The Daily COVID-19 Literature Surveillance Summary

July 1, 2020

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COVID-19 Daily Literature Surveillance

COVID19LST

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LEVEL OF EVIDENCE

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

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

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

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

How to cite the Levels of Evidence Table
OCEBM Levels of Evidence Working Group*. "The Oxford 2011 Levels of Evidence".
Oxford Centre for Evidence-Based Medicine. http://www.cebm.net/index.aspx?o=5653
** OCEBM Table of Evidence Working Group = Jeremy Howick, Iain Chalmers (James Lind Library), Paul Glasziou, Trish Greenhalgh, Carl Heneghan, Alessandro Liberati, Ivan Moschetti, Bob Phillips, Hazel Thornton, Olive Goddard and Mary Hodgkinson*

EXECUTIVE SUMMARY

Epidemiology

- Investigators in Sweden studied the logistics for distributing and collecting SARS-CoV-2 tests via drones and discuss how statistical modeling suggests that testing as little as 3.3% of the population through this method daily could effectively help to flatten the curve.
- A multivariable analysis of 220 hospitalized and 311 non-hospitalized cases of confirmed COVID-19 found that age greater than or equal to 65 years, black race, a history of diabetes mellitus, lack of insurance, male sex, smoking, and obesity were all independently associated with hospitalization.

Transmission & Prevention

- A social psychology survey of 704 participants concluded that people who held individualistic values, in contrast to those with collectivist attitudes, were more likely to harbor feelings of powerlessness and believe in conspiracy theories, and were also less likely to take action to reduce the spread of COVID-19.

Management

- Review of the impact of COVID-19 on immunocompromised patients found that patients with cancer and solid organ transplant may have a higher risk for severe COVID-19, greater use of antiviral and corticosteroid medication, and higher overall mortality rates, though the evidence is unclear for patients who are immunosuppressed for other reasons.

Adjusting Practice During COVID-19

- Guidelines and recommendations for practice during the pandemic include:
    - Cancer radiotherapy
    - Risk stratification and guidance for thalassemia patients
- A group of Canadian physicians recommend that psychiatrists ensure continuity of care during COVID-19 via telepsychiatry but still offer in-person interventions such as electroconvulsive therapy (ECT) to patients with severe psychiatric disease.

R&D: Diagnosis & Treatment

- In order to meet the demand of COVID-19 tests ordered in Portugal, hundreds of volunteers with various skill sets have been trained to help run RT-PCR tests. Through this, Portugal has been able to hugely expand its testing capacity and is now among the top 10 countries in testing per capita with 15% of testing being completed at institutions consisting primarily of volunteers.
- A retrospective study of 802 hospitalized patients with clinical symptoms and/or CT imaging indicative of COVID-19 found that IgM and IgG tend to peak after the ninth week of infection versus nucleic acid testing which peaks during the first week.

Mental Health and Resilience Needs

- A national survey of 10,368 U.S. residents found that 15% of respondents were categorized as high risk on the Suicide Behaviors Questionnaire-Revised (SBQ-R). A higher SBQ-score was associated with Blacks, Native Americans, Hispanics, families with children, the unmarried, and the young.
- A survey of 202 nurses from tertiary hospitals in the Hubei province who were exposed to COVID-19 found a post-traumatic stress disorder rate of 16.83% and note that lower levels of PTSD symptoms were associated with higher job satisfaction, positive coping mechanisms, and male sex.

TABLE OF CONTENTS

A NONLINEAR EPIDEMIOLOGICAL MODEL CONSIDERING ASYMPTOTIC AND QUARANTINE CLASSES FOR SARS COV-2 VIRUS

Mishra AM, Purohit SD, Owolabi KM, Sharma YD.. Chaos Solitons Fractals. 2020 Sep;138:109953. doi: 10.1016/j.chaos.2020.109953. Epub 2020 Jun 4.

Level of Evidence: Other - Modeling

BLUF

An international group of mathematical researchers developed a deterministic compartment model of SARS-CoV-2 transmission with associated sensitivity analysis. Their model found that reducing infection rate (η, see Figure 5) limited disease spread effectively, while changing the asymptomatic infected rate (ρ) and quarantine rate (θ) did not affect the number of infected persons at a large scale (Figures 6 and 7). These results suggest that early, aggressive testing and isolation of infected individuals may be most effective for reducing disease burden. Additionally, their described model may be useful to predict COVID-19 spread and to evaluate future outbreaks.

ABSTRACT

In this article, we develop a mathematical model considering susceptible, exposed, infected, asymptotic, quarantine/isolation and recovered classes as in case of COVID-19 disease. The facility of quarantine/isolation have been provided to both exposed and infected classes. Asymptotic individuals either recovered without undergo treatment or moved to infected class after some duration. We have formulated the reproduction number for the proposed model. Elasticity and sensitivity analysis indicates that model is more sensitive towards the transmission rate from exposed to infected classes rather than transmission rate from susceptible to exposed class. Analysis of global stability for the proposed model is studied through Lyapunov's function.

FIGURES

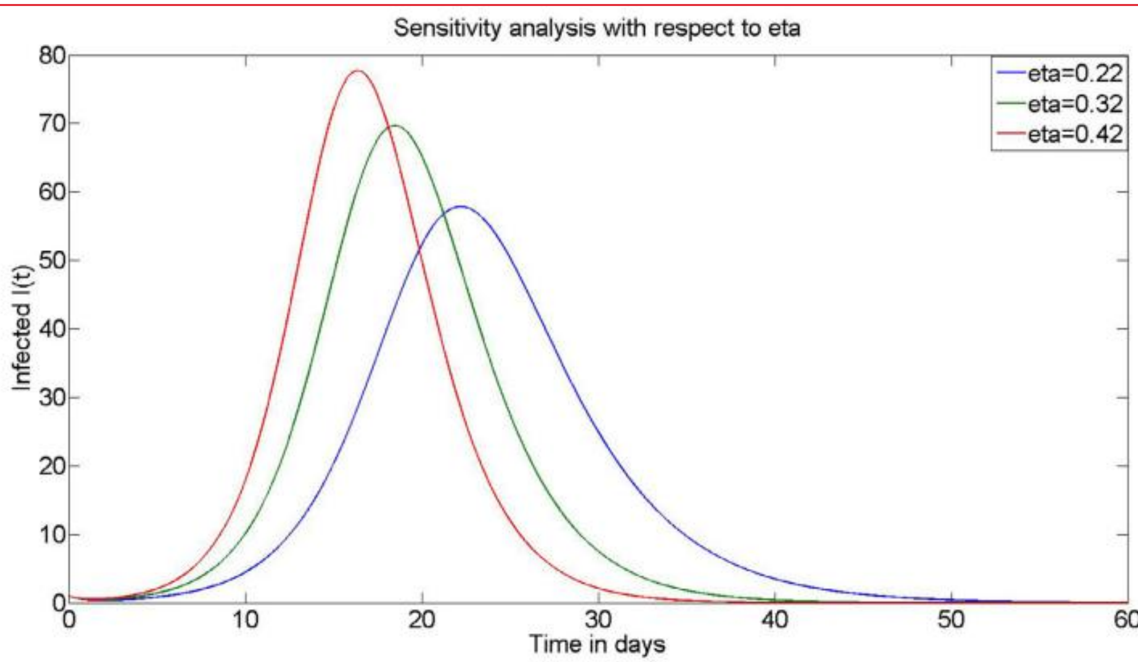

Figure 5. Sensitivity analysis with respect to η.

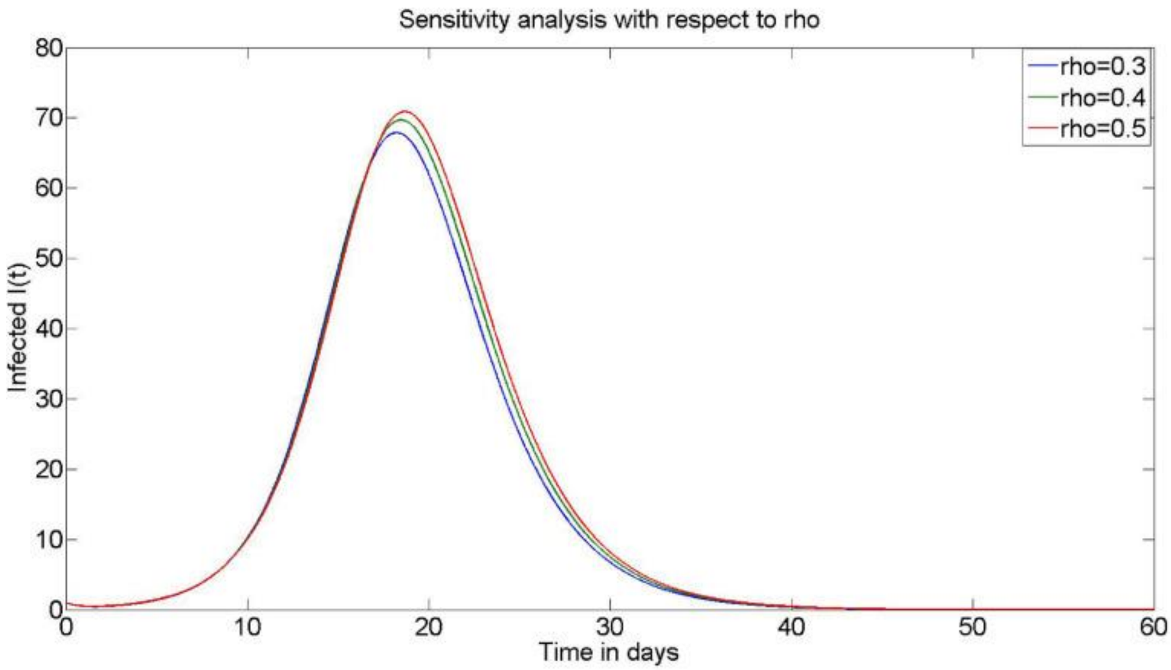

Figure 6. Sensitivity analysis with respect to ρ.

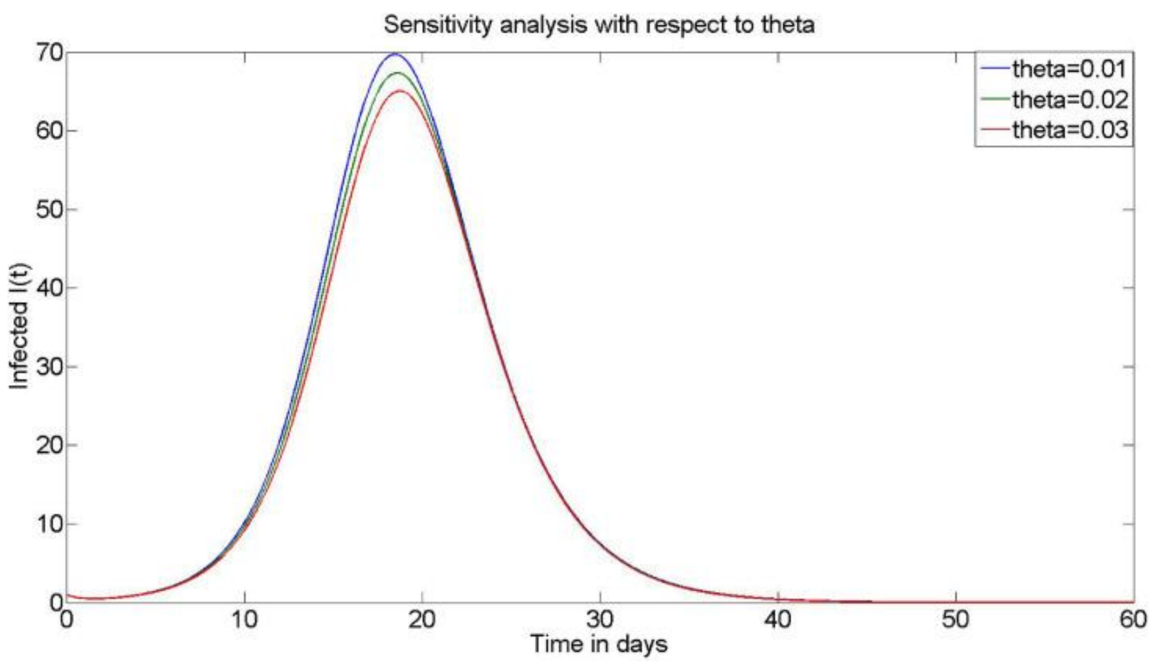

Figure 6. Sensitivity analysis with respect to ρ.

MODELING QUARANTINE DURING EPIDEMICS AND MASS-TESTING USING DRONES

Sedov L, Krasnochub A, Polishchuk V.. PLoS One. 2020 Jun 24;15(6):e0235307. doi: 10.1371/journal.pone.0235307. eCollection 2020.
Level of Evidence: Other - Modeling

BLUF

Researchers studied logistics for distributing and collecting SARS-CoV-2 tests via drones for 102,638 inhabitants across Norrköping, Sweden (Fig. 2). They separately analyzed a susceptible, infected, recovered, quarantine (SIRQ) model, which introduced a "quarantine" category to reflect individuals who are self-isolating at home. They discovered that randomly testing at least 3.3% of the population daily (interval D) would "flatten the curve" of COVID-19 cases significantly (Fig. 4), suggesting that routine testing for SARS-CoV-2 infection and/or immunity, perhaps via the drone method, may help to target asymptomatic spread and successfully address the COVID-19 pandemic in Sweden.

SUMMARY

The authors report 36 Switzerland Matternet drones, each with a carrying capacity of 100 tests were sufficient to distribute, collect and return the tests to the lab. Results from tests were electronically delivered. They acknowledge mass testing with drones is limited by drone battery life which affects their ability to reach rural locations and that cargo/weight capacity of drones varies among different models. They utilized one hospital from which drones were dispatched and returned to, but recommend splitting the geographic area among testing centers to optimize resources. This study has important implications from a public health standpoint as drones mitigate risk associated with visiting hospitals and testing facilities, while enabling the distribution and collection of immunity tests to people in quarantine. The feasibility of mass testing operations warrants further exploration.

