKERS: CROSS-SECTIONAL ANALYSIS OF AN OTOLARYNGOLOGY UNIT

Paderno A, Fior M, Berretti G, Schreiber A, Grammatica A, Mattavelli D, Deganello A.. Otolaryngol Head Neck Surg. 2020 Jun 2:194599820932162. doi: 10.1177/0194599820932162. Online ahead of print.

Level of Evidence: 3

BLUF

In this cross sectional study, the entire staff of an otolaryngology unit (n=58) in a location in Italy with high COVID-19 prevalence was tested for SARS-CoV-2 (by both serology with a SARS-CoV-2 immunoglobulin G (IgG) immunoassay and nasopharyngeal RT-PCR) and staff also filled out a survey regarding exposure history, both in and out of the hospital. Five staff members (9%) tested positive, and subsequent survey results showed that increased out of hospital COVID-19 contact exposure without personal protective equipment (PPE) was associated with a higher risk of infection ($p=0.008$), suggesting that healthcare workers should practice cautious PPE use outside of the hospital.

ABSTRACT

The restart of routine in- and outpatient activity in the COVID-19 postepidemic peak needs to be carefully planned in light of specific patterns of viral diffusion. We evaluated SARS-CoV-2 serology in the entire personnel of a COVID-19-free otolaryngology department in a highly affected area. The aim was to determine the prevalence of SARS-CoV-2 positivity among staff to clarify the impact of different risk factors for infection. The entire staff of the otolaryngology unit was tested for SARS-CoV-2 serology. Symptomatic staff members were tested with nasal/pharyngeal swabs. All answered a survey focused on the number of in- and extrahospital positive contacts and type of activities in the unit. Five (9%) were positive for SARS-CoV-2 infection. The only variable associated with a higher risk of infection was the number of extrahospital contacts without personal protective equipment ($P = .008$). Our study shows that in non-COVID-19 departments, the use of adequate personal protective equipment leads to low rates of infection among health care workers. The prevalent risk of infection was related to extrahospital contact.

IT IS CURRENTLY UNKNOWN WHETHER SARS-COV-2 IS VIABLE IN SEMEN OR WHETHER COVID-19 DAMAGES SPERM

Perry MJ, Arrington S, Neumann LM, Carrell D, Mores CN.. Andrology. 2020 May 29. doi: 10.1111/andr.12831. Online ahead of print.

Level of Evidence: 3

BLUF

This review summarizes the scant current knowledge regarding possible presence and infectivity of SARS-CoV-2 in semen. Given some evidence that SARS-CoV-2 can be found in semen samples, the authors urge increased research on this topic to help understand the true risks and implications for possible sexual transmission and potential impact on assisted reproductive technologies.

SUMMARY

This review sought to summarize the current knowledge regarding the potential presence and effect of SARS-CoV-2 in semen. There are few studies on this topic to date, and most show conflicting results. The article highlights one study of 38 confirmed cases of COVID-19 that found 4 out of 15 patients (26.7%) in the acute stage of infection and 2 out of 23 patients (8.7%) in the recovery phase had detectable levels of SARS-CoV-2 present in semen. The authors state that as there are many asymptomatic carriers of the disease, it is important to determine the virus' presence in semen. This is of special significance as it helps to determine whether COVID-19 is sexually transmitted and as viral transmission may also be seen during assisted reproductive technologies, including intracytoplasmic sperm injection, which may have an effect on early embryogenesis and fetal development.

ABSTRACT

Research is needed to understand the presence of the SARS-CoV-2 virus in semen, sexual transmissibility, and impact on sperm quality. Several studies have examined men recovering from COVID-19, but large-scale community-based testing is needed to ascertain the effects on the male reproductive tract, and the potential for prolonged transmission.

UNIVERSAL MASKING IN THE COVID-19 ERA

Klompas M, Morris CA, Shenoy ES.. N Engl J Med. 2020 Jun 3. doi: 10.1056/NEJMc2020836. Online ahead of print.

Level of Evidence: Other

BLUF

Boston physicians respond to critique that their previous article seemed to discredit universal public face masking. They clarify their emphasis was on low transmission risk in brief, passing encounters and that masks appear most useful in preventing transmission for sustained interactions in enclosed spaces where people cannot maintain a distance of 6 ft.

DEVELOPMENTS IN TRANSMISSION & PREVENTION

SURGICAL MASK PARTITION REDUCES THE RISK OF NON-CONTACT TRANSMISSION IN A GOLDEN SYRIAN HAMSTER MODEL FOR CORONAVIRUS DISEASE 2019 (COVID-19)

Chan JF, Yuan S, Zhang AJ, Poon VK, Chan CC, Lee AC, Fan Z, Li C, Liang R, Cao J, Tang K, Luo C, Cheng VC, Cai JP, Chu H, Chan KH, To KK, Sridhar S, Yuen KY.. Clin Infect Dis. 2020 May 30:ciaa644. doi: 10.1093/cid/ciaa644. Online ahead of print.

Level of Evidence: 4

BLUF

Chinese researchers performed 3 experiments and demonstrated that surgical mask partitioning significantly reduced non-contact (respiratory droplet or aerosol) transmission of SARS-CoV-2 from infected hamsters.

- Infected challenged index hamsters (total n= 13; 5, 4, 4 for experiment 1, 2, 3)
- Exposed naïve hamsters (total n=26; 10, 8, 8 for experiment 1, 2, 3)
- Without masking, they found 6 out of 10 naïve hamsters were infected after being exposed to challenged index hamsters and that masking the SARS-CoV-2 challenged index hamsters provided a statistically significant reduction in virus transmission compared to masking the naïve hamsters ($p=0.018$ for any masking) (Table 3).
- See Figure 1 and Figure 6 for further details on experimental set-up and results.

Given that SARS-CoV-2 can be transmitted from asymptomatic infected individuals, the researchers encourage community-wide masking in order to reduce disease spread.

ABSTRACT

BACKGROUND: Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is believed to be mostly transmitted by medium-to-large sized respiratory droplets although airborne transmission is theoretically possible in healthcare settings involving aerosol-generating procedures. Exposure to respiratory droplets can theoretically be reduced by surgical mask usage. However, there is a lack of experimental evidence supporting surgical mask usage for prevention of COVID-19.

METHODS: We used a well-established golden Syrian hamster SARS-CoV-2 model. We placed SARS-CoV-2-challenged index hamsters and naive hamsters into closed system units each comprising two different cages separated by a polyvinyl chloride air porous partition with unidirectional airflow within the isolator. The effect of a surgical mask partition placed in between the cages was investigated. Besides clinical scoring, hamster specimens were tested for viral load, histopathology, and viral nucleocapsid antigen expression.

RESULTS: Non-contact transmission was found in 66.7% (10/15) of exposed naive hamsters. Surgical mask partition for challenged index or naive hamsters significantly reduced transmission to 25% (6/24, $P=0.018$). Surgical mask partition for challenged index hamsters significantly reduced transmission to only 16.7% (2/12, $P=0.019$) of exposed naive hamsters. Unlike the severe COVID-19 manifestations of challenged hamsters, infected naive hamsters had lower clinical scores, milder histopathological changes, and lower viral nucleocapsid antigen expression in respiratory tract tissues.

CONCLUSIONS: SARS-CoV-2 could be transmitted by respiratory droplets or airborne droplet nuclei in the hamster model. Such transmission could be reduced by surgical mask usage, especially when masks were worn by infected individuals.

FIGURES

Group	5 dpi	P-value ^a	7 dpi	P-value ^a	Total	P-value ^a
Naïve (no mask)	6/10 (60.0%)		4/5 (80.0%)		10/15 (66.7%)	
Naïve (any mask)	4/16 (25.0%)	0.109	2/8 (25.0%)	0.103	6/24 (25.0%)	0.018
Naïve (masked index)	1/8 (12.5%)	0.066	1/4 (25.0%)	0.206	2/12 (16.7%)	0.019
Naïve (masked naïve)	3/8 (37.5%)	0.637	1/4 (25.0%)	0.206	4/12 (33.3%)	0.128

^aP-values represent comparison between the naïve (no mask) group with the other groups (Fisher's exact test).

Table 3. Non-contact transmission rate from challenged hamsters to exposed naïve hamsters with or without surgical mask partition.

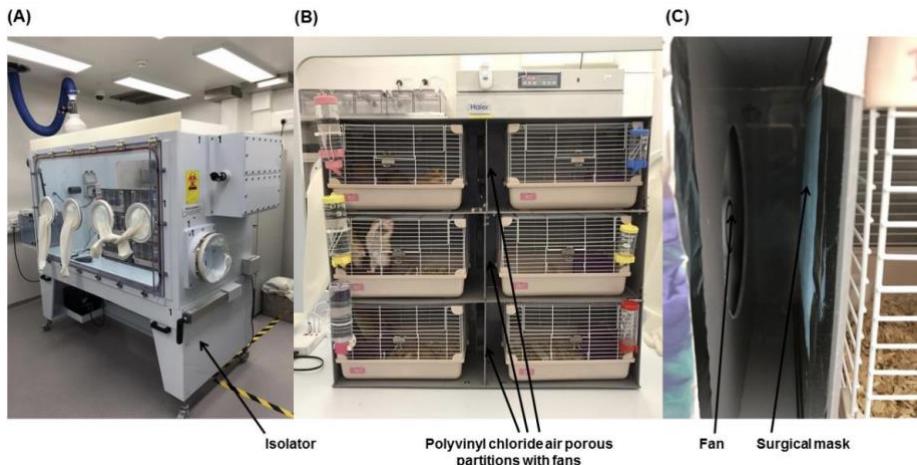


Figure 1. Non-contact transmission of SARS-CoV-2 in the Syrian hamster model. (A)

The closed systems housing the hamsters were placed in the isolator in a Biosafety Level-3 laboratory. (B) Enlarged view of the closed systems used in the non-contact transmission studies. Each system contained two cages (left and right) separated by a polyvinyl chloride air porous partition. An electrically powered fan was installed at the polyvinyl chloride air porous partition to ensure unidirectional airflow from the cage housing the challenged index hamsters to the cage housing the naïve hamsters. (C) Surgical mask partition with the blue external surface facing the challenged hamsters in experiment 3.

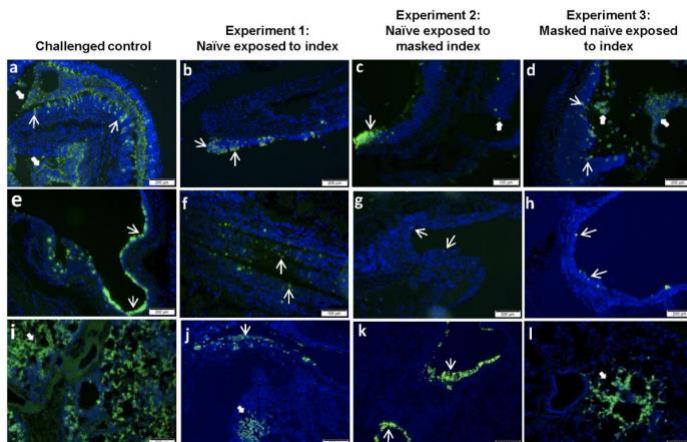


Figure 1. Non-contact transmission of SARS-CoV-2 in the Syrian hamster model. (A)

The closed systems housing the hamsters were placed in the isolator in a Biosafety Level-3 laboratory. (B) Enlarged view of the closed systems used in the non-contact transmission studies. Each system contained two cages (left and right) separated by a polyvinyl chloride air porous partition to ensure unidirectional airflow from the cage housing the challenged index hamsters to the cage housing the naïve hamsters. (C) Surgical mask partition with the blue external surface facing the challenged hamsters in experiment 3.

DETECTABLE SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2 (SARS-CoV-2) IN HUMAN BREAST MILK OF A MILDLY SYMPTOMATIC PATIENT WITH CORONAVIRUS DISEASE 2019 (COVID-19)

Tam PCK, Ly KM, Kernich ML, Spurrier N, Lawrence D, Gordon DL, Tucker EC.. Clin Infect Dis. 2020 May 30:ciaa673. doi: 10.1093/cid/ciaa673. Online ahead of print.

Level of Evidence: 5

BLUF

A case study in Australia of a 40-year-old mother with mild symptoms of COVID-19 and her 8-month old son in March 2020 found what may be the first case of SARS-CoV-2 RNA detected in breast milk via RT-PCR. The patient was actively breastfeeding until symptom onset and samples were obtained 5 days later. The significance of this finding is unclear, as only 2 of 7 serial breast milk samples returned positive results, and the sample showed the presence of RNA, but did not test viral activity or infectivity (figure 1). The eight-month old son also tested positive via oropharyngeal swab, and he secreted SARS-CoV-2 RNA in his stool for 66 days.

ABSTRACT

SARS-CoV-2 is a novel coronavirus and causative pathogen to the pandemic illness COVID-19. Although RNA has been detected in various clinical samples, no reports to date have documented SARS-CoV-2 in human milk. This case report describes an actively breastfeeding patient with COVID-19 infection with detectable viral RNA in human milk.

FIGURES

Figure 1

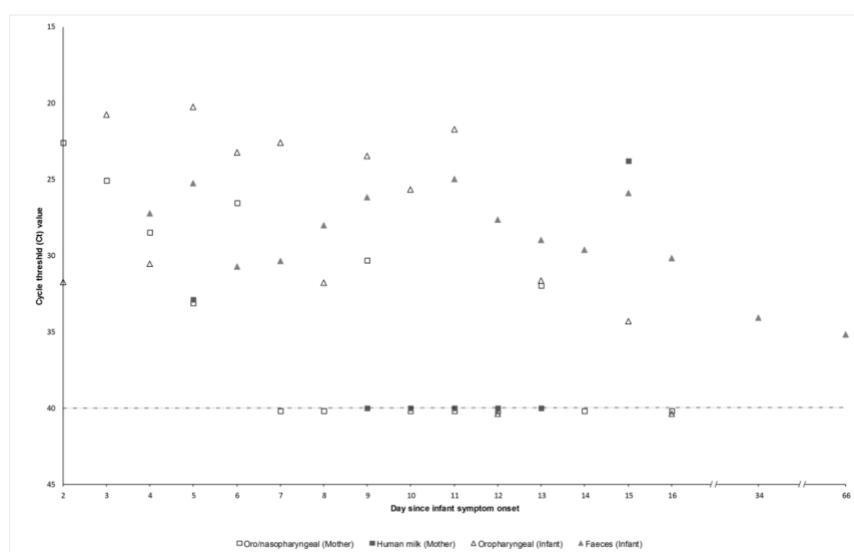


Figure 1: Cycle thresholds (Ct) values for the envelope protein gene (E-gene) target for collected specimens. A single flock swab was used in the mother to collect combined oral and nasopharyngeal samples. A Ct value ≥ 40 is interpreted as undetectable.

VENTILATED UPPER AIRWAY ENDOSCOPIC ENDONASAL PROCEDURE MASK: SURGICAL SAFETY IN THE COVID-19 ERA

Helman SN, Soriano RM, Tomov ML, Serpooshan V, Levy JM, Pradilla G, Solares CA.. Oper Neurosurg (Hagerstown). 2020 May 30:opaa168. doi: 10.1093/ons/opaa168. Online ahead of print.

Level of Evidence: Other

BLUF

In an effort to create a safer working environment for the surgical team during skull base surgery in the COVID19 era, clinicians from Emory University developed and tested a 3D-printed upper airway endoscopic procedure mask. The mask was demonstrated to reduce aerosolized particle transmission while maintaining "surgical freedom (SF)" for skull base surgery. They also tested a modified nasal trocar that can be used in facilities without 3D-printing capabilities. This method also resulted in decreased particle transmission in posterior nasal surgery, but less so than the 3D-mask. The modified trochar was

considered less effective for anterior nasal procedures. Of note, the tests were performed on cadavers, not live subjects. See Table 1 and 2 and Figure 3 for additional details.

SUMMARY

Using both experimental devices discussed above (3D-mask and modified nasal tracer) surgical freedom (SF) and aerosolization of particles were compared in endoscopic procedures performed on two cadaveric specimens.

1. Aerosolization

-Particles were sprayed into the cadaver's nasal cavities, the body was ventilated, and aerosols were measured in a 4-quadrant field (Figure 3).

- 2.5 mL of fluorescein (AK-FLOR® 10%, 100 mg/mL) was used to coat the nasal cavity for each trial

- Analysis Protocol: "Endoscopic images of each quadrant were exported for analysis and uploaded to Image J (version 1.52v). Images underwent brightness and contrast adjustment to 0-pixel intensity and filtering with a minimum of 1 pixel and were converted into grayscale and underwent thresholding with a lower limit of 0 and an upper limit of 100. Images with droplets present underwent particle analysis to determine the number of droplets present in each image."

- Both devices resulted in subjective reductions in the amount of "spillage" of particles compared to no device (Table 1 and 2).

2. Surgical freedom (SF)

- Defined as the "maximum area in which a surgeon is able to move the proximal end of the instrument while the distal end is fixed on a target."

- The 3D-printed mask allowed for the highest degree of SF (100%) in both posterior and anterior nasal procedures.

- The modified trocar reduced SF (55%) in anterior nasal procedures, but maintained subjectively 'appropriate' SF in posterior procedures from the testing surgeon's experience.

ABSTRACT

BACKGROUND: COVID-19 poses a risk to the endoscopic skull base surgeon. Significant efforts to improving safety have been employed, including the use of personal protective equipment, preoperative COVID-19 testing, and recently the use of a modified surgical mask barrier.

OBJECTIVE: To reduce the risks of pathogen transmission during endoscopic skull base surgery.

METHODS: This study was exempt from Institutional Review Board approval. Our study utilizes a 3-dimensional (3D)-printed mask with an anterior aperture fitted with a surgical glove with ports designed to allow for surgical instrumentation and side ports to accommodate suction ventilation and an endotracheal tube. As an alternative, a modified laparoscopic surgery trocar served as a port for instruments, and, on the contralateral side, rubber tubing was used over the endoscrub endosheath to create an airtight seal. Surgical freedom and aerosolization were tested in both modalities.

RESULTS: The ventilated mask allowed for excellent surgical maneuverability and freedom. The trocar system was effective for posterior surgical procedures, allowing access to critical paramedian structures, and afforded a superior surgical seal, but was limited in terms of visualization and maneuverability during anterior approaches. Aerosolization was reduced using both the mask and nasal trocar.

CONCLUSION: The ventilated upper airway endoscopic procedure mask allows for a sealed surgical barrier during endoscopic skull base surgery and may play a critical role in advancing skull base surgery in the COVID-19 era. The nasal trocar may be a useful alternative in instances where 3D printing is not available. Additional studies are needed to validate these preliminary findings.

FIGURES

**TABLE 1. Results of Aerosolization Test in the Anterior Nasal Cavity.
Results Reported in Number (n) of Droplets**

	NO mask (n)	Mask (n)	Mask, spillage reduction (%)
Quadrant A	5	2	60%
Quadrant B	137	11	92%
Quadrant C	9	3	67%
Quadrant D	24	9	63%
Total	175	25	86%

Table 1. Results of aerosolization test in anterior nasal cavity

TABLE 2. Results of Aerosolization Test in the Posterior Nasal Cavity. Results Reported in Number (n) of Droplets

	NO mask (n)	Mask (n)	Trocars (n)	Mask, spillage reduction (%)	Trocars, spillage reduction (%)
Quadrant A	3	1	0	67%	100%
Quadrant B	20	4	1	80%	95%
Quadrant C	5	1	0	80%	100%
Quadrant D	10	5	0	50%	100%
Total	38	11	1	71%	97%

Table 2. Results of aerosolization test in posterior nasal cavity

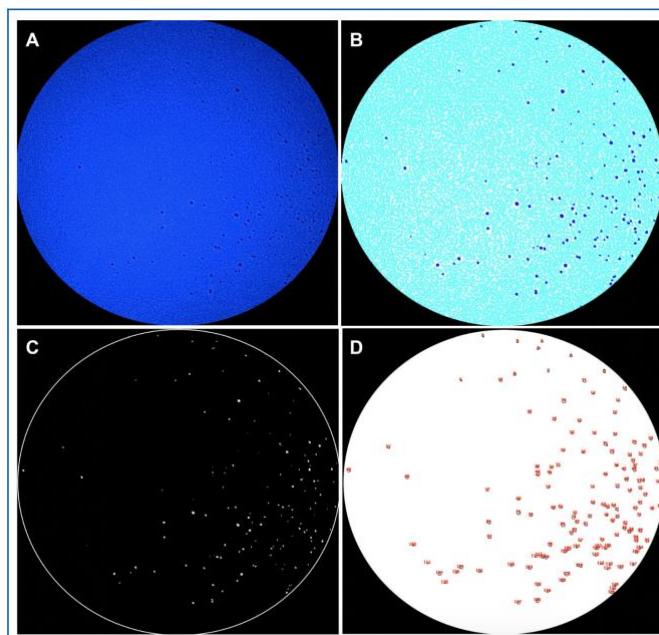


Figure 3. Representative images demonstrating the original cropped image A. image following brightness and contrast adjustment B and thresholding C. with visible, accentuated droplets in both images C.D, Analysis of particles with quantification of droplets.

	NO mask (n)	Mask (n)	Trocars (n)	Mask, spillage reduction (%)	Trocars, spillage reduction (%)
Quadrant A	3	1	0	67%	100%
Quadrant B	20	4	1	80%	95%
Quadrant C	5	1	0	80%	100%
Quadrant D	10	5	0	50%	100%
Total	38	11	1	71%	97%

Figure 3. Representative images demonstrating the original cropped image A. image following brightness and contrast adjustment B and thresholding C. with visible, accentuated droplets in both images C.D, Analysis of particles with quantification of droplets.

PREVENTION IN THE COMMUNITY

HOUSEHOLD MATERIALS SELECTION FOR HOMEMADE CLOTH FACE COVERINGS AND THEIR FILTRATION EFFICIENCY ENHANCEMENT WITH TRIBOELECTRIC CHARGING

Zhao M, Liao L, Xiao W, Yu X, Wang H, Wang Q, Lin YL, Kilinc-Balci FS, Price A, Chu L, Chu MC, Chu S, Cui Y.. Nano Lett. 2020 Jun 2. doi: 10.1021/acs.nanolett.0c02211. Online ahead of print.

Level of Evidence: 5

BLUF

This study examines the filtration efficiency of various household materials used to make non-medical face coverings and suggests that the filtration efficiency of some facial coverings may be enhanced if these coverings are triboelectrically charged (Table 2). Future studies are warranted to investigate the filtration efficiency of non-medical face coverings and the effectiveness of triboelectric charging of these coverings in a free-living setting, taking into account real-world scenarios (i.e., leakage around the edges).