ABSTRACT

We extend the classical SIR epidemic spread model by introducing the "quarantined" compartment. We solve (numerically) the differential equations that govern the extended model and quantify how quarantining "flattens the curve" for the proportion of infected population over time. Furthermore, we explore the potential of using drones to deliver tests, enabling mass-testing for the infection; we give a method to estimate the drone fleet needed to deliver the tests in a metropolitan area. Application of our models to COVID-19 spread in Sweden shows how the proposed methods could substantially decrease the peak number of infected people, almost without increasing the duration of the epidemic.

FIGURES

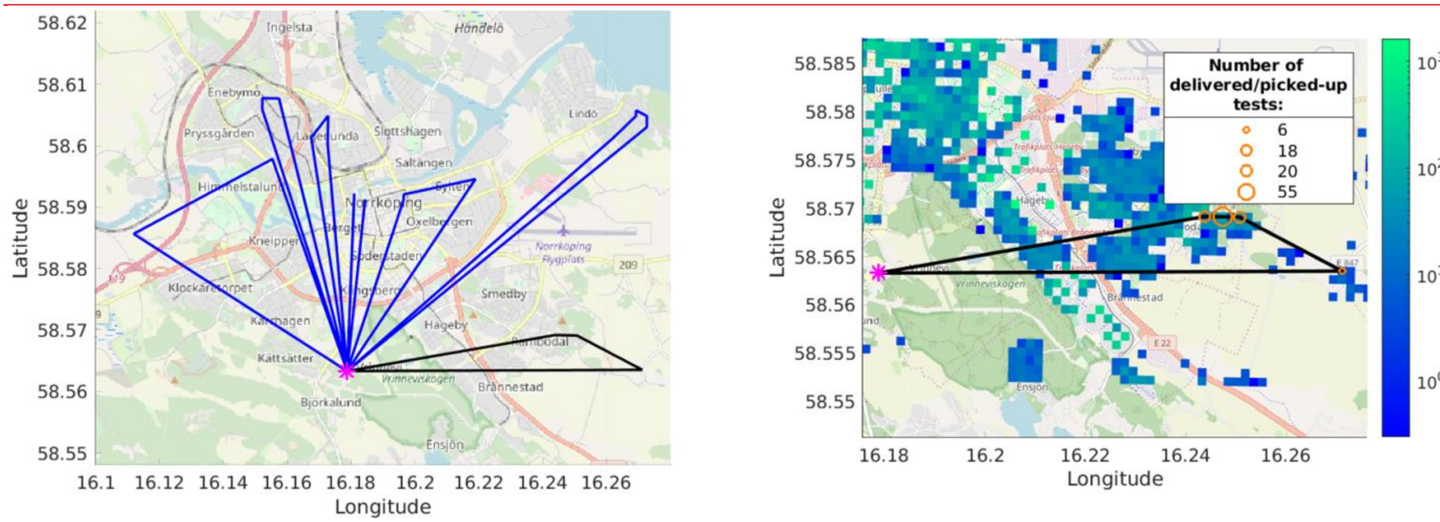

Fig 2. Drone routes.

Left: An example route of a drone with capacity 100; one of the tours in the route is shown black. Pink asterisk is the hospital. Right: A zoom in on the black tour: the orange circles depict the tests delivery/pickup locations; circle size is proportional to the number of tests delivered/picked-up at the location (99 tests are delivered on this tour). The underlying heatmap is the population density. The background map was rendered on the authors' machines from OpenStreetMap data [13] with OpenStreetMap Carto style [14] using the code available from [15].

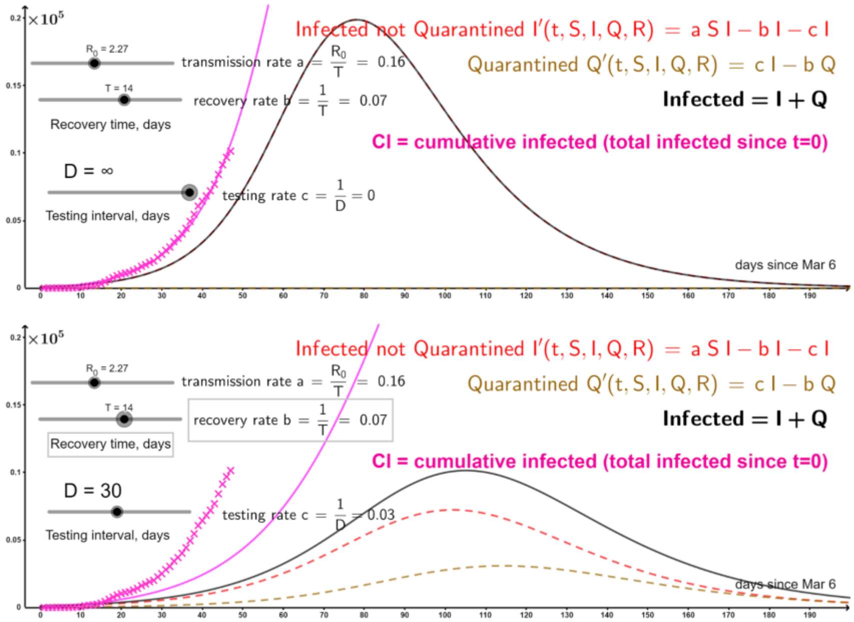

Fig 4. COVID-19 cases growth (starting from 100 cases) in Sweden [42] shown with pink crosses.
Top: SIR model (S and R not shown). Bottom: Mass-testing even as rarely as every D = 30 days flattens the curve.

SYMPTOMS AND CLINICAL PRESENTATION

COVID-19 SYMPTOMS PREDICTIVE OF HEALTHCARE WORKERS' SARS-COV-2 PCR RESULTS

Lan FY, Filler R, Mathew S, Buley J, Iliaki E, Bruno-Murtha LA, Osgood R, Christophi CA, Fernandez-Montero A, Kales SN..
PLoS One. 2020 Jun 26;15(6):e0235460. doi: 10.1371/journal.pone.0235460. eCollection 2020.
Level of Evidence: 3 - Local non-random sample

BLUF

A retrospective cohort study conducted in Massachusetts from March 9 to April 15, 2020 by Harvard University found that healthcare workers with three or more symptoms were more likely to test positive for SARS-CoV-2 [1.95 (95% CI: 1.10–3.64)], while healthcare workers with isolated nasal congestion, sore throat or no symptoms were more likely to test negative (p = 0.006) (Table 2). It was determined that fever, myalgia, and anosmia/ageusia were most predictive of positive testing for SARS-CoV-2 (Table 1, Figure 1), suggesting that certain symptoms may be more predictive of positive SARS-CoV-2 testing in healthcare workers.

ABSTRACT

BACKGROUND: Coronavirus 2019 disease (COVID-19) is caused by the virus SARS-CoV-2, transmissible both person-to-person and from contaminated surfaces. Early COVID-19 detection among healthcare workers (HCWs) is crucial for protecting patients and the healthcare workforce. Because of limited testing capacity, symptom-based screening may prioritize testing and increase diagnostic accuracy.
METHODS AND FINDINGS: We performed a retrospective study of HCWs undergoing both COVID-19 telephonic symptom screening and nasopharyngeal SARS-CoV-2 assays during the period, March 9-April 15, 2020. HCWs with negative assays but progressive symptoms were re-tested for SARS-CoV-2. Among 592 HCWs tested, 83 (14%) had an initial positive SARS-CoV-2 assay. Fifty-nine of 61 HCWs (97%) who were asymptomatic or reported only sore throat/nasal congestion had negative SARS-CoV-2 assays (P = 0.006). HCWs reporting three or more symptoms had an increased multivariate-adjusted odds of having positive assays, 1.95 (95% CI: 1.10-3.64), which increased to 2.61 (95% CI: 1.50-4.45) for six or more symptoms. The multivariate-adjusted odds of a positive assay were also increased for HCWs reporting fever and a measured temperature >= 37.5 C (3.49 (95% CI: 1.95-6.21)), and those with myalgias (1.83 (95% CI: 1.04-3.23)). Anosmia/ageusia (i.e. loss of smell/loss of taste) was reported less frequently (16%) than other symptoms by HCWs with positive assays, but was associated with more than a seven-fold multivariate-adjusted odds of a positive test: OR = 7.21 (95% CI: 2.95-17.67). Of 509 HCWs with initial

negative SARS-CoV-2 assays, nine had symptom progression and positive re-tests, yielding an estimated negative predictive value of 98.2% (95% CI: 96.8-99.0%) for the exclusion of clinically relevant COVID-19.
CONCLUSIONS: Symptom and temperature reports are useful screening tools for predicting SARS-CoV-2 assay results in HCWs. Anosmia/ageusia, fever, and myalgia were the strongest independent predictors of positive assays. The absence of symptoms or symptoms limited to nasal congestion/sore throat were associated with negative assays.

FIGURES

Table 1. Symptom and body temperature distributions at time of triage among healthcare workers (HCWs) by SARS-CoV-2 test results.

	Overall (N = 592)	Positive (N = 83)	Negative (N = 509)	P value
Age	43.6 (12.9)	43.9 (12.7)	43.6 (12.9)	0.843
Female	467 (78.9%)	60 (72.3%)	407 (80.0%)	0.149
Fever	182 (30.7%)	46 (55.4%)	136 (26.7%)	**<0.001**
Measured Temperature (°C)	37.68 (0.71) (n = 161)	37.95 (0.69) (n = 40)	37.60 (0.69) (n = 121)	**0.006**
Temperature ≥ 37.5°C	102 (63.4%) (102/161)	34 (85.0%) (34/40)	68 (56.2%) (68/121)	**0.002**
Cough	365 (61.7%)	59 (71.1%)	306 (60.1%)	0.074
Shortness of breath	111 (18.8%)	14 (16.9%)	97 (19.1%)	0.747
Myalgia	225 (38.0%)	47 (56.6%)	178 (35.0%)	**<0.001**
Malaise	274 (46.3%)	47 (56.6%)	227 (44.6%)	0.055
Sore throat	320 (54.1%)	38 (45.8%)	282 (55.4%)	0.131
Nasal symptoms (runny, sneezing, congestion, sinus)	293 (49.5%)	29 (34.9%)	264 (51.9%)	**0.006**
Gastrointestinal symptoms (nausea/ vomiting/ diarrhea)	151 (25.5%)	20 (24.1%)	131 (25.7%)	0.856
Rash	10 (1.7%)	3 (3.6%)	7 (1.4%)	0.154[a]
Anosmia/Ageusia	27 (4.6%)	13 (15.7%)	14 (2.8%)	**<0.001**
Headache	175 (29.6%)	34 (41.0%)	141 (27.7%)	**0.020**

Mean (SD) for age and body temperature, count (percentage) for all other variables.
[a] Based on Fisher's exact test.

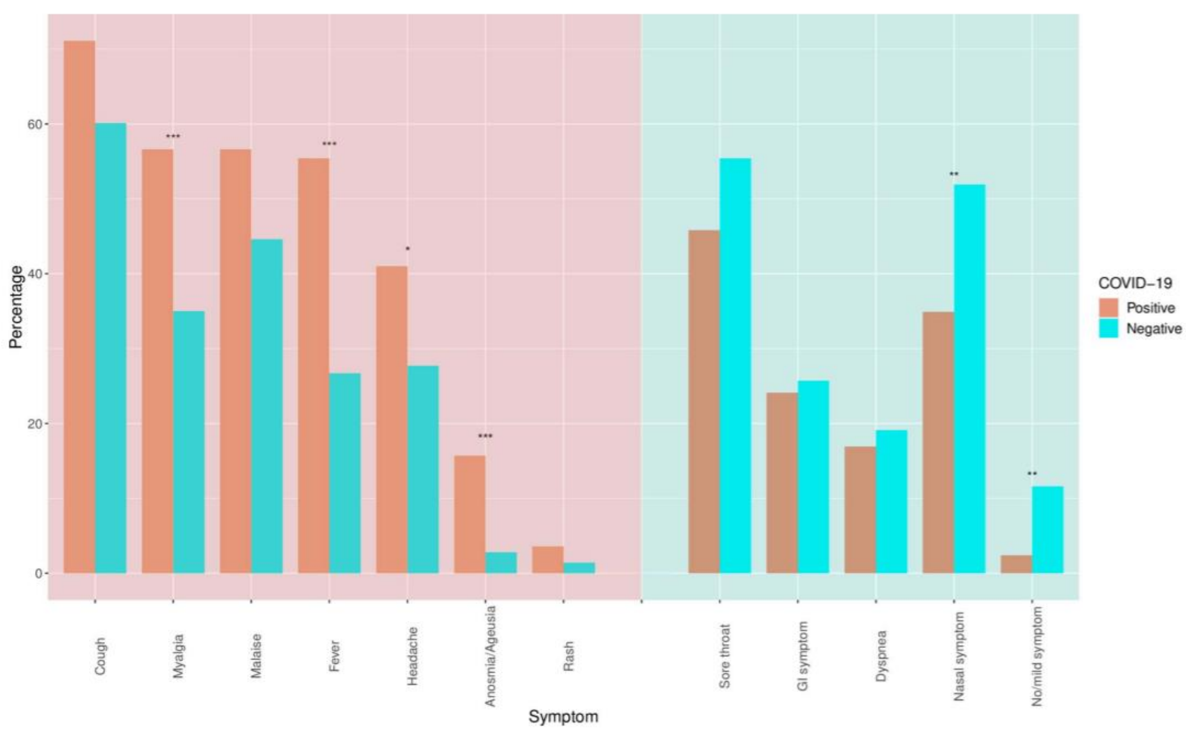

Fig 1. Symptom distributions among HCWs with initial SARS-CoV-2 (the virus causing COVID-19) testing results. The symptoms shaded in salmon-red are the symptoms more frequently seen with positive tests, and the symptoms shaded in blue-green are more frequently seen with negative tests. GI symptom denotes a gastrointestinal symptom (nausea/ vomiting/ diarrhea). Nasal symptom includes runny nose, sneezing, congestion, and sinus symptoms. No/mild symptom denotes no symptom or only sore throat and/or nasal symptoms. The asterisks above the bars denote different statistically significance levels when comparing HCWs with positive assays and HCWs with negative assays (*: P<0.05, **: P<0.01, ***: P<0.001).