ABSTRACT

The COVID-19 pandemic is currently causing a severe disruption and shortage in the global supply chain of necessary personal protective equipment (e.g., N95 respirators). The U.S. CDC recommended use of household cloth by the general public to make cloth face coverings as a method of source control. We evaluated the filtration properties of natural and synthetic materials using a modified procedure for N95 respirator approval. Common fabrics of cotton, polyester, nylon, and silk had filtration efficiency of 5-25%, polypropylene spunbond had filtration efficiency 6-10%, and paper-based products had filtration efficiency of 10-20%. An advantage of polypropylene spunbond is that it can be simply triboelectrically charged to enhance the filtration efficiency (from 6 to >10%), without any increase in pressure (stable overnight and in humid environments). Using the filtration quality factor, fabric microstructure, and charging ability, we are able to provide an assessment of suggested fabric materials for homemade facial coverings.

FIGURES

$\sim Q$ (kPa ⁻¹)	~Filtration Efficiency (%)	Material	Comments
>100	>95	Polypropylene meltblown (charged)	Material found in FFRs (used for reference)
30	10-20	Charged polypropylene (PP-4)	Charged value after overnight, polypropylene spunbonds can vary (different basis weight has different efficiency), charging increased the Q in all cases
15	5-10	Uncharged polypropylene (PP-4)	Initial polypropylene spunbond fabrics can vary in efficiency, but most tested had low pressure drops
5-10	5-20	Cotton	Cotton fabrics can vary in initial pressure drop, select cotton fabrics without any visible pores under light illumination or use multilayer configurations
5-10	20	Polyester	Similar properties and comments as cotton
5	30	Polypropylene meltblown (uncharged)	Material found in medical face masks (used for reference)
5	10-20	Tissue paper, paper towel	Low mechanical strength, but may be possible to integrate into some masks with other cloths as a composite material
<5	5	Silk	Silk can be considered for use if cotton and/or polyester are unavailable
<1	20	Nylon (woven)	The nylon tested in this study had very high pressure drop. If using nylon for masks the fabric needs to have a lower pressure drop to be effective

Table 2. Summary and ranking of materials tested here based on filtration quality factor, Q , with relevant comments for each material.

PREVENTION IN THE HOSPITAL

DETECTION OF AIR AND SURFACE CONTAMINATION BY SARS-COV-2 IN HOSPITAL ROOMS OF INFECTED PATIENTS

Chia PY, Coleman KK, Tan YK, Ong SWX, Gum M, Lau SK, Lim XF, Lim AS, Sutjipto S, Lee PH, Son TT, Young BE, Milton DK, Gray GC, Schuster S, Barkham T, De PP, Vasoo S, Chan M, Ang BSP, Tan BH, Leo YS, Ng OT, Wong MSY, Marimuthu K; Singapore 2019 Novel Coronavirus Outbreak Research Team.. Nat Commun. 2020 May 29;11(1):2800. doi: 10.1038/s41467-020-16670-2.

Level of Evidence: 3

BLUF

A cross-sectional study conducted at the National Centre for Infectious Diseases in Singapore found that 56.7% of the 245 surface and air samples from 2 of the 3 airborne infection isolation rooms (AIIR) of COVID-19 positive patients had SARS-CoV-2 RNA, with data trending toward higher surface/air contamination rates within the first week of illness (Figure 2). The authors support the need for further investigation into airborne transmission of SARS-CoV-2 and factors contributing to surface contamination with SARS-CoV-2.

ABSTRACT

Understanding the particle size distribution in the air and patterns of environmental contamination of SARS-CoV-2 is essential for infection prevention policies. Here we screen surface and air samples from hospital rooms of COVID-19 patients for SARS-CoV-2 RNA. Environmental sampling is conducted in three airborne infection isolation rooms (AIIRs) in the ICU and 27 AIIRs in the general ward. 245 surface samples are collected. 56.7% of rooms have at least one environmental surface contaminated. High touch surface contamination is shown in ten (66.7%) out of 15 patients in the first week of illness, and three (20%) beyond the first week of illness ($p = 0.01$, chi² test). Air sampling is performed in three of the 27 AIIRs in the general ward, and detects SARS-CoV-2 PCR-positive particles of sizes >4 microm and 1-4 microm in two rooms, despite these rooms having 12 air changes per hour. This warrants further study of the airborne transmission potential of SARS-CoV-2.

FIGURES

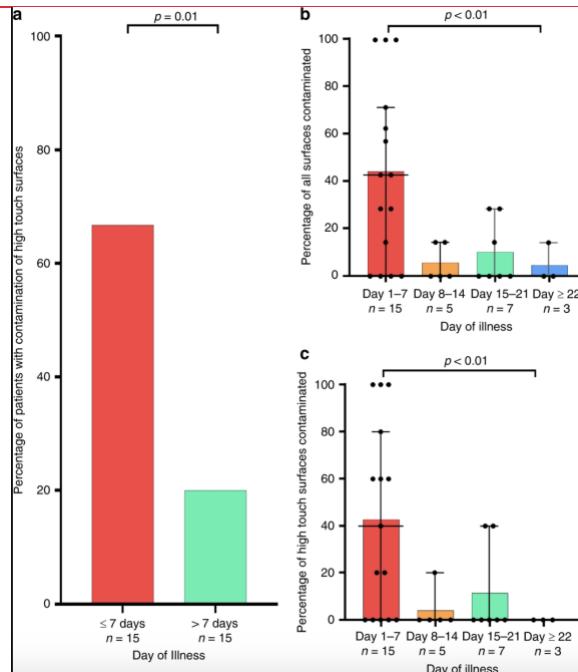


Figure 2: Extent of environmental contamination correlated with day of illness timepoint. a) Percentage of patients with contamination of high-touch surfaces in the first week of illness compared with more than first week of illness, n = 15 in both groups. b) Percentage of surfaces contaminated across weeks of illness with median and 95% confidence intervals. c) Percentage of high-touch surfaces contaminated across weeks of illness with median and 95% confidence intervals.

CONTAINMENT OF A TRACEABLE COVID-19 OUTBREAK AMONG HEALTHCARE WORKERS AT A HEMATOPOIETIC STEM CELL TRANSPLANTATION UNIT

Buchtele N, Rabitsch W, Knaus HA, Wohlfarth P.. Bone Marrow Transplant. 2020 Jun 1. doi: 10.1038/s41409-020-0958-6.

Online ahead of print.

Level of Evidence: 4

BLUF

Physicians in a Vienna hematopoietic stem cell transplantation unit describe the results of contact tracing of COVID-19 and successful containment to five nurses out of 18 personnel and 11 patients. Using a protocol based on stringent testing, self-quarantine with symptom presentation, hand hygiene, appropriate PPE, and high efficiency particulate air (HEPA) filter positive-pressure lock systems, they demonstrate successful transmission prevention by tracing initial symptoms from a nurse to all subsequent contacts, regardless of contact duration.

MANAGEMENT

WHAT IS THE ROLE OF SARS-COV-2 PCR TESTING IN DISCONTINUATION OF TRANSMISSION-BASED PRECAUTIONS FOR COVID-19 PATIENTS?

Abu Raya B, Goldfarb DM, Sadarangani M.. Clin Infect Dis. 2020 May 30:ciaa671. doi: 10.1093/cid/ciaa671. Online ahead of print.

Level of Evidence: Other

BLUF

Authors argue that the recommendation for maintaining isolation and transmission-based precautions for COVID-19 patients until they have two consecutive negative PCR tests is not yet justified by data. Recent studies have shown that RT-PCR detection of SARS-CoV-2 can persist for longer than live viral shedding and that almost 1/5 patients have a positive test after two negative tests. They suggest that more rigorous data is needed to support the need for two consecutive negative PCR tests, particularly considering how this guideline may impact testing resources and personal protective equipment use.

ACUTE CARE

TREATMENT ALGORITHM FOR COVID-19: A MULTIDISCIPLINARY POINT OF VIEW

Galluccio F, Ergonenc T, Garcia Martos A, Allam AE, Pérez-Herrero M, Aguilar R, Emmi G, Spinicci M, Terrancle Juan I, Fajardo-Pérez M.. Clin Rheumatol. 2020 May 29. doi: 10.1007/s10067-020-05179-0. Online ahead of print.

Level of Evidence: 1

BLUF

Based on a review of literature on COVID-19 treatments published from January 2020 to April 2, 2020, an international multidisciplinary group of rheumatologists, immunologists, infectious disease experts, and anesthesiologists recommend a multidisciplinary management approach for COVID-19, as outlined in Figure 1. They highlight the importance of early identification of COVID-19 patients and correct timing of treatments to avoid severe complications.

ABSTRACT

The novel coronavirus (Sars-CoV-2) pandemic has spread rapidly, from December to the end of March, to 185 countries, and there have been over 3,000,000 cases identified and over 200,000 deaths. For a proportion of hospitalized patients, death can occur within a few days, mainly for adult respiratory distress syndrome or multi-organ dysfunction syndrome. In these patients, clinical signs and symptoms, as well as laboratory abnormalities, suggest a cytokine storm syndrome in response to the viral infection. No current targeted treatment is yet available for COVID-19, an unknown disease up to 2 months ago, which challenges doctors and researchers to find new drugs or reallocate other treatments for these patients. Since the beginning of the COVID-19 outbreak, a growing body of information on diagnostic and therapeutic strategies has emerged, mainly based on preliminary experience on retrospective studies or small case series. Antivirals, antimalarials, corticosteroids, biotechnological and small molecules, convalescent plasma and anticoagulants are among the drugs proposed for the treatment or in tested for COVID-19. Given the complexity of this new condition, a multidisciplinary management seems to be the best approach. Sharing and integrating knowledge between specialists, to evaluate the correct timing and setting of every treatment, could greatly benefit our patients. We reviewed the literature, combining it with our experiences and our specialist knowledge, to propose a management algorithm, correlating the clinical features with laboratory and imaging findings to establish the right timing for each treatment.

Key Points Critically ill COVID-19 patients show signs of cytokine storm syndrome. No current targeted therapy is available, but a lot of drugs are in tested. A multidisciplinary approach is crucial to manage COVID-19. Choosing the correct timing of treatment is of pivotal importance to avoid the most severe complications.

CLINICAL OUTCOMES OF COVID-19 WITH EVIDENCE-BASED SUPPORTIVE CARE

Larson DT, Sherner JH, Gallagher KM, Judy CL, Paul MB, Mahoney AM, Weintraub PJ.. Clin Infect Dis. 2020 May 30:ciaa678. doi: 10.1093/cid/ciaa678. Online ahead of print.

Level of Evidence: 4

BLUF

A retrospective observational case series of 135 reverse transcriptase (RT)-PCR confirmed COVID-19 patients conducted at Fort Belvoir Community Hospital (Virginia, US) between March 6 and April 22, 2020 showed that utilizing only pre-COVID-19 evidence-based best practice medical therapy for acute respiratory viral infections without the use of investigational therapies resulted in favorable outcomes for their COVID-19 patients (median age of 46.5 years [33-56] and comorbidities reflective of a normal community hospital). No patients progressed to sepsis or similar levels of organ dysfunction, and no patients needed intubation, suggesting that supportive treatment in line with current best practice guidelines may provide the best patient outcomes in the absence of genuine evidence of the efficacy of experimental treatments for SARS-CoV-2.

SUMMARY

"We believe this is attributable to multiple factors including a focus on supportive care that is well established to benefit patients and a conservative intubation strategy. Our population likely also benefited from having later occurrence of widespread community transmission as lessons learned from regions previously affected were able to be incorporated into local care, and care was provided in a facility that was not taxed by an overwhelming surge. Limitations of this study are notable for being retrospective in design, a younger population, and the lack of long term follow up data."

ABSTRACT

Calls for adherence to evidence-based medicine have emerged during the initial wave of the COVID-19 pandemic but reports of outcomes are lacking. This retrospective study of a single-institution cohort including 135 patients with confirmed COVID-19 demonstrates positive outcomes when institutional standards of care consist of evidence-based supportive therapies.

CRITICAL CARE

FEASIBILITY OF TOCILIZUMAB IN ICU PATIENTS WITH COVID-19

Issa N, Dumery M, Guisset O, Mourissoux G, Bonnet F, Camou F.. J Med Virol. 2020 Jun 2. doi: 10.1002/jmv.26110. Online ahead of print.

Level of Evidence: 4

BLUF

A retrospective case series of 10 ICU COVID-19 patients in France who were admitted between 15 March and 30 April 2020 found that the use of tocilizumab was associated with rapid reduction in fever, possible reduced length of hospitalization, and improvement in biological parameters of inflammation (Table 1). These findings, combined with the fact tocilizumab is often well tolerated, suggest that the use of this medication in critically ill patients may be in line with current compassionate use guidelines.

ABSTRACT

Severe COVID-19 causes cytokine release syndrome and is associated with high mortality. In this retrospective case series, all patients diagnosed with COVID-19 by semi quantitative RT-PCR and hyperinflammatory markers were treated with tocilizumab. The use of tocilizumab was associated with rapid apyrexia, improvement of respiratory, biological parameters and short length of hospitalization (11 days). Moreover, no adverse effect attributed to the treatment was noticed. Tocilizumab seems to be a promising and safe therapy in severe patients. This article is protected by copyright. All rights reserved.

FIGURES

	Normal range	Before tocilizumab	D+3 after tocilizumab
PaO ₂ /FiO ₂ (mmHg)	> 400	94 (75;130)	230 (171;278)
CRP (mg/L)	0-5	246 (216;274)	43 (21;52)
D-Dimers (ng/mL)	0-500	1,354 (749;3,992)	1,931 (1,515;5,000)
Fibrinogen (g/L)	2-5	10 (9;10)	6 (5;6)
Procalcitonin (µg/mL)	0-0.5	0.47 (0.33;1.22)	0.30 (0.22;0.75)
Ferritin (ng/mL)	5-200	2,751 (2,300;3,815)	2,265 (1,633;2,730)

Data are medians (interquartile 1; interquartile 3). D, day after tocilizumab infusion day, CRP C-reactive protein

Table 1: Laboratory tests before and after tocilizumab

MEDICAL SUBSPECIALTIES

CARDIOLOGY

INCIDENCE OF NEW-ONSET AND WORSENING HEART FAILURE BEFORE AND AFTER THE COVID-19 EPIDEMIC LOCKDOWN IN DENMARK: A NATIONWIDE COHORT STUDY

Andersson C, Gerds T, Fosbøl E, Phelps M, Andersen J, Lamberts M, Holt A, Butt JH, Madelaire C, Gislason G, Torp-Pedersen C, Køber L, Schou M. Circ Heart Fail. 2020 Jun 2:CIRCHEARTFAILURE120007274. doi: 10.1161/CIRCHEARTFAILURE.120.007274. Online ahead of print.

Level of Evidence: 1

BLUF

In this nationwide observational study, researchers compare the incidence of new-onset heart failure (HF) and worsening HF before and after the COVID-19 lockdown in Denmark in 2020 versus 2019. They found that during the lockdown period, rates of new-onset HF and hospitalizations for worsening HF were significantly lower in 2020 than in 2019. These findings may be concerning for the undertreatment of HF during the COVID-19 lockdown; however, this has not yet affected mortality on a population level.

ABSTRACT

BACKGROUND: The Danish government ordered a public lockdown on March 12, 2020, because of the coronavirus disease 2019 (COVID-19) pandemic. We investigated the immediate consequences of such a lockdown for patients with heart failure (HF).

METHODS: Using the Danish nationwide administrative databases, we investigated the incidence of new-onset HF and hospitalizations for worsening HF before and after the lockdown (January 1 to March 11 versus March 12 to March 31) in 2020 versus 2019. We also investigated the mortality for all patients with HF and in COVID-19-infected patients with HF.

RESULTS: Rates of new-onset HF between January 1 and March 11 were comparable for 2020 and 2019 (1.83 versus 1.78 per 10 000 person-years; P=0.19), while hospitalizations for worsening HF were slightly higher in 2020 versus 2019 (1.04 versus 0.93 per 1000 person-years; P=0.02). In the lockdown period, rates of new-onset HF diagnoses (1.26 versus 2.25 per 1000 person-years) and of hospitalizations for worsening HF (0.63 versus 0.99 per 1000 person-years) were significantly lower in 2020 versus 2019 (P for both, <0.0001). Mortality was similar before and after the national lockdown for the population with HF. We observed 90 HF patients with diagnosed COVID-19 infection, of whom 37% (95% CI, 23%-50%) died within 15 days.

CONCLUSIONS: The number of patients hospitalized with worsening HF or diagnosed with new-onset HF was markedly reduced after lockdown but has not yet impacted mortality in HF patients at a population-based level. However, these data raise concerns for a potential undertreatment of HF currently that may impact prognosis in the longer term.

FIGURES

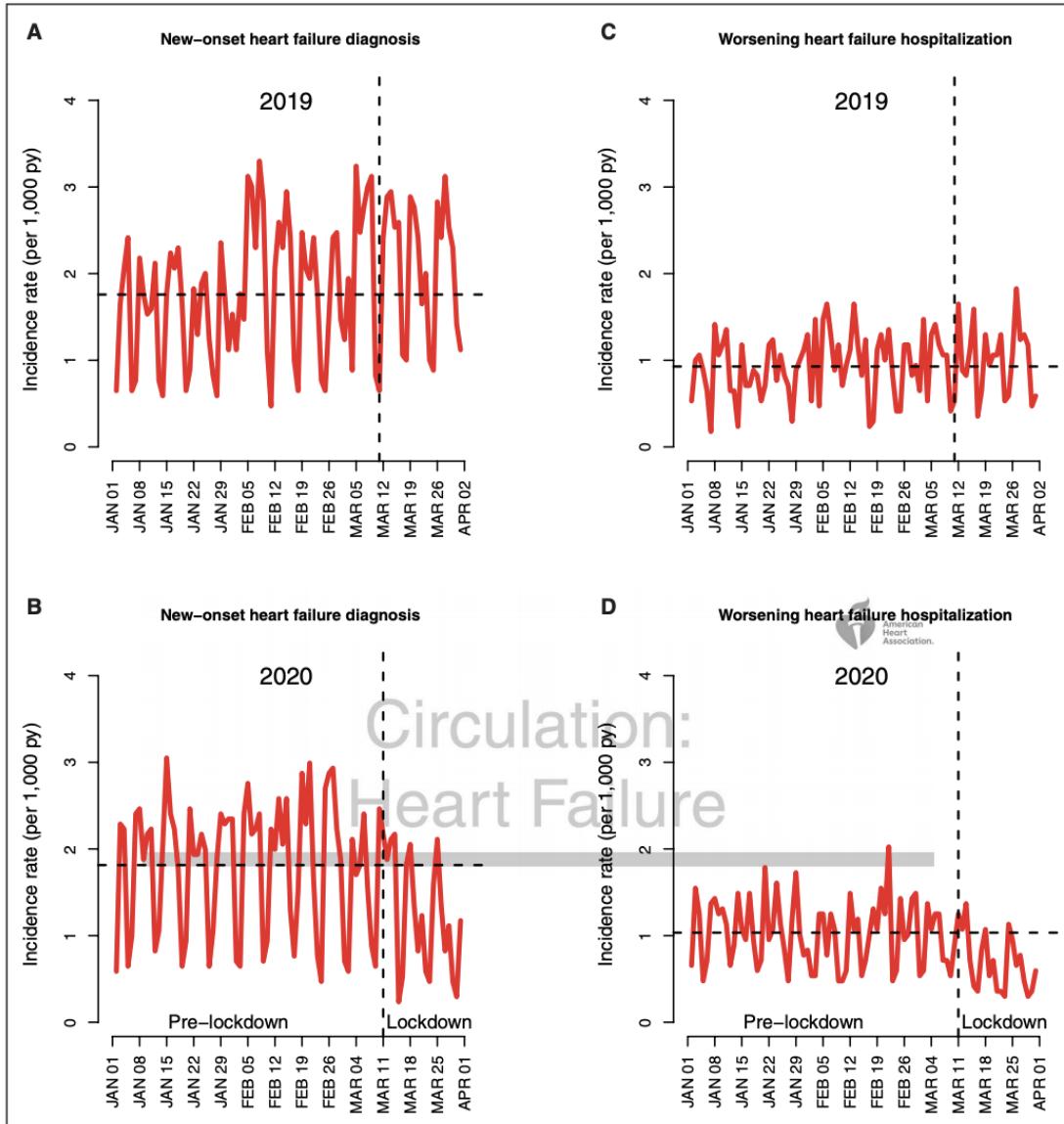


Figure 1. Daily incidence rates (per 1000 person-years) of new-onset diagnoses of heart failure (HF) and hospitalizations for worsening HF in the period January 1 to March 31, 2019 and 2020, respectively.

Horizontal lines represent the average incidence rates in the prelockdown period. Vertical lines represent the day of lockdown.