Table 2. SARS-CoV-2 test results in asymptomatic healthcare workers (HCWs) and HCWs with only nasal/throat symptoms.

	Positive (N = 83)	Negative (N = 509)	P value [a]
No symptom	2 (2.4%)	25 (4.9%)	0.406
Only sore throat	0 (0%)	12 (2.4%)	0.390
Only nasal symptoms	0 (0%)	7 (1.4%)	0.601
Only sore throat and/or nasal symptoms	0 (0%)	34 (6.7%)	**0.009**
No symptom or Only sore throat and/or nasal symptoms	2 (2.4%)	59 (11.6%)	**0.006**

[a] Fisher's exact test

ADULTS

CHARACTERISTICS ASSOCIATED WITH HOSPITALIZATION AMONG PATIENTS WITH COVID-19 - METROPOLITAN ATLANTA, GEORGIA, MARCH-APRIL 2020

Killerby ME, Link-Gelles R, Haight SC, Schrodt CA, England L, Gomes DJ, Shamout M, Pettrone K, O'Laughlin K, Kimball A, Blau EF, Burnett E, Ladva CN, Szablewski CM, Tobin-D'Angelo M, Oosmanally N, Drenzek C, Murphy DJ, Blum JM, Hollberg J, Lefkove B, Brown FW, Shimabukuro T, Midgley CM, Tate JE; CDC COVID-19 Response Clinical Team.. MMWR Morb Mortal Wkly Rep. 2020 Jun 26;69(25):790-794. doi: 10.15585/mmwr.mm6925e1.
Level of Evidence: 3 - Local non-random sample

BLUF

A multivariable analysis conducted by researchers at the Centers for Disease Control and Prevention reviewed 220 hospitalized and 311 non-hospitalized cases of confirmed COVID-19 from March 1st through April 7th, 2020 in metropolitan Atlanta, Georgia. They found that age greater than or equal to 65 years, black race, a history of diabetes mellitus, lack of insurance, male sex, smoking, and obesity were all independently associated with hospitalization (Figure). The authors indicate the findings highlight the importance of preventative measures such as social distancing, staying at home, management of underlying conditions, and wearing a cloth face covering for those at highest risk of hospitalization.

ABSTRACT

The first reported U.S. case of coronavirus disease 2019 (COVID-19) was detected in January 2020 (1). As of June 15, 2020, approximately 2 million cases and 115,000 COVID-19-associated deaths have been reported in the United States.* Reports of U.S. patients hospitalized with SARS-CoV-2 infection (the virus that causes COVID-19) describe high proportions of older, male, and black persons (2-4). Similarly, when comparing hospitalized patients with catchment area populations or nonhospitalized COVID-19 patients, high proportions have underlying conditions, including diabetes mellitus, hypertension, obesity, cardiovascular disease, chronic kidney disease, or chronic respiratory disease (3,4). For this report, data were abstracted from the medical records of 220 hospitalized and 311 nonhospitalized patients aged >=18 years with laboratory-confirmed COVID-19 from six acute care hospitals and associated outpatient clinics in metropolitan Atlanta, Georgia. Multivariable analyses were performed to identify patient characteristics associated with hospitalization. The following characteristics were independently associated with hospitalization: age >=65 years (adjusted odds ratio [aOR] = 3.4), black race (aOR = 3.2), having diabetes mellitus (aOR = 3.1), lack of insurance (aOR = 2.8), male sex (aOR = 2.4), smoking (aOR = 2.3), and obesity (aOR = 1.9). Infection with SARS-CoV-2 can lead to severe outcomes, including death, and measures to protect persons from infection, such as staying at home, social distancing (5), and awareness and management of underlying conditions should be emphasized for those at highest risk for hospitalization with COVID-19. Measures that prevent the spread of infection to others, such as wearing cloth face coverings (6), should be used whenever possible to protect groups at high risk. Potential barriers to the ability to adhere to these measures need to be addressed.

FIGURES

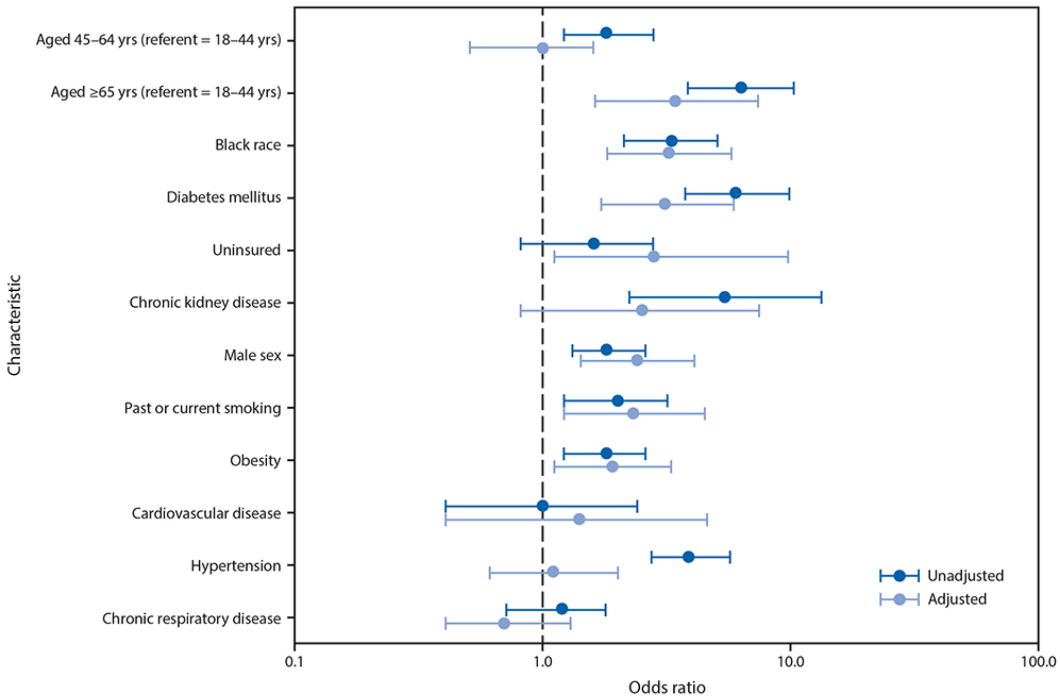

Figure. Unadjusted and adjusted* odds ratios and 95% confidence intervals for hospitalizations in COVID-19 patients (n = 506†) evaluated at six acute care hospitals and associated outpatient clinics, by selected characteristics — metropolitan Atlanta, Georgia, March 1–April 7, 2020. * Adjusted for age, sex, race, obesity, past or current smoking, insurance status, obesity, and other underlying conditions (hypertension, diabetes mellitus, cardiovascular disease, chronic respiratory disease, and chronic kidney disease). † Complete case analysis was used for multivariable analyses; therefore, n = 368 for the multivariable model.

MANIFESTATIONS OF BLOOD COAGULATION AND ITS RELATION TO CLINICAL OUTCOMES IN SEVERE COVID-19 PATIENTS: RETROSPECTIVE ANALYSIS

Zhang Y, He L, Chen H, Lu S, Xiong Y, Liu J, Zheng Y, Wang S, Liu L.. Int J Lab Hematol. 2020 Jun 27. doi: 10.1111/ijlh.13273. Online ahead of print.
Level of Evidence: 4 - Case-control studies, or "poor or non-independent reference standard

BLUF

A retrospective case-control study of 71 patients (compared to 61 healthy controls) who manifested with severe COVID-19 disease and received treatment at Wuhan First Hospital between February 12 to March 20, 2020 found that coagulation and liver function tests correlated with disease severity and outcome (Table 3). COVID-19 patients tended to have higher coagulation parameters than controls (Table 2) and patients with aggravated disease were found to have elevated coagaulation parameters, liver function tests, and inflammatory markers compared to those with non-aggravated disease (Table 3). The authors recommend early diagnosis and treatment of coagulopathy disorders as a means to arrest disease progression in COVID-19 patients.

ABSTRACT

INTRODUCTION: Characteristics of blood coagulation and its relation to clinical outcomes in COVID-19 patients are still rarely reported. We aimed to investigate the blood coagulation function and its influences on clinical outcomes of patients with syndrome coronavirus 2 (SARS-CoV-2) infection.
METHODS: A total of 71 severe patients with confirmed SARS-CoV-2 infection who were treated in Wuhan First Hospital from February 12 to March 20, 2020, were enrolled. The blood coagulation data in these patients and in 61 healthy controls were collected. The patients with COVID-19 were divided into two groups: the aggravated group and the nonaggravated group, respectively, basing on whether the patients' conditions turned to critically ill or not after admission. RESULTS: Compared with healthy controls, patients with COVID-19 had significant performances with coagulation dysfunction, including dramatically elevated values of FIB, PT, APTT, INR, FDP, and D-Dimers but markedly reduced AT value (P < .05). Importantly,

more noteworthy coagulation disorders similar to the differences between patients and controls were found in the aggravated patients with conditions deterioration after admission than those in the nonaggravated patients without conditions deterioration ($P < .05$). Moreover, the aggravated patients possessed a longer hospital stay and a higher mortality compared with the nonaggravated patients ($P < .001$). The coagulation parameters of COVID-19 patients were widely and closely related to the indexes of liver function and inflammation ($P < .05$), indicating the coagulation dysfunction of these patients may be caused by liver injury and inflammatory storm. CONCLUSION: Severe patients with SARS-CoV-2 infection often possess coagulation dysfunction on admission. A certain correlation exists in coagulation disorder and adverse clinical outcome among severe COVID-19 patients.

FIGURES

Parameters	Aggravated (N = 17)	Nonaggravated (N = 54)	P value
Coagulation function test			
FIB (g/L; normal range 2.00-4.00)	3.84 (3.51-4.40)	3.96 (3.42-4.17)	.532
Increased	8 (47.1)	19 (35.2)	.379
APTT (s; normal range 20.00-40.00)	30.40 (24.30-34.65)	26.10 (24.10-28.43)	.027
Increased	0 (0.0)	0 (0.0)	>.99
PT (s; normal range 9.00-13.00)	12.00 (11.75-12.80)	11.50 (10.90-11.83)	<.001
Increased	3 (17.6)	3 (5.6)	.144
TT (s; normal range 14.00-21.00)	17.20 (16.95-19.35)	18.10 (17.30-19.00)	.200
INR (normal range 0.70-1.30)	1.07 (1.05-1.14)	1.02 (0.96-1.05)	<.001
Increased	1 (5.9)	0 (0.0)	.239
FDP (mg/L; normal range 0.0-5.0)	13.00 (5.50-65.05)	2.40 (1.70-5.00)	<.001
Increased	14 (82.4)	13 (24.1)	<.001
D-D (mg/L; normal range 0.00-0.55)	5.95 (1.23-20.08)	0.44 (0.25-1.19)	<.001
Increased	15 (88.2)	18 (33.3)	<.001
AT (%; normal range 75.0-141.0)	76.10 (63.40-81.35)	84.25 (79.48-91.95)	<.001
Decreased	7 (41.2)	5 (9.3)	.007
Liver function test			
ALT (U/L; normal range 7-45)	25.00 (15.50-112.00)	24.50 (13.75-40.00)	.217
Increased	7 (41.1)	12 (22.2)	.220
AST (U/L; normal range 13-35)	38.00 (24.50-88.50)	23.00 (17.75-35.00)	.003
Increased	9 (52.9)	12 (22.2)	.016
TBiL (μmol/L; normal range 2.0-24.0)	14.30 (11.45-18.55)	11.30 (8.58-15.03)	.036
Increased	2 (11.8)	3 (5.6)	.587
DBiL (μmol/L; normal range 0.0-7.0)	2.80 (1.30-4.45)	1.50 (1.08-2.35)	.026
Increased	1 (5.9)	1 (1.9)	.424
Diagnostic enzyme index			
LDH (U/L; normal range 114-250)	382.00 (271.00-515.00)	180.00 (157.00-218.00)	<.001
Increased	14 (82.4)	6 (11.1)	<.001
CRP (mg/L; normal range 0.00-5.00)	73.20 (31.50-128.00)	3.11 (3.11-12.45)	<.001
Increased	16 (94.1)	19 (35.2)	<.001

Note: Data are median (IQR) or n (%).P values comparing patients in the aggravated group and in the nonaggravated group are from Chi-square test, Fisher's exact test, or Mann-Whitney *U* test.

Aggravated, patients in the aggravated group; Nonaggravated, patients in the nonaggravated group.

Abbreviations: ALT, alanine aminotransferase; APTT, activated partial thromboplastin time; AST, aspartate aminotransferase; AT, antithrombin; CRP, C-reactive protein; DBiL, direct bilirubin; D-D, D-Dimers; FDP, fibrin/fibrinogen degradation products; FIB, fibrinogen; INR, international normalized ratio; LDH, lactate dehydrogenase; PT, prothrombin time; TBiL, total bilirubin; TT, thrombin time.

Table 3. Laboratory findings on admission and clinical outcomes of COVID-19 patients.

PEDIATRICS

FIRST PAEDIATRIC COVID-19 ASSOCIATED DEATH IN ITALY

Mercolini F, Donà D, Girtler Y, Mussner KA, Biban P, Bordugo A, Molinaro G.. J Paediatr Child Health. 2020 Jun 27. doi: 10.1111/jpc.14994. Online ahead of print.
Level of Evidence: 5 - Case report

BLUF

A case report of a five year old female from Italy with a history of mucolipidosis type II who had symptoms of fever, rhinorrhea, dyspnea and bilateral opacification on chest x-ray (Figure 1) and tested positive for COVID-19 by nasopharyngeal swab. Treatment with Ceftriaxone, Azithromycin, and Methylprednisolone was unsuccessful and the patient passed away several days after beginning treatment. This case study highlights how preexisting metabolic and degenerative disorders can negatively impact a pediatric patient's COVID-19 prognosis and suggests that new guidelines need to be established for the care of such patients.