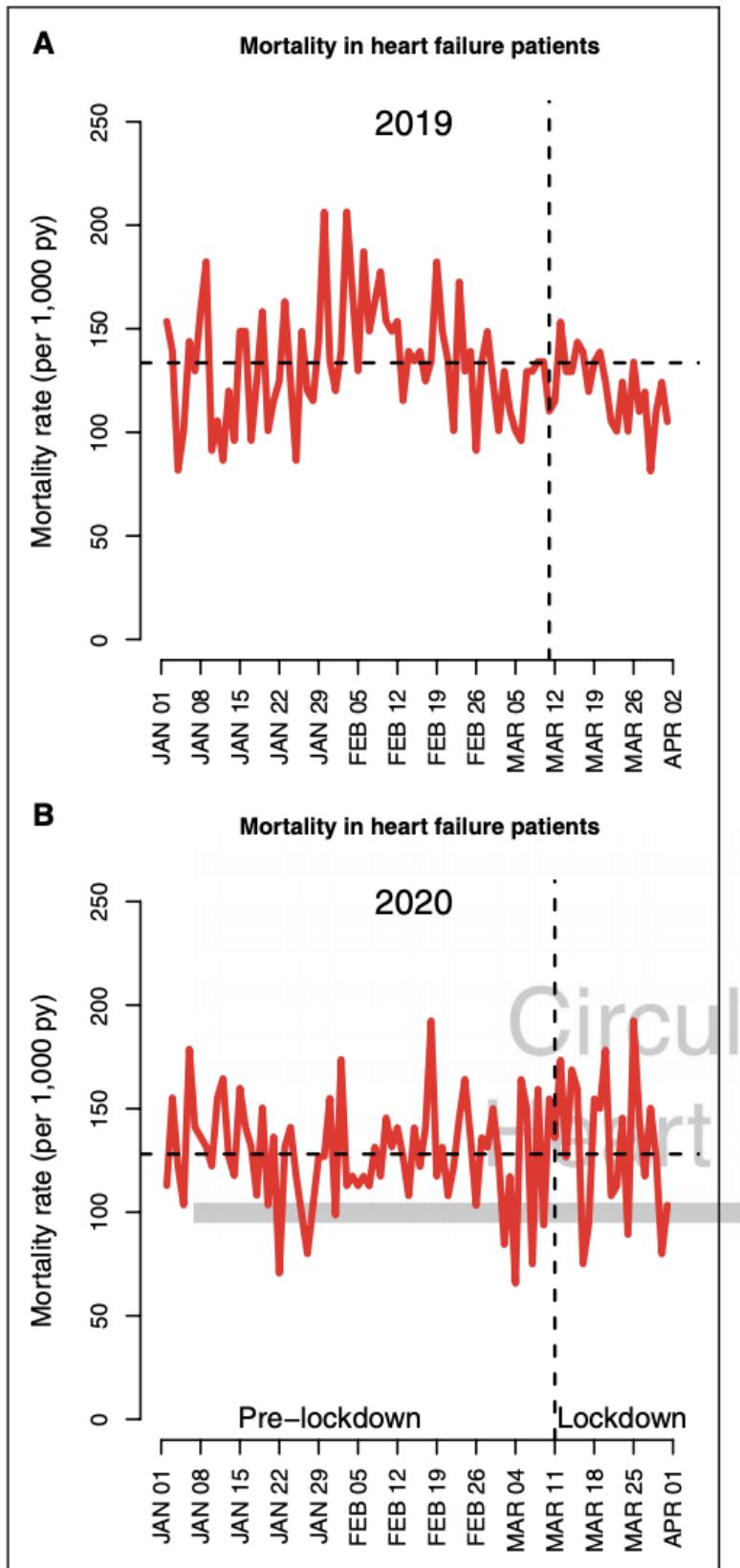


Figure 2. Daily mortality rates in patients with heart failure in the period January 1 to March 31, 2020 vs 2019.

Horizontal lines represent the average mortality rates in the prelockdown period. Vertical lines represent the day of lockdown.

ADJUSTING PRACTICE DURING COVID-19

FOR HEALTHCARE PROFESSIONALS

KEEPING JOURNAL CLUB RELEVANT IN A PANDEMIC: THE 'RAPID FIRE' 5-MINUTE FORMAT

Chu DC.. Med Educ. 2020 May 29. doi: 10.1111/medu.14259. Online ahead of print.

Level of Evidence: Other

BLUF

A physician at Penn State describes the adaptations they have made in their journal club to accommodate the “explosion of data” that has flooded the medical community during the pandemic. They have begun asking each fellow to choose a paper that they believed would change the management of COVID-19, and present it to the group in five minutes as opposed to the traditional format of dissecting one paper over the full hour. The author states that fellows and faculty have favored this new technique, and that it helps to standardize care for complex patients, promote further research, and encouraged collaboration between specialties.

ABSTRACT

There has been an explosion of data published in a short period of time about COVID-19. It can be difficult for learners to stay on top of the latest information while also critically appraising each new piece of information. As a result, there can be a lack of local consensus on how to best manage these patients as new data continually becomes available.

MEDICAL SUBSPECIALTIES

CELLULAR PATHOLOGY IN THE COVID-19 ERA: A EUROPEAN PERSPECTIVE ON MAINTAINING QUALITY AND SAFETY

Gosney JR, Hofman P, Troncone G, Lopez-Rios F.. J Clin Pathol. 2020 Jun 1:jclinpath-2020-206789. doi: 10.1136/jclinpath-2020-206789. Online ahead of print.

Level of Evidence: Other

BLUF

A set of guidelines constructed by a collaboration of pathologists in the United Kingdom, France, Italy, and Spain for maintaining safety in pathology laboratories through preanalytical, analytical, and post-analytical considerations, to ensure that pathologists can continue to perform their duties in laboratories, while mitigating the risk of COVID-19 as much as possible:

- Pre-analytical considerations: personnel wearing appropriate personal protective equipment, proper transporting and containment of specimens, and minimizing staff present.
- Analytical considerations: following the Royal College of Pathologists advice, treating specimens from COVID-19 patients as category 3 and treating specimens without confirmed COVID-19 as category 2, utilizing biological safety cabinets when necessary.
- Post-analytic considerations: the utilization of technology whenever possible, such as for conferring with other pathologists and making electronic reports.

ABSTRACT

COVID-19 is a zoonotic viral infection that originated in Wuhan, China, in late 2019. WHO classified the resulting pandemic as a 'global health emergency' due to its virulence and propensity to cause acute respiratory distress syndrome. The COVID-19 pandemic has had a major impact on diagnostic laboratories, particularly those handling cell and tissue specimens. This development carries serious implications for laboratory practice in that safety of personnel has to be balanced against high-quality analysis and timely reporting of results. The aim of this article is to present some recommendations for the handling of

such specimens in the preanalytical, analytical and postanalytical phases of laboratory testing and analysis in an era of high COVID-19 prevalence, such as that seen, for example, in the UK, Spain, Italy and France.

SURGICAL SUBSPECIALTIES

TRANSPLANT SURGERY

EXPEDITED SARS-COV-2 SCREENING OF DONORS AND RECIPIENTS SUPPORTS CONTINUED SOLID ORGAN TRANSPLANT

Lieberman JA, Mays JA, Wells C, Cent A, Bell D, Bankson DD, Greninger AL, Jerome KR, Limaye AP.. Am J Transplant. 2020 Jun 1. doi: 10.1111/ajt.16081. Online ahead of print.

Level of Evidence: 4

BLUF

A case series conducted in Seattle, Washington during 15 March through 5 April 2020 at the University of Washington Medical Center found that creating an expedited process (Figure 1) to screen transplant donors and recipients for COVID-19 did not hinder successful and timely organ transplantation (Table 2) and only one transplant was delayed briefly due to testing, suggesting that this process could be implemented to prevent inactivation of transplant wait lists as health care institutions manage the COVID-19 pandemic. This allowed for:

- 38 organs recovered from 14 donors resulting in 32 transplants compared to the same time period in 2019 where 70 organs were collected from 23 donors.
- A turnaround time for this process for donors and recipients was 6.8 and 6.5 hours respectively, which was faster than inpatient specimen turnaround time (Figure 2).
- Inactivation of transplant wait list decreased significantly in the Northwest region between week 1 and 2 of this study.

ABSTRACT

Universal screening of potential organ donors and recipients for SARS-CoV-2 is now recommended prior to transplantation in the United States during the COVID-19 pandemic. Challenges have included limited testing capacity, short windows of organ viability, brief lead time for notification of potential organ recipients, and the need to test lower respiratory donor specimens to optimize sensitivity. In an early US epicenter of the outbreak, we designed and implemented a system to expedite this testing and here report results from the first three weeks. The process included a Laboratory Medicine designee for communication with organ recovery and transplant clinical staff, specialized sample labeling and handoff, and priority processing. Thirty-two organs recovered from 14 of 17 screened donors were transplanted versus 70 recovered from 23 donors during the same period in 2019. No pre-transplant or organ donors tested positive for SARS-CoV-2. Median turnaround time from specimen receipt was 6.8h (donors), 6.5h (recipients): 4.5h faster than daily inpatient median. No organ recoveries or transplants were disrupted by a lack of SARS-CoV-2 testing. Waitlist inactivations for COVID-19 precautions were reduced in our region. Systems that include specialized ordering pathways and adequate testing capacity can support continued organ transplantation even in a SARS-CoV-2 hyperendemic area.

FIGURES

Table 2: Impact of SARS-CoV-2 Test Results on Procedures

	Potential Cases	Cases Discontinued for SARS-CoV-2	Cases with Organs Recovered or Transplanted	Cases with Tissue Recovered
Donors	17	0	14	7
Potential Recipients	13	0	8	n/a
Post-Transplant Patients	4	0	n/a	n/a

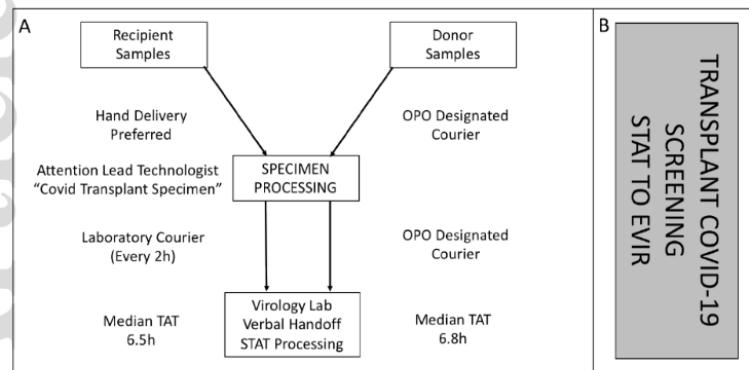


Figure 1. Overview of Expedited Workflow and Specimen Identifiers. Specimens for both potential organ donors and recipients were collected and transported to the laboratory, where specimens were immediately accessioned and logged by a lead technologist, A. From there, specimens were transported to the Virology laboratory, where they became the next specimens processed. OPO-designated couriers maintained custody of donor specimens throughout. Median TAT from specimen receipt are displayed. Verbal handoffs played an important role in identifying these to laboratory personnel for proper handling, as did a flag, B, that was attached to each specimen requisition. “EVIR” indicates the Clinical Virology laboratory.

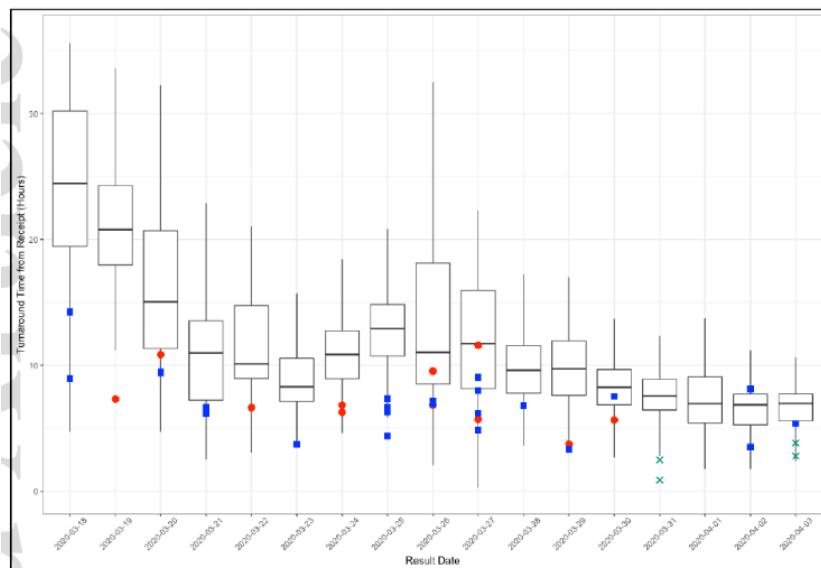


Figure 2. Donor and Recipient SARS-CoV-2 Turnaround Times Compared to Routine Inpatient Result Times. Box and whisker plots show the calculated median inpatient TAT by day. Individual TATs for transplant patients, red circles. Individual TATs for transplant patients performed on rapid tests, green exes. Individual TATs for donor specimens, blue squares. Two-tailed Wilcoxon signed rank test indicates a significant difference ($p = 6.557 \times 10^{-9}$) between the expedited sample TAT vs. daily median TAT for routine samples.