ADVANCED AGE

ORBITOFRONTAL INVOLVEMENT IN A NEUROCOVID-19 PATIENT

Le Guennec L, Devianne J, Jalin L, Cao A, Galanaud D, Navarro V, Boutolleau D, Rohaut B, Weiss N, Demeret S.. Epilepsia. 2020 Jun 26. doi: 10.1111/epi.16612. Online ahead of print.
Level of Evidence: Other - Case Report

BLUF

Authors present the case of a SARS-CoV-2-positive 69-year-old man in France presenting with anosmia and in status epilepticus, with a brain MRI showing hyperintensity of the right orbital prefrontal cortex near the olfactory bulb. Although the patient recovered after one week, MRI on day 15 showed hyperintensity of the right caudate nucleus and decreased prefrontal cortex hyperintensity (Figure 2) in addition to the patient experiencing symptoms of frontal lobe syndrome. Based on these findings, the authors support the claim that SARS-CoV-2 brain infiltration may occur through the olfactory pathway, hypothesizing several mechanisms (direct neuronal injury, immune-mediated encephalitis, etc.) for CNS involvement during infection.

ABSTRACT

Neurological manifestations of COVID-19 such as encephalitis and seizures have been increasingly reported, but our understanding of COVID-related brain injury is still limited. Herein we describe prefrontal involvement in a COVID-19 patient who presented prior anosmia, raising the question of a potential trans-olfactory-bulb brain invasion.

FIGURES

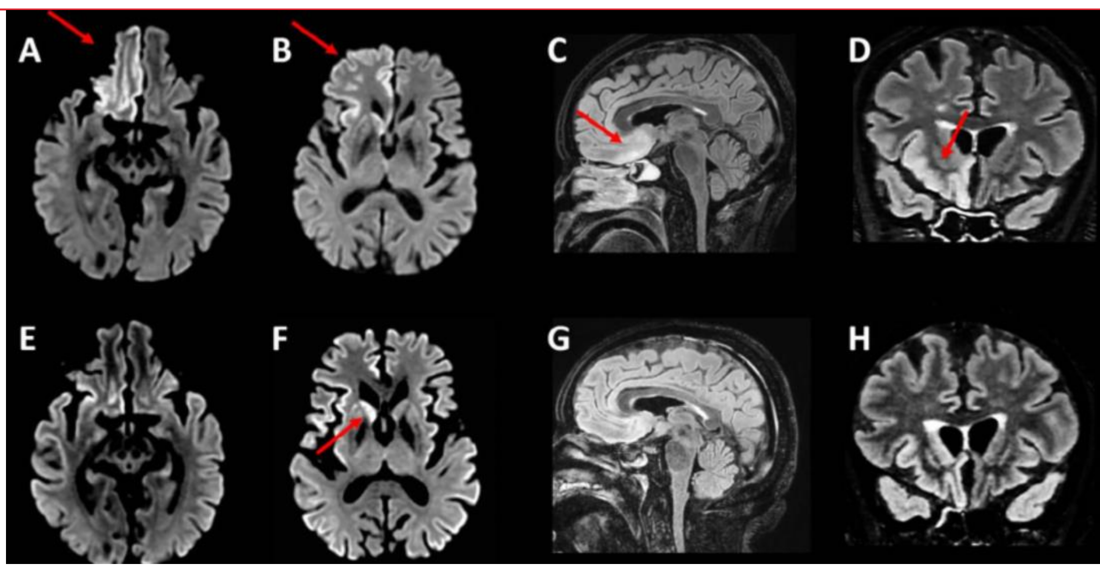

Figure 2. Brain MRI Upper panel : Brain MRI on admission : (A, B) Axial Diffusion-weighted image (DWI) showing right orbitofrontal cortex and caudate nucleus hyperintensity (tip of the red arrow). (C) Sagital fluid-attenuated inversion recovery (T2/FLAIR) showing right orbitofrontal cortico subcortical hyperintensity toward caudate nucleus (tip of the red arrow). (D) Coronal T2/FLAIR showing an orbitofrontal hyperintensity (tip of the red arrow). Lower panel: Brain MRI on day 15: (E, F) Axial DWI showing decrease of the hyperintensity within the right orbitofrontal cortex but persistance on the right caudate nucleus (tip of the red arrow). (G) Sagital and (H) coronal T2/FLAIR showing decrease of the hyperintensity within the right orbitofrontal cortex.

UNDERSTANDING THE PATHOLOGY

RELATIONSHIP BETWEEN ACE2 AND OTHER COMPONENTS OF THE RENIN-ANGIOTENSIN SYSTEM

Cohen JB, Hanff TC, Bress AP, South AM.. Curr Hypertens Rep. 2020 Jun 26;22(7):44. doi: 10.1007/s11906-020-01048-y.
Level of Evidence: Other - Review / Literature Review

BLUF

In this review article, the authors detail the role of angiotensin-converting enzyme 2 (ACE2) in the renin-angiotensin system (Figure 1) and its association with COVID-19. ACE2 facilitates SARS-CoV-2 entry into endothelial cells during infection, but it may also play a protective role against severe lung injury given its vasodilatory, natriuretic, anti-inflammatory, and anti-fibrotic effects. The authors suggest further research is necessary to better manage patients on drug therapies targeting the renin-angiotensin system in the setting of COVID-19, especially given that down regulation of ACE2 leads to increased Angiotensin II, which may be associated with hypercoagulability and vasculopathy during infection.

ABSTRACT

PURPOSE OF THE REVIEW: Angiotensin-converting enzyme 2 (ACE2) is a key counter-regulatory component of the renin-angiotensin system. Here, we briefly review the mechanistic and target organ effects related to ACE2 activity, and the importance of ACE2 in SARS-CoV-2 infection. RECENT FINDINGS: ACE2 converts angiotensin (Ang) II to Ang-(1-7), which directly opposes the vasoconstrictive, proinflammatory, and prothrombotic effects of Ang II. ACE2 also facilitates SARS-CoV-2 viral entry into host cells. Drugs that interact with the renin-angiotensin system may impact ACE2 expression and COVID-19 pathogenesis; however, the magnitude and direction of these effects are unknown at this time. High quality research is needed to improve our understanding of how agents that act on the renin-angiotensin system impact ACE2 and COVID-19-related disease outcomes.

IN SILICO

TIME SERIES PREDICTION OF COVID-19 BY MUTATION RATE ANALYSIS USING RECURRENT NEURAL NETWORK-BASED LSTM MODEL

Pathan RK, Biswas M, Khandaker MU.. Chaos Solitons Fractals. 2020 Sep;138:110018. doi: 10.1016/j.chaos.2020.110018. Epub 2020 Jun 13.
Level of Evidence: Other - Modeling

BLUF

Researchers studied the mutation rate of SARS-CoV-2 by analyzing its genomic sequence in 3408 infected patients from 33 countries across the world from 12th January to 11th May 2020 via the NCBI GenBank database (Table 1). They found higher rates of mutation between Thymine (T) and Adenine (A) nucleotides and that codons as a whole were less susceptible to change with a mutation rate of 0.12% (Fig 4). Using a recurrent neural network (RNN) based Long Short Term Memory (LSTM) model, an algorithm was developed to predict the mutation rate of SARS-CoV-2 in future time (Fig 10). The authors suggest their model may be useful to predict future SARS-CoV-2 mutations to inform viral evolution and its implications for virulence, risk assessment, and vaccine development.

ABSTRACT

SARS-CoV-2, a novel coronavirus mostly known as COVID-19 has created a global pandemic. The world is now immobilized by this infectious RNA virus. As of June 15, already more than 7.9 million people have been infected and 432k people died. This RNA virus has the ability to do the mutation in the human body. Accurate determination of mutation rates is essential to comprehend the evolution of this virus and to determine the risk of emergent infectious disease. This study explores the mutation rate of the whole genomic sequence gathered from the patient's dataset of different countries. The collected dataset is processed to determine the nucleotide mutation and codon mutation separately. Furthermore, based on the size of the dataset, the determined mutation rate is categorized for four different regions: China, Australia, the United States, and the rest of the World. It has been found that a huge amount of Thymine (T) and Adenine (A) are mutated to other nucleotides for all regions, but codons are not frequently mutating like nucleotides. A recurrent neural network-based Long Short Term Memory

(LSTM) model has been applied to predict the future mutation rate of this virus. The LSTM model gives Root Mean Square Error (RMSE) of 0.06 in testing and 0.04 in training, which is an optimized value. Using this train and testing process, the nucleotide mutation rate of 400th patient in future time has been predicted. About 0.1% increment in mutation rate is found for mutating of nucleotides from T to C and G, C to G and G to T. While a decrement of 0.1% is seen for mutating of T to A, and A to C. It is found that this model can be used to predict day basis mutation rates if more patient data is available in updated time.

FIGURES

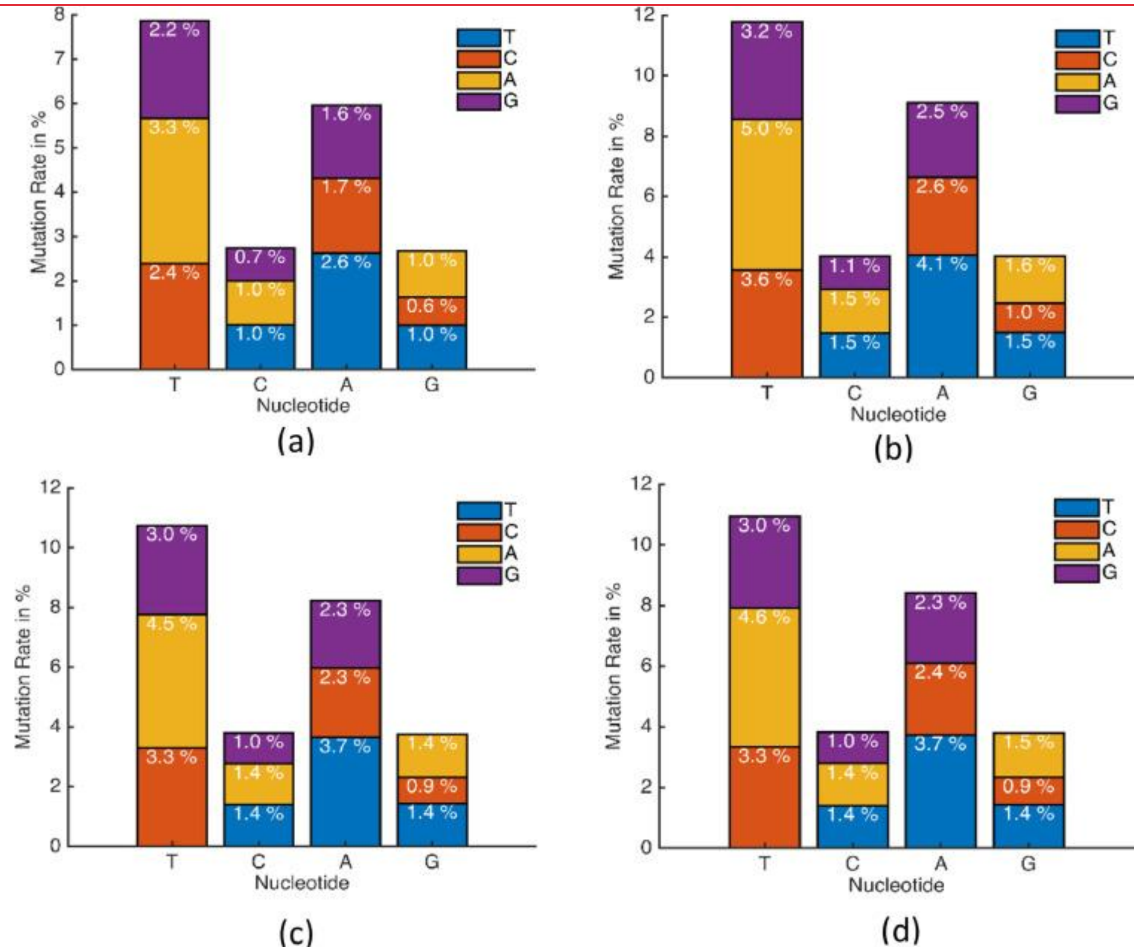

Fig. 4. Nucleotide mutation rate for (a) China, (b) Australia, (c) The USA, (d) Rest of the World.

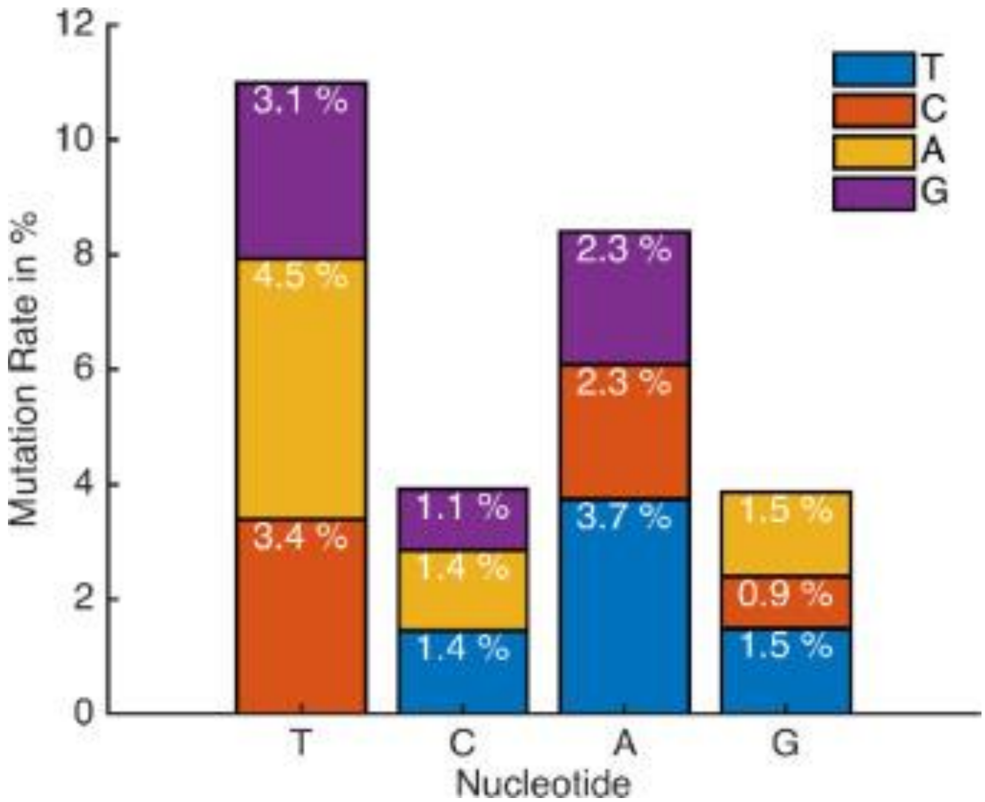

Fig. 10. Predicted mutation rate for 400th future patient.

Country	Number of Patient	Country	Number of Patient
Australia	925	Malaysia	4
Brazil	3	Nepal	1
China	60	Netherlands	1
Colombia	1	Pakistan	2
Czech Republic	7	Peru	1
Finland	1	Puerto Rico	13
France	1	Serbia	1
Germany	1	South Africa	1
Greece	4	South Korea	1
Hong Kong	20	Spain	12
India	46	Sri Lanka	4
Iran	2	Sweden	1
Israel	2	Taiwan	22
Italy	2	Thailand	23
Japan	5	Turkey	1
Kazakhstan	4	United States	2103
Vietnam	2		

Fig. 10. Predicted mutation rate for 400th future patient.

POSITIVE SARS-COV-2 RNA RECURS REPEATEDLY IN A CASE RECOVERED FROM COVID-19: DYNAMIC RESULTS FROM 108 DAYS OF FOLLOW-UP

Liu F, Cai ZB, Huang JS, Yu WY, Niu HY, Zhang Y, Sui DM, Wang F, Xue LZ, Xu AF.. Pathog Dis. 2020 Jun 27:ftaa031. doi: 10.1093/femspd/ftaa031. Online ahead of print.
Level of Evidence: Other - Case Report

BLUF

Authors at Xixi Hospital in Hangzhou, China examine a case study of a previously healthy 35-year-old man with multiple COVID-19 recurrences to assess the role of post-discharge isolation and surveillance in preventing disease transmission. Following each apparent recovery (no clinical symptoms, normal CT imaging) and negative nasopharyngeal and stool swabs, the patient was discharged from the hospital and placed under a two week surveillance. Nasopharyngeal swabs revealed positive results during both the first and second isolation periods, thus requiring rehospitalization each time. He was followed for 108 days in total (Figure 1, 2), with 65 days of viral shedding. Authors advocate for reappraisal of criteria regarding hospital discharge and suggest that post discharge isolation and surveillance allows for containment of COVID-19 infection.

ABSTRACT

The evidence of long-term clinical dynamic on Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) RNA re-positive case are less. We performed a 108 days follow-up on dynamic clinical presentations in a case, who hospitalized three times due to the positive recurrence of SARS-CoV-2 RNA after discharge, to understand the prognosis of the 2019-Coronavirus disease (COVID-19). In this case, positive SARS-CoV-2 recurred even after apparent recovery (normal CT imaging, no clinical symptoms, negative SARS-CoV-2 on stool sample and negative serum IgM test) from COVID-19, viral shedding duration lasted for 65 days, the time from symptom onset to disappearance was up to 95 days. Erythrocyte-associated indicators, liver function and serum lipid metabolism presented abnormal throughout during the observation period. Awareness of atypical presentations such as this one is important to prompt the improvement of the management of COVID-19.

FIGURES

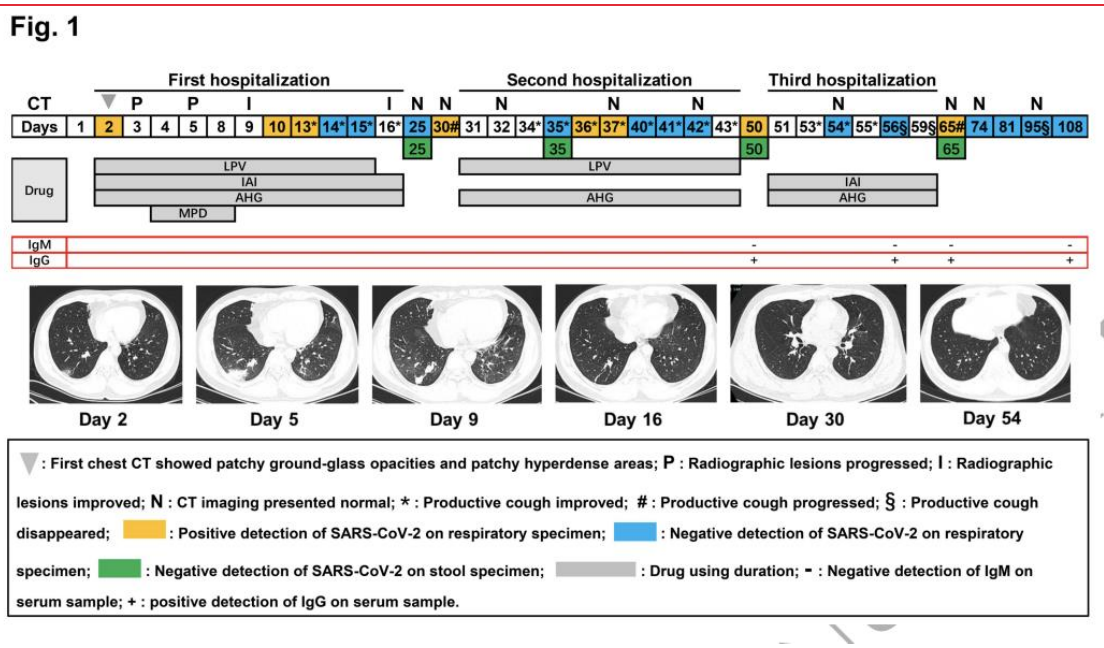

Figure 1: Time dynamics of virus, chest radiograph and clinical symptom on a case recovered from COVID-19 during the observation period. LPV: lopinavir; IAI: interferon α2b atomization inhalation; AHG: arbidol hydrochloride granules; MPD: methylprednisolone.

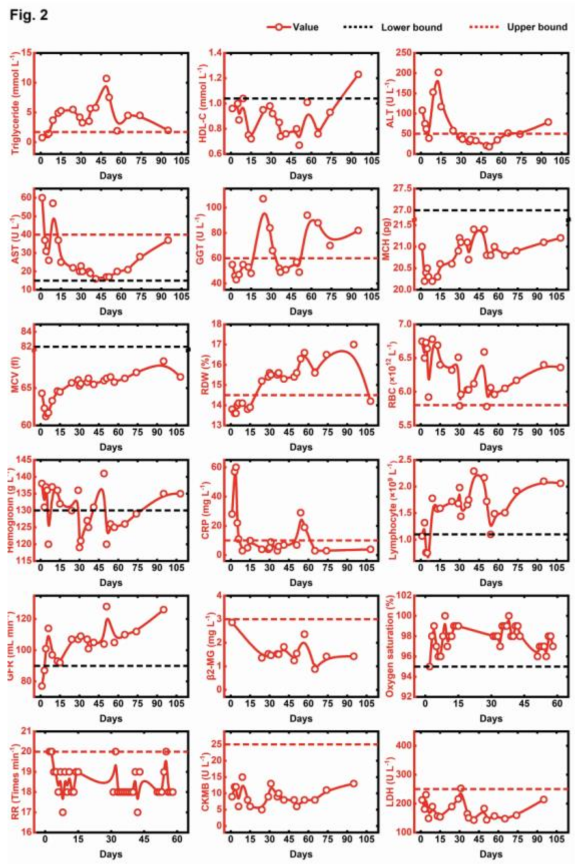

Figure 2: The temporal changes of laboratory indicators in a patient recovered from COVID-19.

Figure 2 Legend: HDL-C: high-density lipoprotein cholesterol; ALT: alanine transaminase; AST: aspartate aminotransferase; GGT: gamma-glutamyltransferase; MCH: mean corpuscular hemoglobin; MCV: mean corpuscular volume; RDW: red cell distribution width; RBC: red blood cell count; CRP: rapid c-reactive protein; GFR: glomerular filtration rate; β2-MG: β2-macroglobulin; RR: respiratory rate; CKMB: creatine kinase isoenzyme; LDH: lactate dehydrogenase

PREVENTION IN THE COMMUNITY

CULTURAL ORIENTATION, POWER, BELIEF IN CONSPIRACY THEORIES, AND INTENTIONS TO REDUCE THE SPREAD OF COVID-19

Biddlestone M, Green R, Douglas KM.. Br J Soc Psychol. 2020 Jun 27. doi: 10.1111/bjso.12397. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

Researchers from the University of Kent in the United Kingdom used a Qualtrics survey administered to 704 participants from April 4 to April 13, 2020 on several social media platforms to assess individuals' attitudes towards social distancing and hygiene measures. They then evaluated whether these results correlated with individualist versus collectivist ideals using confirmatory factor analysis (CFA) and structural equation modeling (SEM). They concluded that those who held individualistic values, in contrast to those with collectivist attitudes, were more likely to harbor feelings of powerlessness and believe in conspiracy theories, and were also less likely to take action to reduce the spread of COVID-19 (Figures 1 and 2). Limitations to the study include limited generalizability as well as a small effect size, suggesting "many other factors influence the COVID-19 response."

ABSTRACT

The current study investigated cultural and psychological factors associated with intentions to reduce the spread of COVID-19. Participants (n = 704) completed measures of individualism-collectivism, belief in conspiracy theories about COVID-19,

feelings of powerlessness, and intentions to engage in behaviours that reduce the spread of COVID-19. Results revealed that vertical individualism negatively predicted intentions to engage in social distancing, directly and indirectly through both belief in COVID-19 conspiracy theories and feelings of powerlessness. Vertical collectivism positively predicted social distancing intentions directly. Horizontal collectivism positively predicted social distancing intentions indirectly through feelings of powerlessness. Finally, horizontal collectivism positively predicted hygiene-related intentions both directly and indirectly through lower feelings of powerlessness. These findings suggest that promoting collectivism may be a way to increase engagement with efforts to reduce the spread of COVID-19. They also highlight the importance of examining the interplay between culture and both personal feelings (powerlessness) and information consumption (conspiracy theories) during times of crisis.

FIGURES

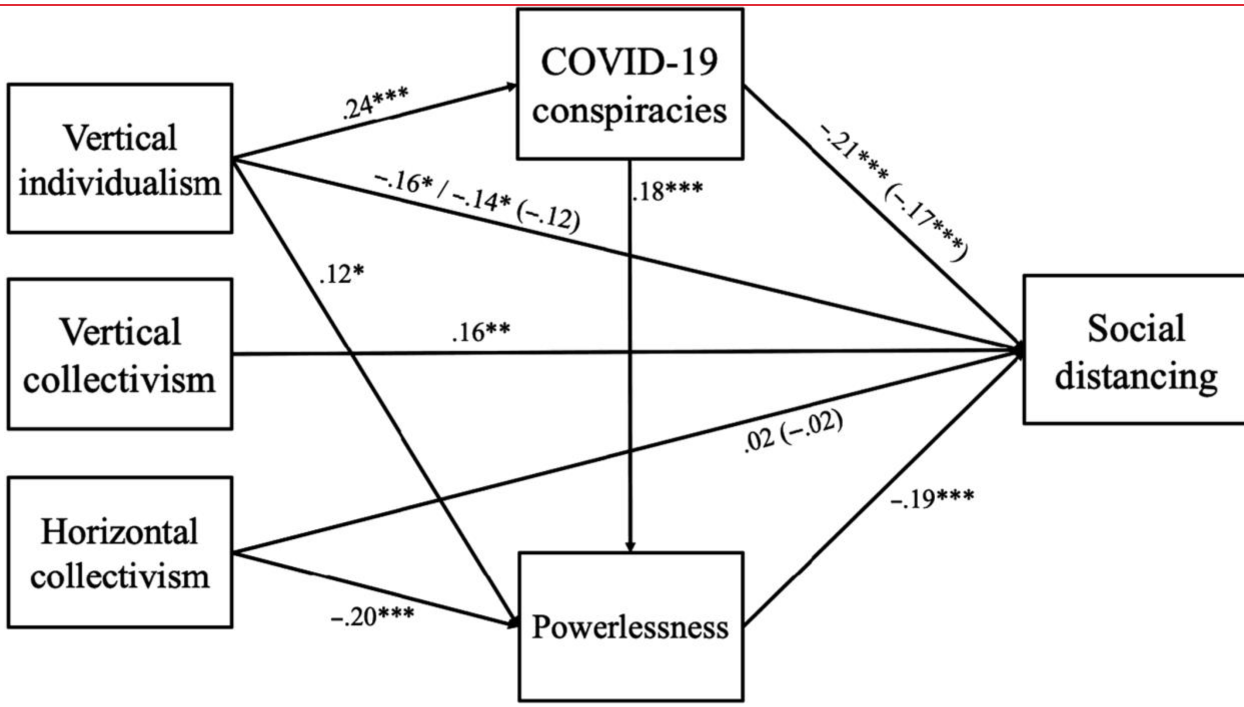

Figure 1. Predictors of social distancing intentions in the final SEM model (controlling for demographics). Non-significant paths, demographic paths, and paths predicting hygiene intentions have been removed for ease of viewing. Direct effects are reported in parentheses, and total effects are reported without parentheses. The total effect of vertical individualism on social distancing is firstly reported through conspiracy beliefs, and secondly through powerlessness. All values are standardised beta coefficients.