R&D: DIAGNOSIS & TREATMENTS

EFFECT OF IMPLEMENTING SIMULATION EDUCATION ON HEALTH CARE WORKER COMFORT WITH NASOPHARYNGEAL SWABBING FOR COVID-19

Mark ME, LoSavio P, Husain I, Papagiannopoulos P, Batra PS, Tajudeen BA.. Otolaryngol Head Neck Surg. 2020 Jun 2:194599820933168. doi: 10.1177/0194599820933168. Online ahead of print.

Level of Evidence: 3

BLUF

A study with 46 healthcare workers (HCW) conducted at Rush University Medical Center found that lecture in conjunction with simulation training on nasopharyngeal swabbing significantly increased HCW's confidence in performing swabs for COVID-19, with post-training self-assessments showing a mean score of 4.54/5 compared to a pre-training average score of 3.13 ($p < 0.0001$, Figure 1, Table 1). These findings reveal that simulation-based training can improve familiarity and confidence with nasopharyngeal swabbing among HCW, which ultimately could help lower the incidence of false-negative testing results.

ABSTRACT

OBJECTIVE: To determine if rapid implementation of simulation training for the nasopharyngeal swab procedure can increase provider confidence regarding procedure competency.

METHODS: A simulation training exercise was designed as a departmental initiative to improve competency performing nasopharyngeal swabs during the COVID-19 pandemic. Sixty-one health care workers attended teaching sessions led by the Department of Otorhinolaryngology on proper nasopharyngeal swab technique. After a brief lecture, participants practiced their swab technique using a high-fidelity airway simulation model. Pre- and postintervention self-evaluations were measured via standardized clinical competency questionnaires on a 5-point Likert scale ranging from "No knowledge, unable to perform" up to "Highly knowledgeable and confident, independent."

RESULTS: Forty-six participants in this study submitted pre- and postintervention self-assessments. Postintervention scores improved on average 1.41 points (95% CI, 1.10-1.73) out of 5 from a mean score of 3.13 to 4.54 ($P < .0001$). This reflects a large effect size with a Glass's delta value of 1.3.

DISCUSSION: Lecture coupled with simulation-based teaching can significantly improve health care workers' confidence in performing nasopharyngeal swabs. Proper training for frontline workers performing swabs for COVID-19 is essential to improving testing accuracy and can be achieved in a simple and timely manner.

IMPLICATIONS FOR PRACTICE: To meet the testing needs of the growing pandemic, many health care workers who are unfamiliar with nasopharyngeal swabs have been asked to perform this test. Simulation-based teaching sessions may improve health care workers' confidence and help prevent false-negative results. This intervention is easily reproducible in any setting where frequent nasopharyngeal swab testing occurs.

LEVEL OF EVIDENCE/STUDY DESIGN: Prospective cohort study.

FIGURES

Nasopharyngeal Swab Self-Assessment

Please rate your confidence with performing a nasopharyngeal swab for COVID-19 in a real-life scenario

by selecting the appropriate response (*circle choice*):

- 1 – No knowledge, unable to perform
- 2 – Some knowledge but need a lot of guidance
- 3 – Basic knowledge but guidance still needed
- 4 – Reasonably confident, some guidance needed
- 5 – Highly knowledgeable and confident, independent

Figure 1. A 5-point Likert scale self-assessment for competence performing a nasopharyngeal swab for COVID-19.

Simulation training (N = 46)		
	Preintervention	Postintervention
Likert scale score		
1	3	0
2	10	0
3	16	2
4	12	17
5	5	27
Mean	3.13	4.54
SD	1.09	0.59
Mean change (95% CI)	—	1.41 (1.10-1.73)^a

^aMean self-assessed competency scores for performing nasopharyngeal swabs improved 1.41 points from 3.13 to 4.54 after the intervention ($P < .0001$).

Table 1. Self-assessment of Competency Performing Nasopharyngeal Swab: Pre- and Postintervention Scores.

CURRENT DIAGNOSTICS

CLINICAL PERFORMANCE OF THE LUMINEX NXTAG COV EXTENDED PANEL FOR SARS-COV-2 DETECTION IN NASOPHARYNGEAL SPECIMENS OF COVID-19 PATIENTS IN HONG KONG

Chen JH, Yip CC, Chan JF, Poon RW, To KK, Chan KH, Cheng VC, Yuen KY.. J Clin Microbiol. 2020 Jun 1:JCM.00936-20. doi: 10.1128/JCM.00936-20. Online ahead of print.

Level of Evidence: 3

BLUF

Researchers in Hong Kong compared the diagnostic capabilities of the Luminex NxTAG CoV Extended panel to the standard testing protocol used at Queen Mary Hospital (LightMix Sarbeco V E-gene kit and RdrP/HeL RT-PCR assay). Using archived nucleic acid extracts (via eMAG extraction system) from nasopharyngeal swab specimens of 214 patients who previously presented with suspected COVID-19, they found that there was no statistically significant difference between the two diagnostic protocols (Table 1), suggesting that the NxTAG CoV extended panel could be used as an effective screening tool for suspected COVID-19 cases.

ABSTRACT

In December 2019, the coronavirus disease 2019 (COVID-19) pandemic caused by the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) was first reported in the Hubei Province of China and later spread all over the world. There was an urgent need of a high-throughput molecular testing for screening the COVID-19 patients in the community. The Luminex NxTAG CoV Extended Panel is a high-throughput FDA emergency use authorized molecular diagnostic assay for SARS-CoV-2 detection. This system targets three genes (ORF1ab, N and E gene) of SARS-CoV-2, ORF1ab region of SARS-CoV and ORF5 region of MERS-CoV. In this study, we evaluated the diagnostic performance of this system with nasopharyngeal swab specimens of 214 suspected COVID-19 patients in Hong Kong. The results were compared with our routine COVID-19 RT-PCR protocol with LightMix SarbecoV E-gene kit and an in-house RdRp/HeL RT-PCR assay. The NxTAG CoV Extended panel demonstrated a 97.8% sensitivity and 100% specificity to SARS-CoV-2 in nasopharyngeal specimens. On low viral load specimens, the sensitivity of the NxTAG panel could still maintain at 85.71%. High agreement was observed between the NxTAG panel and the routine COVID-19 RT-PCR protocol (κ value = 0.98). Overall the E gene target of the NxTAG panel demonstrated the highest sensitivity among the three SARS-CoV-2 targets while the N gene targets demonstrated the least. In conclusion, the NxTAG CoV Extended Panel is simple to use and it has high diagnostic sensitivity and specificity to SARS-CoV-2.

in nasopharyngeal specimens. we recommend this diagnostic system for high-throughput COVID-19 screening in the community.

FIGURES

Routine COVID-19 RT-PCR protocol (LightMix E-gene + RdRp/Hei RT-PCR)	NxTAG CoV Extended Panel			Kappa value (95% CI)	McNemar's test
	Positive	Negative	Total		
Positive	89 *	2 *	91	0.98	
Negative	0	123	123	(0.95-1.00)	$p = 0.500$
Total	89	125	214		

* There are in total 2 samples with LightMix E-gene PCR positive and RdRp/Hei RT-PCR negative. The samples were further confirmed to be SARS-CoV-2 positive by the government reference laboratory.

Table 1. Results of comparative evaluation of the NxTAG CoV Extended Panel and routine COVID-19 RT PCR protocol of 214 nasopharyngeal samples.

DEVELOPMENTS IN DIAGNOSTICS

SEROCONVERSION RATE AND DIAGNOSTIC ACCURACY OF SEROLOGICAL TESTS FOR COVID-19

Nagappa B, Marimuthu Y.. Clin Infect Dis. 2020 May 30:ciaa676. doi: 10.1093/cid/ciaa676. Online ahead of print.
Level of Evidence: Other

BLUF

This article details the authors' concerns about Zhao J et al's study on antibody responses due to SARS-CoV-2 infection including their methodology (inconsistency in reported sample size), sensitivity calculation (error in calculations), interpretation of the results (failed to consider confounding variables), and potential bias.

DEVELOPMENTS IN TREATMENTS

CELL-BASED THERAPY TO REDUCE MORTALITY FROM COVID-19: SYSTEMATIC REVIEW AND META-ANALYSIS OF HUMAN STUDIES ON ACUTE RESPIRATORY DISTRESS SYNDROME

Qu W, Wang Z, Hare JM, Bu G, Mallea JM, Pascual JM, Caplan AI, Kurtzberg J, Zubair AC, Kubrova E, Engelberg-Cook E, Nayfeh T, Shah VP, Hill JC, Wolf ME, Prokop LJ, Murad MH, Sanfilippo FP.. Stem Cells Transl Med. 2020 May 29. doi: 10.1002/sctm.20-0146. Online ahead of print.

Level of Evidence: 1

BLUF

The authors performed a systematic review and meta-analysis to evaluate the potential efficacy of mesenchymal stem cells (MSCs) in treating acute respiratory distress syndrome (ARDS) associated with COVID-19 infection, which yielded nine studies with an overall patient population of 200 (Table 1), and displayed a trend towards reduced mortality in patients treated with MSCs that did not end up being statistically significant (Figure 2, Table 5). However, there have been no serious adverse events associated with MSC treatment, so these authors conclude that the risk-benefit ratio of using MSC to treat ARDS supports further research into this potential treatment.

ABSTRACT

Severe cases of COVID-19 infection, often leading to death, have been associated with variants of acute respiratory distress syndrome (ARDS). Cell therapy with mesenchymal stromal cells (MSCs) is a potential treatment for COVID-19 ARDS based on preclinical and clinical studies supporting the concept that MSCs modulate the inflammatory and remodeling processes and

restore alveolo-capillary barriers. The authors performed a systematic literature review and random-effects meta-analysis to determine the potential value of MSC therapy for treating COVID-19-infected patients with ARDS. Publications in all languages from 1990 to March 31, 2020 were reviewed, yielding 2691 studies, of which nine were included. MSCs were intravenously or intratracheally administered in 200 participants, who were followed for 14 days to 5 years. All MSCs were allogeneic from bone marrow, umbilical cord, menstrual blood, adipose tissue, or unreported sources. Combined mortality showed a favorable trend but did not reach statistical significance. No related serious adverse events were reported and mild adverse events resolved spontaneously. A trend was found of improved radiographic findings, pulmonary function (lung compliance, tidal volumes, $\text{PaO}_2 / \text{FiO}_2$ ratio, alveolo-capillary injury), and inflammatory biomarker levels. No comparisons were made between MSCs of different sources.