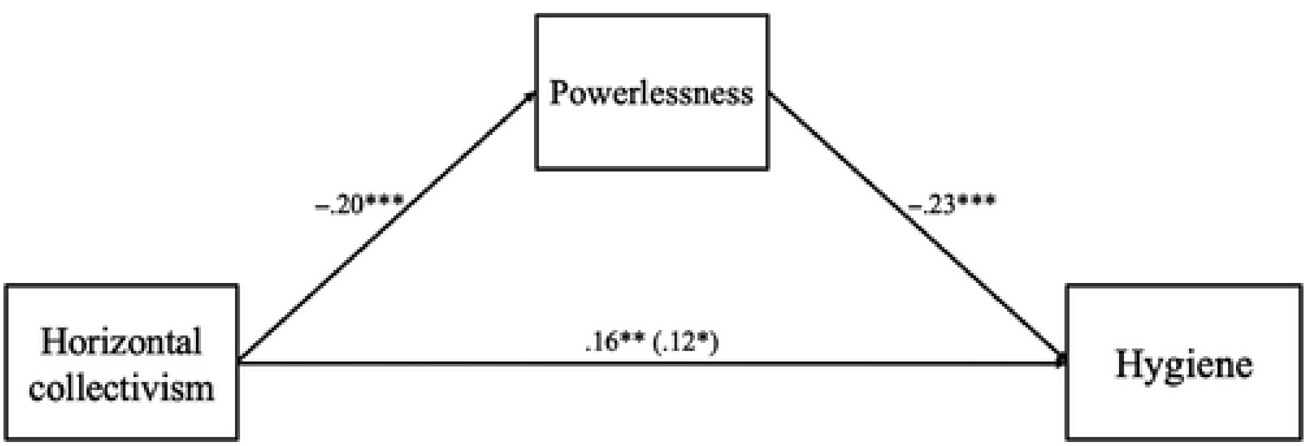

Figure 2. Predictors of hygiene intentions in the final SEM model (controlling for demographics). Non-significant paths, demographic paths, and paths predicting social distancing intentions have been removed for ease of viewing. Direct effects are reported in parentheses, and total effects are reported without parentheses. All values are standardised beta coefficients.

COVID-19 IN IMMUNOCOMPROMISED HOSTS: WHAT WE KNOW SO FAR

Fung M, Babik JM.. Clin Infect Dis. 2020 Jun 27:ciaa863. doi: 10.1093/cid/ciaa863. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

Authors from the University of California San Francisco review the impact of COVID-19 on immunocompromised patients, namely patients with cancer, solid organ transplant (SOT), and those on biologics and disease modifying anti-rheumatic drugs (DMARDS). Their findings reveal that cancer and SOT patients may have a higher risk for severe COVID-19, greater use of antiviral and corticosteroid medication, and higher overall mortality rates. In contrast, patients on biologics do not appear to suffer severe COVID-19, suggesting a possible protective effect, and the authors urge for prospective studies to investigate the attributable risk of immunocompromised status on COVID-19 outcomes.

ABSTRACT

The coronavirus disease 2019 (COVID-19) pandemic caused by SARS coronavirus 2 (SARS-CoV-2) has caused significant morbidity and mortality for patients and stressed healthcare systems worldwide. The clinical features and outcomes of COVID-19 among immunosuppressed patients, who are at presumed risk for more severe disease but who may also have decreased detrimental inflammatory responses, are not well characterized. We review the existing literature on COVID-19 among immunocompromised populations ranging from cancer patients and solid organ transplant recipients to patients with HIV and those receiving immunomodulatory therapy for autoimmune disease. Patients with malignancy and solid organ transplant recipients may be at increased risk of severe COVID-19 disease and death whereas for those with other types of immunocompromise, current evidence is less clear. Overall, further prospective, controlled studies are needed to determine the attributable risk of immunocompromising conditions and therapies on COVID-19 disease prognosis.

DIAGNOSTIC RADIOLOGY

CHEST CT OF COVID-19 IN PATIENTS WITH A NEGATIVE FIRST RT-PCR TEST: COMPARISON WITH PATIENTS WITH A POSITIVE FIRST RT-PCR TEST

Chen ZH, Li YJ, Wang XJ, Ye YF, Wu BL, Zhang Y, Xuan WL, Bao JF, Deng XY.. Medicine (Baltimore). 2020 Jun 26;99(26):e20837. doi: 10.1097/MD.0000000000020837.
Level of Evidence: 3 - Non -randomized controlled cohort/follow-up study

BLUF

A retrospective study evaluating data from 24 January to 6 February 2020 in Hangzhou, China compared clinical and CT imaging features between COVID-19 patients with initially negative reverse transcription polymerase chain reaction (RT-PCR) tests (n=12) and positive RT-PCR tests (n=21). The results suggest that CT lesions in the positive group were more likely to be peripheral (83.6% vs 68.2%, [P< .05]) and appear as pure ground-glass opacities (GGO) or GGO with interlobular septal thickening (P<.05), while lesions in the negative group were more likely to appear as GGO with consolidation followed by pure GGO (Table 3). Patients in the positive RT-PCR test group were more likely to have a fever than patients in the negative RT-PCR test group (85.7% vs 50%, [P < .05]), while other clinical features were variable (Table 1). Follow-up data of the negative group showed consolidation increased in frequency while pure GGOs decreased in frequency (Table 4). Authors conclude that recognition of typical chest CT features such as GGO and consolidation is an important step in preventing public risks by diagnosing early COVID-19 cases in patients with negative first RT-PCR test.

ABSTRACT

To compare clinical and imaging features between patients with an initial negative reverse-transcription-polymerase chain-reaction (RT-PCR) test and patients with an initial positive RT-PCR test. CT follow-up analysis in the negative RT-PCR group is also described.Thirty-three patients with SARS-CoV-2 infection confirmed by RT-PCR, with 216 lesions upon CT, were included. Demographic information and chest CT imaging features were collected.The average age in the whole study group

was 46.9 +- 11.1 years, with 18 males and 15 females. Patients in the positive RT-PCR test group were more likely to have a fever than patients in the negative RT-PCR test group (85.7% vs 50%, P < .05). Lesions in the positive group were more likely to be located in the peripheral area than lesions in the negative group (83.6% vs 68.2%, P < .05). Regarding the appearance of 216 lesions, ground-glass opacities (GGOs) with consolidation (43.2%) was the most common appearance in the negative group, followed by pure GGOs (31.8%), while in the positive group, pure GGOs (32%) and GGOs with interlobular septal thickening (32.8%) were both most frequent, and the difference between them was evident (P < .05). For the follow-up analysis, the largest short-axis of a lesion was smaller upon follow-up (median size 13.6 mm vs 14 mm), albeit by a smaller margin. Pure GGOs decreased in frequency, from 31.3% to 21.3%, while consolidation increased in frequency, from 7.5% to 12.5%.The manifestations of COVID-19 in patients with a first negative RT-PCR test and patients with a positive first RT-PCR test are different to some extent. The consolidation component may increase after follow-up.

FIGURES

	All subjects (n=33)	Negative (n=12)	Positive (n=21)	*P* value
Age (yr)	46.9±11.1	47.6±13.4	46.5±9.9	.788
Gender				.245*
Male	18 (54.5)	8 (66.7)	10 (47.6)	
Female	15 (45.5)	4 (33.3)	11 (52.4)	
Symptomatic				
Fever	24 (72.7)	6 (50)	18 (85.7)	**.036***
Cough	19 (57.6)	7 (58.3)	12 (57.1)	.947
Fatigue	6	3	3	–
Headache	4	0	4	–
Chest distress	3	1	2	–
Muscular soreness	1	0	1	–
Throat discomfort and pain	6	2	4	–
Contact history				**.042***
Travel to Wuhan	7 (21.2)	0 (0)	7 (33.3)	
Exposure to infected patient	19 (57.6)	10 (83.3)	9 (42.9)	
Unknown reasons	7 (21.2)	2 (16.7)	5 (23.8)	
Days from symptom onset to admit to hospital	2 (1–4.5)	2 (1–6)	2 (1.5–4.5)	.593
Comorbidity				–
Hypertension	2	0	2	
Diabetes	1	0	1	
Liver cirrhosis	1	0	1	
Lung cancer	1	1	0	
Hashimoto thyroiditis	1	0	1	
Laboratory examination				
Elevation of C-reaction protein (0–10) mg/L	16 (48.5)	6 (50)	10 (47.6)	.895
Normal white blood cell count (4–10) *10^9/L	31 (93.9)	11 (91.7)	20 (95.2)	.602
Lower lymphocyte count (1.1–3.2) *10^9/L	15 (45.5)	3 (25)	12 (57.1)	.077

* Fisher exact test.

Table 1: Baseline demographic and clinical characteristics of 33 patients with COVID-19.

	All subjects (n=216)	Negative (n=88)	Positive (n=128)	*P* value
Largest short-axis of lesion (mm)	13.7 (9.5–22.3)	14 (8.8–28.3)	13.7 (9.8–20.7)	.472
Involve lung lobes				**.037**
Right superior lobe	40 (18.5)	23 (26.1)	17 (13.3)	
Right middle lobe	22 (10.2)	12 (13.6)	10 (7.8)	
Right inferior lobe	65 (30.1)	24 (27.3)	41 (32)	
Left superior lobe	39 (18.1)	15 (17)	24 (18.8)	
Left inferior lobe	50 (23.1)	14 (15.9)	36 (28.1)	
Predominant distribution				**.022**
Peripheral area	167 (77.3)	60 (68.2)	107 (83.6)	
Central area	24 (11.1)	15 (17)	9 (7)	
Both area related	25 (11.6)	13 (14.8)	12 (9.4)	
Performance of lesions				**.020**
Pure GGO	69 (31.9)	28 (31.8)	41 (32)	
GGO with interlobular septal thickening	57 (26.4)	15 (17)	42 (32.8)	
GGO with consolidation	71 (32.9)	38 (43.2)	33 25.8)	
Consolidation	19 (8.8)	7 (8)	12 (9.4)	
Bronchiectasis	85 (39.4)	15 (17)	70 (54.7)	**<.001**
Air bronchogram	37 (17.1)	25 (28.4)	12 (9.4)	**<.001**

GGO=ground-glass opacities.

Table 3: CT imaging characteristics of 216 lesions from COVID-19 patients.

	Negative (n=80)	Follow-up (n=80)	*P* value
Largest short-axis of lesion	14 (8.8–28.3)	13.7 (9.8–20.7)	.310
Performance of lesions			**.007**
Pure GGO	25 (31.3)	17 (21.3)	
GGO with interlobular septal thickening	13 (16.3)	15 (18.8)	
GGO with consolidation	36 (45)	38 47.5)	
Consolidation	6 (7.5)	10 (12.5)	

Table 3: CT imaging characteristics of 216 lesions from COVID-19 patients.

PEDIATRICS

FIRST PAEDIATRIC COVID-19 ASSOCIATED DEATH IN ITALY

Mercolini F, Donà D, Girtler Y, Mussner KA, Biban P, Bordugo A, Molinaro G.. J Paediatr Child Health. 2020 Jun 27. doi: 10.1111/jpc.14994. Online ahead of print.
Level of Evidence: Other - Case Report

BLUF

A case report of a 5 year-old Italian girl with mucolipidosis type II who died from COVID-19 pneumonia, thus emphasizing that children with chronic medical conditions may have worse prognoses with COVID-19 infections. The authors suggest managing higher-risk patients at home, abiding by infection prevention rules, ensuring that all healthcare personnel close contacts use proper PPE, regularly communicating with the hospital team, and educating caregivers to improve outcomes.

SUMMARY

A 5-year-old girl with mucolipidosis type II, associated hypertrophic cardiomyopathy, and previously stable cardiac and pulmonary function developed SARS-CoV-2 pneumonia and acute respiratory distress syndrome. There were multiple sick family contacts. The patient decompensated and was given supplemental oxygen, parenteral hydration, and intravenous antibiotics (ceftriaxone and azithromycin) and corticosteroids (methylprednisolone 1 mg/kg/day). Hydroxychloroquine was considered but the decompensation was deemed too rapid. Over the next 24 hours mask oxygen requirement increased to 7-8 L/min but she was not intubated due to her underlying disease and the patient continued to deteriorate over the next few days and passed away

HEMATOLOGY AND ONCOLOGY

PRACTICE RECOMMENDATIONS FOR LUNG CANCER RADIOTHERAPY DURING THE COVID-19 PANDEMIC: AN ESTRO-ASTRO CONSENSUS STATEMENT

Guckenberger M, Belka C, Bezjak A, Bradley J, Daly ME, DeRuysscher D, Dziadziuszko R, Faivre-Finn C, Flentje M, Gore E, Higgins KA, Iyengar P, Kavanagh BD, Kumar S, Le Pechoux C, Lievens Y, Lindberg K, McDonald F, Ramella S, Rengan R, Ricardi U, Rimner A, Rodrigues GB, Schild SE, Senan S, Simone Ii CB, Slotman BJ, Stuschke M, Videtic G, Widder J, Yom SS, Palma D.. Int J Radiat Oncol Biol Phys. 2020 Jul 15;107(4):631-640. doi: 10.1016/j.ijrobp.2020.05.012.
Level of Evidence: Other - Guidelines and Recommendations

BLUF

A survey performed by 32 experts in lung cancer radiotherapy explored opinions about practice recommendations for patients with 6 different types of lung cancer in two different COVID-19 scenarios. This survey found consensus in not deviating from guideline-recommended radiotherapy practice while also avoiding exposure of cancer patients and hospital staff to COVID-19 patients. In the later phases of this pandemic, important factors for triage of COVID-19 patients must be considered (Table 8).