FIGURES

TABLE 1 Patient character

TABLE 1 (Continued)

Author	Country	Study type	Total n	Mean age(y)	MFC	Comorbidity	Bathing procedure history	Bathing procedure MFC	Bathwater microbial load	Bathwater microbial load MFC	E/FU	ABRS case	ABRS severity
Dhang et al ¹⁰	South Korea	Case report	1/1	59	—	—	—	—	—	—	100	Neutropenia	NE
Menssen et al ¹¹	Sweden	Case series	2/2	49	—	HT, CDM, A/H	HT, CDM, A/H	CFU/ml, total was 550-560 CFU/ml	CFU/ml, total was 550-560 CFU/ml	NE	2M	Infection	Severe

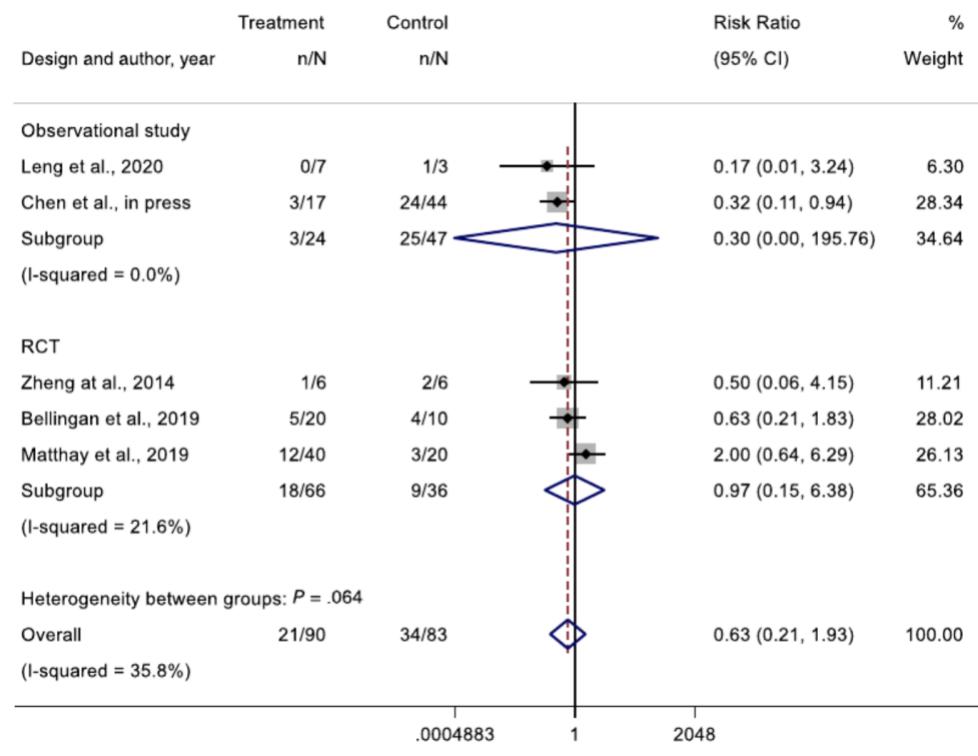
TABLE 5 Clinical, laboratory, and imaging outcomes

Author	Mortality MSCs (Median [IQR])	Mortality in control (Deaths/I)	Pulmonary function outcomes	Systemic outcomes	Inflammatory markers	Imaging
Long et al ²⁰	0/7	1/3	All 2-4 d after MSC transplantation, all patients disappeared (disappeared to <95% at rest, or with or without oxygen uptake (L/min))	All 2-4 d after MSC transplantation, all patients disappeared (disappeared in all patients)	MSC group: Decrease in TNF α , IL-6, IL-8, IL-10, IL-12, IL-13, IL-15, IL-16, IL-17, IL-20, IL-25, CCR4, CXCL10, CXCL13, CCR5 + cells and CXCR3+ cells.	The patient in the most critical condition had signs of pneumonia and was treated with IV CTX, improvement in CT by day 4 after MSCs.
Wilson et al ²¹	2/9	NA	Mean IL-6 expression between baseline and D13 in three groups (mean, SD): control, 10.1 (4.7) pg/ml; trend, no effect (ECMO, 2.9 vs control, 2.1 pg/ml), P = 0.03 (not statistically significant).	Mean SVA score declined in all 2-4 d after treatment group, with the last 2 d.	Median levels of IL-6, IL-8, RAGE declined between baseline and D3 (P = 0.001, P = 0.001, P = 0.001, respectively)	NR
Zhang et al ²²	1/6	2/6	Ventilator-free days and K10 free days were significantly lower than control in both groups (PaO ₂ /FiO ₂ did not significantly differ between MSCs and placebo group at all time points).	Length of hospital stay, at D3 after treatment was similar	MSC group: mean IL-6 levels at day 3 were significantly higher than at day 0 (Change in IL-6 levels: log ₁₀ fold change = 0.4, P = 0.001). No significant difference in IL-6 compared with day 0, but not statistically significant.	NR
Bellinger et al ²³	5/26	4/10	ICU-free days: 30.3 ± 6.7, MSC group; 20.7 ± 10.7 in the control group (P = 0.02) (Fig 2D) (as in the control group).	NR	NR	NR
Muthay et al ²⁷	15/40 (in day 40)	5/20 (by day 40)	Mortality higher in the MSC group (thought to be due to higher baseline risk). In the MSC group, ventilator-free and oxygen saturation times were all lower in the MSC group than in the placebo group (all significant). At 2 d after treatment, the mortality index in the MSC group reduced from 1.0 to 0.5, while the placebo group (consequently similar	Number of ventilator-free and organ failure-free days were significantly lower in the MSC group than in the placebo group (all significant). The number of intensive-care days was significantly higher in the MSC group than in the placebo group.	Concentrations of arginase1 2 fold reduced to 0.6 after the start of treatment. No significant changes from baseline were seen for IL-6, IL-8, IL-10, IL-12, IL-13, IL-15, IL-16, IL-17, IL-20, IL-25, CCR4, CXCL10, CXCL13, CCR5 + cells and CXCR3+ cells.	NR

TABLE 5 (Cont.)

Author	Mortality MTCs (death/n)	Mortality in control (death/n)	Primary function addressed	Systemic outcomes	Inflammatory markers	Imaging
Vip et al ²⁷	3/9	NA	Level of improvement in FIO ₂ : FIO ₂ /FiO ₂ free days were 12.9 (10-17) and in ICU-free days was 20.3 (8-35)	Two patients who died improved initially. Clinical improvement after the first 24 hours of therapy was associated with another 10% of improvement in the subsequent 24 hours due to severe septic shock.	Serum biomarker analysis of circulating inflammatory markers were progressively reduced. Serum lactate levels were notably increased after cell infiltration.	Liver ultrasound implementation Level 2: 25% complete resolution, 3-25% progressive improvements, 3-25% mixed results; Level 3: mixed results
Chen et al ²⁸	3/17	24/44	Fractional O ₂ patients followed up for 1 month. No significant difference among patients in the resp. function (FVC, FEV ₁ , FEF ₂₅₋₇₅ and FEF _{50%})	After following up for 2 x 1 month, the patients in the 3D did not show any signs of improvement during the follow-up.	NR	After MSC transplantation for 20 days, 10/14 patients showed improvement on CT
Cheng et al ²⁷	1/5	NA	CD3 improvement from 191 to 324 (224±100). CD4 improvement from 111 to 196. CD8 improved from 24 to 46. dynamic compliance improvement from 22.3 to 26.5, 27.3 and 27.9 ml/cmH ₂ O at 24 h, 24 h, and 23 h, respectively.	Mental status, lung compliance, oxygen saturation, heart rate, chest improvement over the course of at least 3 d	NR	Chest radiograph slight decrease in bilateral infiltrates

Abbreviations: APACHE: Acute Physiology and Chronic Health Evaluation; BAI, bronchial airway image; CCT, cardiac computed tomography; CT, computed tomography; CXR, chest X-ray; D: day; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; LSI, lung injury score; MCT, mesenchymal stromal cell; NA, not applicable; NR, not reported; PaO₂/FiO₂, arterial oxygen partial pressure/fraction inspired oxygen; patient, $n=36$; 36-month Fair Use; SGRQ, self-reported quality of life assessment score.



NOTE: Weights are from random-effects model; continuity correction applied to studies with zero cells

REMDESIVIR AND TOCILIZUMAB: MIX OR MATCH

Akinosoglou K, Velissaris D, Ziazias D, Davoulou C, Tousis A, Tsoutsios K, Kalogeropoulou C, Spyridonidis A, Marangos M, Fligkou F, Gogos C.. J Med Virol. 2020 Jun 3. doi: 10.1002/jmv.26117. Online ahead of print.

Level of Evidence: 4

BLUF

In this letter to the editor, researchers from the University General Hospital of Patras in Greece detail two well-matched cases of patients with COVID-19 who were hospitalized with respiratory failure and treated with tocilizumab. One of the patients also received remdesivir. Notably, the patient treated with tocilizumab alone did develop hemophagocytic syndrome. Despite this, both patients ultimately improved and were discharged in stable condition, suggesting that tocilizumab +/- remdesivir may be useful in the treatment of COVID-19. The authors note that results from randomized clinical trials are needed to support this.

WHY NOT TO USE COLCHICINE IN COVID-19? AN OLD ANTI-INFLAMMATORY DRUG FOR A NOVEL AUTO-INFLAMMATORY DISEASE

Piantoni S, Patroni A, Toniati P, Furloni R, Franceschini F, Andreoli L, Scarsi M.. Rheumatology (Oxford). 2020 May 30:keaa217. doi: 10.1093/rheumatology/keaa217. Online ahead of print.

Level of Evidence: 5

BLUF

A letter written by Italian authors reviews research on cytokine storm in association with COVID-19 severity and describes alternative treatments to minimize this pro-inflammatory state by using anti-rheumatic drugs (colchicine, chloroquine/hydrochloroquine, tocilizumab, adalimumab, and ruxolitinib). The authors emphasize the use of colchicine due to its disruption of microtubule polymerization which has a role in auto-inflammation. They recommend future studies focus on identifying and selecting ideal patient populations and timing of administration in COVID-19 patients.

CHARACTERISTICS OF REGISTERED STUDIES FOR CORONAVIRUS DISEASE 2019 (COVID-19): A SYSTEMATIC REVIEW

Level of Evidence: Other

BLUF

A literature search of clinical trials related to COVID-19 diagnosis, treatment, and prevention between January 23 and March 3, 2020 worldwide identified 393 clinical trials, 96.7% of which were from mainland China (Tables 1-2 & 4). The authors found that most studies from China were limited by inappropriate outcome setting, delayed recruitment, and small sample sizes, suggesting that global collaborative efforts are necessary for efficient and comprehensive research and data sharing, and to reduce duplicate studies.

ABSTRACT

Background: The World Health Organization characterized the Coronavirus disease 2019 (COVID-19) as a pandemic on March 11th. Many clinical trials on COVID-19 have been registered, and we aim to review the study characteristics and provide guidance for future trials to avoid duplicated effort.

Methods: Studies on COVID-19 registered before March 3rd, 2020 on eight registry platforms worldwide were searched and the data of design, participants, interventions, and outcomes were extracted and analyzed.

Results: Three hundred and ninety-three studies were identified and 380 (96.7%) were from mainland China, while 3 in Japan, 3 in France, 2 in the US, and 3 were international collaborative studies. Two hundred and sixty-six (67.7%) aimed at therapeutic effect, others were for prevention, diagnosis, prognosis, etc. Two hundred and two studies (51.4%) were randomized controlled trials. Two third of therapeutic studies tested Western medicines including antiviral drugs (17.7%), stem cell and cord blood therapy (10.2%), chloroquine and derivatives (8.3%), 16 (6.0%) on Chinese medicines, and 73 (27.4%) on integrated therapy of Western and Chinese medicines. Thirty-one studies among 266 therapeutic studies (11.7%) used mortality as primary outcome, while the most designed secondary outcomes were symptoms and signs (47.0%). Half of the studies (45.5%) had not started recruiting till March 3rd.