ABSTRACT

BACKGROUND: The COVID-19 pandemic has caused radiotherapy resource pressures and led to increased risks for lung cancer patients and healthcare staff. An international group of experts in lung cancer radiotherapy established this practice recommendation pertaining to whether and how to adapt radiotherapy for lung cancer in the COVID-19 pandemic.
METHODS: For this ESTRO & ASTRO endorsed project, 32 experts in lung cancer radiotherapy contributed to a modified Delphi consensus process. We assessed potential adaptations of radiotherapy in two pandemic scenarios. The first, an early pandemic scenario of risk mitigation, is characterized by an altered risk-benefit ratio of radiotherapy for lung cancer patients due to their increased susceptibility for severe COVID-19 infection, and minimization of patient travelling and exposure of radiotherapy staff. The second, a later pandemic scenario, is characterized by reduced radiotherapy resources requiring patient triage. Six common lung cancer cases were assessed for both scenarios: peripherally located stage I NSCLC, locally advanced NSCLC, postoperative radiotherapy after resection of pN2 NSCLC, thoracic radiotherapy and prophylactic cranial irradiation for limited stage SCLC and palliative thoracic radiotherapy for stage IV NSCLC.
RESULTS: In a risk-mitigation pandemic scenario, efforts should be made not to compromise the prognosis of lung cancer patients by departing from guideline-recommended radiotherapy practice. In that same scenario, postponement or interruption of radiotherapy treatment of COVID-19 positive patients is generally recommended to avoid exposure of cancer patients and staff to an increased risk of COVID-19 infection. In a severe pandemic scenario characterized by reduced resources, if patients must be triaged, important factors for triage include potential for cure, relative benefit of radiation, life expectancy, and performance status. Case-specific consensus recommendations regarding multimodality treatment strategies and fractionation of radiotherapy are provided.
CONCLUSION: This joint ESTRO-ASTRO practice recommendation established pragmatic and balanced consensus recommendations in common clinical scenarios of radiotherapy for lung cancer in order to address the challenges of the COVID-19 pandemic.

FIGURES

Table 8 Prioritization of lung cancer patients and factor for triaging of patients

Prioritization of lung cancer patients			
Rank	Case*	Relative Priority Compared All Other Types Cancer Cases in Department**	Top 5 factors for triaging patients across all radiotherapy cases
1.	Stage III NSCLC	Very high/high (71% consensus)	1. Potential for cure
2.	LS-SCLC SCLC	Very high/high (78% consensus)	2. Relative benefit of RT vs. other treatment options
3.	Stage I NSCLC	High/average (near consensus: 65%)	3. Active COVID-19 infection (absence thereof)
4.	Palliative NSCLC	No consensus. Widely dispersed responses.	4. Life expectancy
5.	PORT NSCLC	Low/very low (68% consensus)	5. Performance Status
6.	SCLC PCI	Low/very low (81% consensus)	

* The six cases were ranked, with 6 points given for a #1 ranking, 5 points for #2, etc, and the average number of points was determined. The average scores, in order of ranking as listed in the table, were 5.2, 4.9, 4.1, 3.0, 2.1 and 1.7, respectively.
** Respondents were asked to prioritize each case as very high, high, average, low, or very low, corresponding to quintiles of priority (e.g. very high = top 20%, very low = bottom 20%), compared to all types of cancers treated in their department. Adjacent categories were combined to determine consensus.

COVID-19 AND THALASSAEMIA: A POSITION STATEMENT OF THE THALASSAEMIA INTERNATIONAL FEDERATION

Farmakis D, Giakoumis A, Cannon L, Angastiniotis M, Eleftheriou A.. Eur J Haematol. 2020 Jun 23. doi: 10.1111/ejh.13476. Online ahead of print.
Level of Evidence: Other - Guidelines and Recommendations

BLUF

Experts from the Thalassemia International Federation (TIF) developed guidelines classifying thalassemia patients into three risk categories with corresponding guidance for each (Figure 1). They also provided patient pathways (transfusion and non-transfusion dependent) (Figure 2), strategies to implement effective communication (Figure 3), and additional recommendations for care during the pandemic (discussed in summary). Finally, they developed an international web-based registry to facilitate access to a database of thalassemia patients for improved management.

SUMMARY

The experts from TIF makes the following recommendations for hemoglobinopathy management during COVID-19.
1. Adaptation of hemoglobinopathy patients: Patients are encouraged to follow social distancing measures. Patients presenting with COVID-19 symptoms are to be tested for the SARS-CoV-2 virus, contact the patient's treating physician if the test turns positive and extra attention to patients with comorbidities.
2. TIF recommended patient pathways (transfusion-dependent and independent) and effective communication as discussed in Figures 2 and 3 respectively.
3. Monitoring tests: Routine CBC, pre-transfusion hemoglobin levels, and serum ferritin can be performed. The annual tests may be postponed until after the epidemic. The patients are encouraged to take all the current medications including RAAS inhibitors.
4. Blood transfusions: The COVID-19 patients should defer from blood donation at least 28 days after symptom resolution or treatment completion and the donors are followed up at least 14 and until 28 days post-donation to track their health status.
5. Patient Blood Management (PBM) - optimization of patient's blood volume with erythropoietin analogs, minimizing blood loss, and harnessing physiologic anemia reserve plays a vital role in COVID-19.
6. Lifestyle and Nutritional Management: Sufficient hydration, adequate sleep for at least 7-8 hours, regular exercise, well-balanced diet, stress management, management of existing chronic comorbidities, and consuming natural sources of Vitamins C, D and omega 3 fatty acids.

ABSTRACT

OBJECTIVES: Many patients with haemoglobinopathies, including thalassaemia and sickle cell disease, are at increased risk of developing severe complications from the coronavirus disease 2019 (COVID-19). Although epidemiologic evidence concerning the novel coronavirus (SARS-CoV-2) infection in these patients is currently lacking, the COVID-19 pandemic represents a significant challenge for haemoglobinopathy patients, their families and their attending physicians.

METHODS: The present statement summarizes the key challenges concerning the management of haemoglobinopathies, with particular focus on patients with either transfusion-dependent or non-transfusion-dependent thalassaemia, identifies the gaps in knowledge and suggests measures and strategies to deal with the pandemic, based on available evidence and expert opinions. Key areas covered include patients' risk level, adaptation of haemoglobinopathy care, safety of blood transfusions, blood supply challenges, and lifestyle and nutritional considerations.
CONCLUSIONS: The proposed measures and strategies may be useful as a blueprint for other disorders which require regular hospital visits, as well as for the timely adaptation of patient care during similar future pandemics.

FIGURES

Table 1: Risk levels in patients with haemoglobinopathies and corresponding guidance considerations regarding work, schooling or educational activities.

Risk level	Criteria	Guidance
Group A: Moderate risk	Thalassaemia patient with all of the following: • Optimal transfusions with pre-transfusion Hb 9.5-10.0 g/dl (for ≥3-4 previous years) • Optimal iron chelation with cardiac T2* >20ms, LIC <7mg/g DW or serum ferritin <2000mg/L (for ≥3-4 previous years) • No underlying comorbidities • No splenectomy	Assume work/schooling/education without any additional measures besides national guidelines for general population (distancing, hand washing, wearing mask)
Group B: High risk	Thalassaemia patient with 2 or more of the following: • Sub-optimal transfusions with pre-transfusion Hb 8.0-9.0g/dl (currently and in ≥2-3 previous years) • Moderate iron load with cardiac MRI T2* 10-20 ms, LIC 7-10 mg/g DW or serum ferritin 2000-4000 mg/L (currently and in ≥2-3 previous years) • One underlying comorbidity including diabetes, cardiac, endocrine, hepatic or respiratory disease • Splenectomy	Assume work/schooling/education keeping national guidelines for general population (distancing, hand washing, wearing mask) unless job involves treating/caring patients or other vulnerable groups (e.g., healthcare professionals) or frequent contact with people (e.g., receptionists, shop assistants)
Group C: Highest risk	• Sickle cell disease patient • Thalassaemia patient with 2 or more of the following: ○ Age >50 years ○ Sub-optimal transfusions with pre-transfusion Hb <7 g/dl (currently and in ≥2-3 previous years) ○ Severe iron load with cardiac MRI T2* <10 ms, LIC >10 mg/g DW or serum ferritin >4000 mg/L (currently and in ≥2-3 previous years) ○ One or more underlying comorbidity including diabetes, cardiac, endocrine, hepatic or respiratory disease ○ Splenectomy with one or more of comorbidities	Refrain from any type of work/schooling/education activities and remain at home, avoiding any gatherings or contact with potential COVID-19 (e.g, relative symptoms) until the pandemic is declared well over at country level. Keep national guidelines of distancing, hand washing and wearing mask at least 6 months after the pandemic is declared over at country level

Figure 1. Risk levels in patients with haemoglobinopathies and corresponding guidance considerations regarding work, schooling or educational activities.

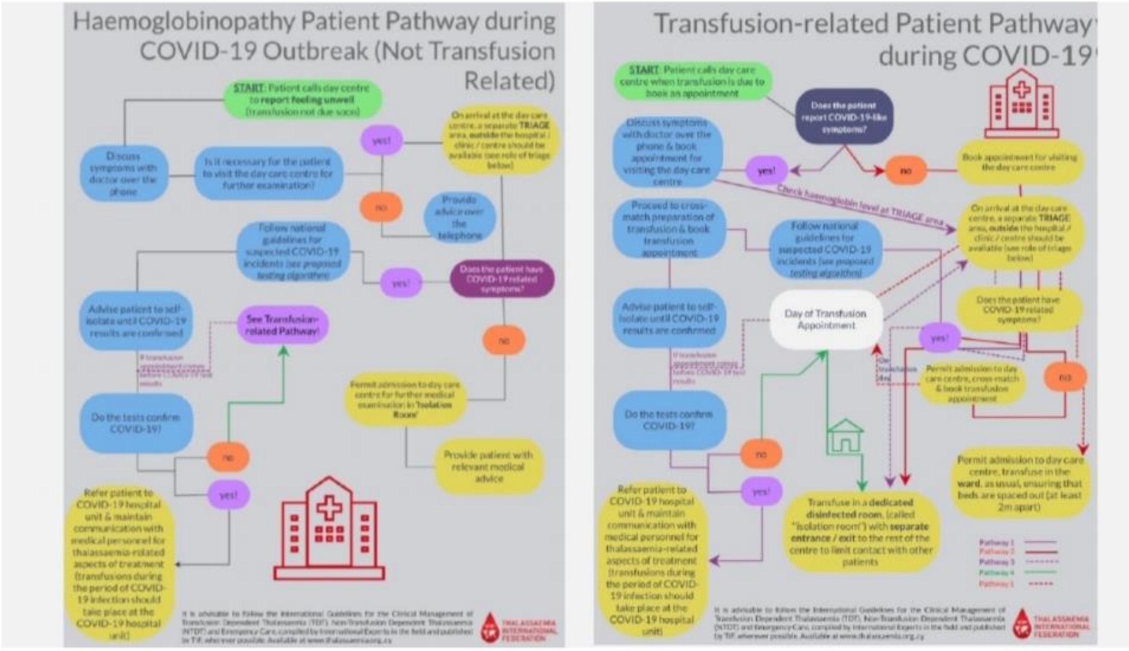

Figure 2. Patient pathways during the pandemic: general pathway (left panel) and transfusion-dependent patient pathway (right panel).

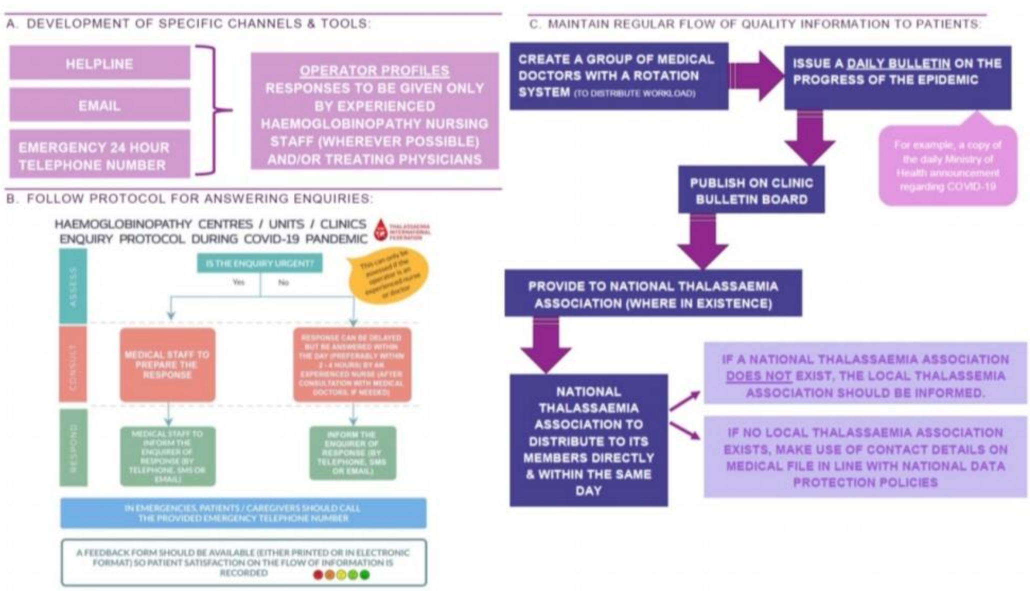

Figure 2. Patient pathways during the pandemic: general pathway (left panel) and transfusion-dependent patient pathway (right panel).

PSYCHIATRY

CLOZAPINE AND COVID-19: THE AUTHORS RESPOND

Siskind D, Honer WG, Clark S, Correll CU, Hasan A, Howes O, Kane JM, Kelly DL, Laitman R, Lee J, MacCabe JH, Myles N, Nielsen J, Schulte PF, Taylor D, Verdoux H, Wheeler A, Freudenreich O.. J Psychiatry Neurosci. 2020 Jul 1;45(4):E1-E2. doi: 10.1503/jpn.2045302.
Level of Evidence: Other - Expert Opinion

BLUF

In this letter to the editor, authors discuss recommendations on clozapine hematologic monitoring as originally outlined in Remington G & Powell V., J Psychiatry Neurosci, 2020, and the authors of the original article respond to their commentary. Authors on both sides agree that providers can safely extend the time between blood monitoring appointments for agranulocytosis on a case by case basis, which will help decrease contact during the pandemic, but the letter writers note that more frequent monitoring based on low absolute neutrophil counts may be an overly conservative recommendation.