Conclusion: Inappropriate outcome setting, delayed recruitment and insufficient numbers of new cases in China implied many studies may fail to complete. Strategies and protocols of the studies with robust and rapid data sharing are warranted for emergency public health events, helping the timely evidence-based decision-making.

FIGURES

Table 1
The Characteristics of the Registered Studies From Eight Registries

Items	Details	n	%
Aim	Prevention	16	4.1
	Therapeutic evaluation	266	67.7
	Diagnosis	25	6.4
	Prognosis	19	4.8
	Others ^a	67	17.0
Setting	Hospital	363	92.4
	Community	4	1.0
	Others (university, online and research institute)	3	0.8
	NA	23	5.9
Study type	RCTs	202	51.4
	CCTs	31	7.9
	Single arm trials	23	5.9
	Observational studies	96	24.4
	Cross-sectional studies	16	4.1
	Diagnostic tests	18	4.6
	Others (basic science/factorial/NA)	7	1.8
	≤100	206	52.4
Sample size	101–300	100	27.0
	301–500	43	10.9
	501–1500	21	5.3
	1500+	14	3.6
	NA	3	0.8
Populations	People exposed to patients	38	9.7
	Suspected infection	9	2.3
	Confirmed or suspected infection	15	3.8
	Mild or moderate	121	30.8
	Moderate or severe	6	1.5
	Severe or critical illness	72	18.3
	Coronavirus patients (without details for stage or all stages included)	96	24.4
	Confirmed patients with complications	7	1.8
	Rehabilitation	9	2.3
	Special population (children, neonates, women, maternal)	6	1.5
Recruitment status	Other diseases without COVID-19	6	1.5
	Others ^b	8	2.0
	Not yet recruiting	179	45.5
	Recruiting	192	48.9
	Completed	4	1.0
	Suspended	3	0.8
	Expanded access ^c	1	0.3
Interventions (therapeutic studies)	NA	14	3.6
	Western medicine	177	66.5
	Chinese medicine	16	6.0
	Integrated therapy	73	27.4
	Conventional therapy	122	45.9
Comparisons (therapeutic studies)	Antiviral drugs	26	9.8
	Placebo	28	10.5
	Blank	11	4.1
	No control group	47	17.7
	Multiple controls	14	5.3
	Others	18	6.8
	Government	106	27.0
	Hospital	74	18.8
	University/Research institute/Academic association	22	5.6
	Multiple funding	18	4.6
Funding source	Industry	44	11.2
	Self-raised	105	26.7
	No funding	7	1.8
	NA	17	4.3
	Yes	268	68.2
	Unclear	125	31.8

^a Other aims: epidemiology research, description of clinical or imaging characteristics, investigation on traditional Chinese medicine (TCM) syndrome.

^b Other populations: health or suspected infectious people, COVID-19 patients and other types of pneumonia, COVID-19 patients and other influenza patients.

^c Expanded access: currently available for this investigational treatment, and patients who are not participants in the clinical study may be able to gain access to the drug, biologic, or medical device being studied.

^d Other comparisons: different dosage or duration of the tested intervention, "historical comparison" (without details), γ-Globulin, bag-valve mask oxygenation Assisted tracheal intubation, psychological intervention (without details), Chinese medicine.

NA, not available; RCT, randomized controlled trial; CCT, controlled clinical trial.

Table 2
Categories of Western Medicine and Chinese Medicine in the Registered Studies

Intervention	Category	n	%
Western medicine	Antiviral drugs	47	17.7
	Stem cell and cord blood therapy	27	10.2
	Chloroquine and derivatives	22	8.3
	Immunology and monoclonal antibodies	15	5.6
	Convalescent plasma	8	3.0
	Inhalation therapy	6	2.3
	Glucocorticoids	6	2.3
	Psychological therapy	4	1.5
	Vitamins	3	1.1
	ECMO	2	0.8
Chinese medicine	Others	36	13.5
	CM with no details	46	17.3
	Patent herbal drugs	17	6.4
	Herbal injections	10	3.8
	Non-pharmaceutical intervention	9	3.4
	Herbal decoctions	6	2.3
	Multiple Chinese medicine therapy	2	0.8

ECMO, Extracorporeal Membrane Oxygenation; TCM, Traditional Chinese Medicine.

Table 4
Primary and Secondary Outcomes Measured in the Registered studies on Therapeutic Effect Evaluation

Outcomes	No. of studies indicated as primary outcomes (%)	No. of studies indicated as secondary outcomes (%)
Mortality	31 (11.7)	67 (25.2)
Exacerbation rate/time	26 (9.8)	62 (23.3)
Length of stay in ICU	2 (0.8)	25 (9.4)
Length of hospital stay	20 (7.5)	58 (21.8)
Cure rate	23 (8.7)	17 (6.4)
Discharge rate	6 (2.3)	4 (1.5)
Lung function	28 (10.5)	30 (11.3)
Mechanical ventilation and oxygen inhalation time/rate	12 (4.5)	52 (19.6)
Imaging examinations (chest CT, X radiograph, etc.)	47 (17.7)	43 (16.2)
Oxygenation indicator	29 (10.9)	28 (10.5)
Symptoms and signs	105 (39.5)	125 (47.0)
Health status/mental state/quality of life	9 (3.4)	18 (6.8)
Viral nucleic acid/viral loads	76 (28.6)	86 (32.3)
Common laboratory tests (blood, urine routine, biochemicals, etc.)	40 (15.0)	109 (41.0)
Safety (adverse events/adverse drug reactions, etc.)	18 (6.8)	67 (25.2)
Complications	4 (1.5)	10 (3.8)
TCM Syndrome score	11 (4.1)	12 (4.5)
Other outcomes	12 (4.5)	17 (6.4)

CT, computerized tomography; ICU, Intensive care unit; TCM, Traditional Chinese Medicine; Viral loads, changes of real-time reverse-transcriptase-polymerase-chain-reaction testing.

MENTAL HEALTH & RESILIENCE NEEDS

COVID-19'S IMPACT ON HEALTHCARE WORKFORCE

PSYCHOTHERAPISTS' VICARIOUS TRAUMATIZATION DURING THE COVID-19 PANDEMIC

Aafjes-van Doorn K, Békés V, Prout TA, Hoffman L.. Psychol Trauma. 2020 Jun 1. doi: 10.1037/tra0000868. Online ahead of print.

Level of Evidence: 3

BLUF

This cross-sectional study from authors at Yeshiva University surveyed 339 psychotherapists on their experiences with the pandemic and found that 62.7% experienced moderate levels of vicarious trauma and 15% experienced high levels, though the study design made it difficult to separate primary trauma from vicarious trauma. Higher levels were associated with "younger age, less clinical experience, and negative online treatment experiences," and the authors conclude that more research into interventions targeted at mediating therapists' symptoms during the COVID-19 pandemic is needed.

ABSTRACT

During the COVID-19, psychotherapists are often exposed to traumatic material in their sessions, potentially leading to vicarious traumatization. We surveyed 339 therapists about their professional practices and experiences during the pandemic. Results showed that on average therapists experienced moderate levels of vicarious trauma, whereas about 15% experienced high levels of vicarious trauma. A higher level of vicarious trauma was associated with younger age, less clinical experience, and negative online treatment experiences. The results imply a need for personal and professional support for therapists working remotely amid a global health crisis.

IMPACT ON PUBLIC MENTAL HEALTH

COVID-19: MISINFORMATION CAN KILL

Aghagoli G, Siff EJ, Tillman AC, Feller ER.. R I Med J (2013). 2020 Jun 1;103(5):12-14.

Level of Evidence: Other

BLUF

This commentary from Brown University shares the prevalence of misinformation regarding the COVID-19 pandemic, potential constructs for rationalizing this misinformation, consequences of consuming misinformation, and methods to avoid and detect misleading messages (Table 1). In sum, individuals should limit their consumption of unreliable information pertaining to the pandemic, and when necessary, consider information and guidelines from reliable sources.

SUMMARY

This commentary focuses on misinformation during the COVID-19 pandemic. Because the overwhelming majority of Americans have access to the internet and regularly consume information that may be inaccurate, misinformation is widespread during this pandemic. In order to make sense of the pandemic, Americans often accept the most simple and unambiguous information as factual, especially information that does not conflict with existing ideals. Believing misinformation can result in direct harm from inaccurate guidelines, or overoptimism from false messages. It is important to monitor internet use and avoid malicious information. People should seek guidance from reliable sources.

FIGURES

MALICIOUS METHODS	DEFINITIONS	MISINFORMATION EXAMPLES	CORRECTIONS
Deception	Inaccurate, false information that is presented as legitimate	Untrue: "COVID-19 can be transmitted through mosquito bites."	True: COVID-19 cannot be transmitted by mosquitos.
Create False Equivalence	Comparing logical, accurate arguments to illogical, inaccurate arguments	Untrue: "Scientists disagree – no COVID-19 consensus exists."	True: Scientists commonly disagree; however, there is widespread scientific consensus about COVID-19.
Favor Simplified Messages	Tendency to favor simple messages over complicated content	Untrue: "Do not take ibuprofen if you have the virus."	True: WHO initially said that those with COVID-19 should avoid ibuprofen, but later retracted this statement.
Amplify Unreliable Messages	Frequently flood Internet with the same malicious content	Untrue: "5G spreads COVID-19."	True: 5G technology does not spread COVID-19.
Downplay Risks	Underestimate risk, overestimate ability to overcome risk	Untrue: "COVID-19 is like the common cold."	True: COVID-19 is not like the common cold; much higher fatality rates than a common cold.
Mix Content Accuracy	Combine accurate and inaccurate information	Untrue: "COVID-19 can kill older people, but it can't harm young people."	True: COVID-19 can infect and be fatal at any age.
Impersonate Reliable Sources	Attribute misinformation to a reliable source or pretend to be a reliable source	Untrue: "Dr. Fauci said social distancing doesn't matter."	True: Dr. Fauci has been a major proponent of social distancing.
Non-Verifiable Predictions	Predictions about future events that cannot be proven or disproven	Untrue: "Schools will re-open in Fall 2020."	True: School re-openings depend on diverse, uncertain scenarios.

Table 1. How Misinformation Spreads: Malicious Methods

RESOURCES

COVID-19 PANDEMIC: A COLLECTION OF RELEVANT PUBLICATIONS FROM MILITARY MEDICINE

Talbot LA, Haffner WHJ, Rice CL, Rothwell SW.. Mil Med. 2020 Jun 2:usaa108. doi: 10.1093/milmed/usaa108. Online ahead of print.

Level of Evidence: Other

BLUF

The authors compiled a list of freely available articles from Military Medicine's database published between July 1940 to February 2020 within the following six topics.

- 1) Experience with influenza epidemics and pandemics
- 2) Encounters with other infectious diseases outbreaks in a deployed environment
- 3) Policy and position articles
- 4) Potential high-risk military groups and environments
- 5) Differential, biological warfare, or natural outbreak
- 6) Pandemic strategies"

The authors hope that the collection of free articles (Table 1 and available at <https://academic.oup.com/milmed>) and wealth of knowledge from the military and military medicine will be useful to the readers during the COVID-19 pandemic.

FIGURES

Experience with influenza epidemics and pandemics
Influenza
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Table 1: Military Medicine Published Articles Organized by Themes

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