ADAPTING TO THE IMPACT OF COVID-19 ON MENTAL HEALTH: AN INTERNATIONAL PERSPECTIVE

Thomas RK, Suleman R, Mackay M, Hayer L, Singh M, Correll CU, Dursun S.. J Psychiatry Neurosci. 2020 Jul 1;45(4):229-233. doi: 10.1503/jpn.200076.
Level of Evidence: Other - Expert Opinion

BLUF

Canadian physicians recommend that psychiatrists ensure continuity of care during COVID-19 via telepsychiatry while still offering in-person interventions such as electroconvulsive therapy (ECT) to patients with severe psychiatric disease. Furthermore, when possible, clinicians should reach out to the general community and particularly individual patients with known mental health disease.

HIGH COVID-19 TESTING RATE IN PORTUGAL

Triunfol M.. Lancet Infect Dis. 2020 Jul;20(7):783. doi: 10.1016/S1473-3099(20)30499-0.
Level of Evidence: Other - Opinion

BLUF

In this news article, the author reports that in order to meet the demand of COVID-19 RT-PCR tests ordered in Portugal, academic and scientific institutions throughout the country have rounded up hundreds of volunteers with various skill sets to run hundreds of PCR tests daily. By taking advantage of available equipment and this volunteer workforce, Portugal has been able to hugely expand its testing capacity and is now among the top 10 countries in testing per capita; currently, 15% of the testing is completed at institutions consisting primarily of volunteers.

THE CYTOKINE STORM AND COVID-19

Hu B, Huang S, Yin L.. J Med Virol. 2020 Jun 27. doi: 10.1002/jmv.26232. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

In this literature review, experts from China identify major cytokines related to cytokine storms in coronaviruses infection (Table 1) and summarize patterns of symptoms, cytokine secretion, and T cell lymphopenia in severe COVID-19 (Table 2). The authors suggest that identifying patients at risk of developing severe COVID-19 and treating the cytokine storm at early stages may improve the clinical outcome of severe COVID-19.

SUMMARY

The authors' recommendations for treatment options for COVID-19 patients with cytokine storm are summarized below:
- Corticosteroids:
Advantages: Reducing hospital stay and mortality
Disadvantages: impaired clearance of viral RNA, adverse events (secondary infection, psychosis, diabetes, and avascular necrosis)
- Hydroxychloroquine and Chloroquine:
Advantages: Reducing viral load, reducing the duration of viral infection
Disadvantages: Arrhythmias, other side effects (retinopathy, cardiomyopathy, myopathy)
- Tocilizumab:
Advantages: improving survival outcome
Disadvantages: adverse events (severe infections, thrombocytopenia, neutropenia, liver damage)
- Mesenchymal stem cells (MSCs):
Advantages: reducing mortality and improving clinical symptoms
Disadvantages: unclear.
- Interleukin-1 receptor antagonist:
Advantages: improving respiratory function, increasing survival rate
Disadvantages: increasing the risk of bacterial infections.
- Janus Kinase (JAK) inhibitors:
Advantages: improving clinical symptoms and respiratory parameters
Disadvantages: locking the production of beneficial cytokine (IFN- α).
- Intravenous immunoglobin (IVIG):
Advantages: exerting various immunomodulatory effects
Disadvantages: severe lung injury, thrombosis.
- Convalescent plasma therapy:
Advantages: obtain artificial passive immunity
Disadvantages: moderate fever, anaphylactic shock.

ABSTRACT

Coronavirus disease 2019 (COVID-19), which began in Wuhan, China in December 2019 has caused a large global pandemic and poses a serious threat to public health. More than four million cases of COVID-19, which is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), have been confirmed as of May 11, 2020. SARS-CoV-2 is a highly pathogenic and transmissible coronavirus that primarily spreads through respiratory droplets and close contact. A growing body of clinical data suggests that a cytokine storm is associated with COVID-19 severity and is also a crucial cause of death from COVID-19. In the absence of antivirals and vaccines for COVID-19, there is an urgent need to understand the cytokine storm in COVID-19. Here, we have reviewed the current understanding of the features of SARS-CoV-2 and the pathological features, pathophysiological mechanisms, and treatments of the cytokine storm induced by COVID-19. Additionally, we suggest that the identification and treatment of the cytokine storm are important components for rescuing patients with severe COVID-19.

FIGURES

Table 1 The major cytokines related to cytokine storms during coronaviruses infection

cytokines	SARS-CoV[41]	MERS-CoV[42]	SARS-CoV-2[2,43,44]
	↑IL-1β	↑IL-15	↑IL-2
	↑IL-6	↑IL-17	↑IL-4
	↑IL-8	↑IFN-γ	↑IL-6
	↑IL-12	↑TNF-α	↑IL-7
	↑IP-10		↑IL-10
	↑MCP-1		↑G-SCF
	↑IFN-γ		↑IP-10
	↓IL-4		↑MCP-1
			↑MIP1A
			↑TNF-α
			↑IFN-γ

↑=increased ↓=decreased. SARS-CoV=Severe Acute Respiratory Syndrome coronavirus. MERS-CoV=Middle East respiratory syndrome coronavirus. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2. IL=interleukins. IFN-γ=interferon γ. IP-10=inducible protein 10. MCP-1=monocyte chemoattractant protein 1. TNF-α=tumor necrosis factor α. G-SCF=granulocyte-colony stimulating factor. MIP1A=macrophage inflammatory protein 1 alpha.

Table 2 Patterns of symptoms, cytokine secretion, and T cell lymphopenia related to the severity of COVID-19[2, 43, 44]

State of COVID-19	Uninfected individual	Mild and moderate COVID-19	Severe COVID-19
symptoms	No symptoms	Fever, myalgia, fatigue or dyspnea	Fever, myalgia, fatigue, dyspnea, ARDS or MOF
Cytokines patterns	No cytokines	↑IL-6,IL-10,TNF-α	↑↑IL-6,IL-10,TNF-α,IL-2,MCP1
T cell lymphopenia	No changes	↓Lymphocytes, (CD4⁺T cells,CD8⁺T cells)	↓↓Lymphocytes, (CD4⁺T cells, especially CD8⁺T cells)

ARDS= acute respiratory distress syndrome. MOF= multiple organ failure. IL= interleukin. TNF-α= tumor necrosis factor-α. MCP1= chemoattractant protein 1

ANALYSIS OF THE DIAGNOSTIC VALUE OF SERUM SPECIFIC ANTIBODY TESTING FOR CORONAVIRUS DISEASE 2019

Yan M, Zheng Y, Sun Y, Wang L, Luan L, Liu J, Tian X, Wan N.. J Med Virol. 2020 Jun 27. doi: 10.1002/jmv.26230. Online ahead of print.

Level of Evidence: 3 - Non -randomized controlled cohort/follow-up study

BLUF

In this retrospective study, researchers from China characterize the development of SARS-CoV-2 antibodies in 802 hospitalized patients with clinical symptoms and/or CT imaging indicative of COVID-19. Key results include:
1. Overall positivity rates of IgM and/or IgG, regardless of timing relative to disease onset, were greater when compared to nucleic acid detection (88% vs. 70%),
2. Distinct differences exist in the timing of peak positivity rates in IgM and/or IgG levels, which peak after the ninth week, versus nucleic acid detection, which peaks during the first week (Figure 1), and
3. Positive antibody tests occurred in 193 out of 238 patients with negative nucleic acid tests.

The authors conclude by arguing that supplementation of nucleic acid testing with antibody testing can reduce the rate of missed COVID-19 diagnoses.

ABSTRACT

The coronavirus disease 2019 (COVID-19) pandemic has spread to various regions worldwide. As of 27 April 2020, according to real-time statistics released by the World Health Organization, there have been 84,341 confirmed cases and 4,643 deaths in China, with more than 2,979,484 confirmed cases and 206,450 deaths outside China. The detection of antibodies produced during the immune response to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has become an important laboratory method for the diagnosis of COVID-19. However, at present, little research on these specific antibodies has been conducted. In this study, retrospective analysis was used to explore the dynamic changes of serum IgM and IgG antibody and factors affecting diagnostic efficacy, so as to provide a theoretical basis for clinical diagnosis and treatment.

FIGURES

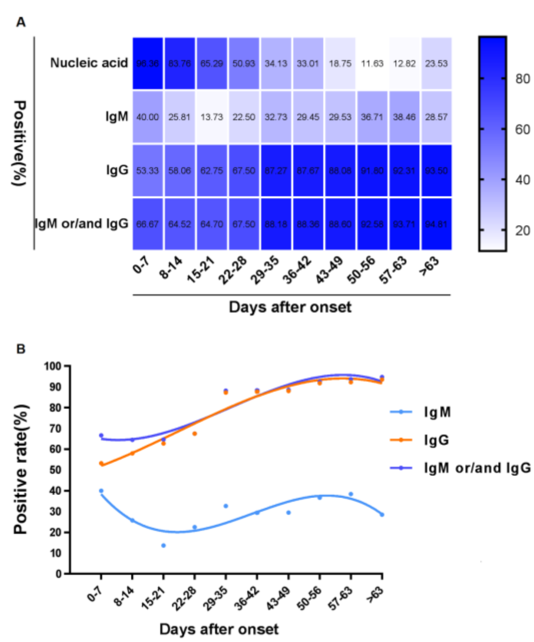

Figure 1. Dynamic changes in the positive rates in patients after the onset of disease. (A) Heat map of changes in the positive rates of antibodies. (B) Changes in the positive rates of nucleic acid and antibodies at different time periods after COVID-19 onset.

POTENTIAL ROLE OF INCRETINS IN DIABETES AND COVID-19 INFECTION: A HYPOTHESIS WORTH EXPLORING

Pantanetti P, Cangelosi G, Ambrosio G.. Intern Emerg Med. 2020 Jun 26. doi: 10.1007/s11739-020-02389-x. Online ahead of print.
Level of Evidence: 5 - Mechanism-based reasoning

BLUF

This review conducted by authors of UO Diabetologia Asur Marche and the Division of Cardiology at the University of Perugia in Italy review literature that suggests dipeptidyl peptidase 4 (DPP4) may have a pro-inflammatory role in diseases such as COVID-19 (Figure 1). This association suggests the potential for DPP4 inhibitors to be used as a treatment in patients with COVID-19, even if they are not diabetic.

ABSTRACT

Patients with diabetes mellitus have been reported to be at a high risk of complications from SARS-CoV2 virus infection (COVID-19). In type 2 diabetes, there is a change in immune system cells, which shift from an anti-inflammatory to a predominantly pro-inflammatory pattern. This altered immune profile may induce important clinical consequences, including increased susceptibility to lung infections; and enhanced local inflammatory response. Furthermore, dipeptidyl peptidase 4 (DPP4) enzyme is highly expressed in the lung, and that it may have additional actions besides its effects on glucose metabolism, which might exert profound pro-inflammatory effects. We briefly review the impact on the inflammatory system of DPP4 for its possible detrimental effect on COVID-19 syndrome, and of DPP4 inhibitors (gliptins), currently used as glucose lowering agents, which may have the potential to exert positive pleiotropic effect on inflammatory diseases, in addition to their effects on glucose metabolism. Thanks to these ancillary effects, gliptins could potentially be "repurposed" as salutary drugs against COVID-19 syndrome, even in non-diabetic subjects. Clinical studies should be designed to investigate this possibility.

FIGURES

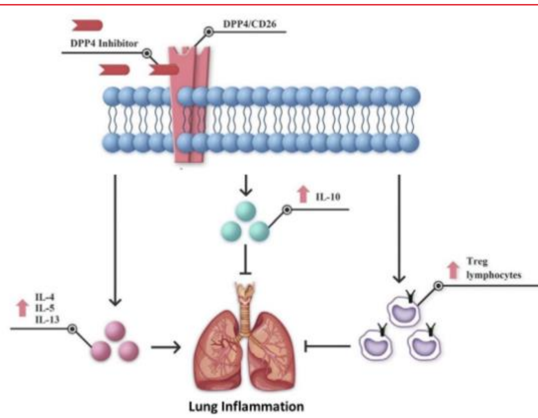

Fig. 1 Mechanistic effects of DPP4 inhibition in lung injury (modified from Shao et al. 2020) [13]

HOW BAD IS IT? SUICIDALITY IN THE MIDDLE OF THE COVID-19 PANDEMIC

Fitzpatrick KM, Harris C, Drawve G.. Suicide Life Threat Behav. 2020 Jun 26. doi: 10.1111/sltb.12655. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

A national survey of U.S. residents (n=10,368), released on 23 March 2020, found that 15% of respondents were categorized as high risk on the Suicide Behaviors Questionnaire-Revised (SBQ-R). A higher SBQ-score was associated with Blacks, Native Americans, Hispanics, families with children, the unmarried, and the young in addition to certain situational factors (food insecurity, physical symptoms, and depressive symptomatology) (Table 2, 3). While limited by response bias, these findings demonstrate that clinicians should be attentive to mental health needs of patients during the pandemic, particularly when risk factors for depression may be present.

ABSTRACT

OBJECTIVE: The current paper examines the intersection between social vulnerability, individual risk, and social/psychological resources with adult suicidality during the COVID-19 pandemic. METHOD: Data come from a national sample (n =10, 368) of U.S. adults. Using an online platform, information was gathered the third week of March 2020, and post-stratification weighted to proportionally represent the U.S. population in terms of age, gender, race/ethnicity, income, and geography. RESULTS: Nearly 15 percent of sampled respondents were categorized as high risk, scoring 7+ on the Suicide Behaviors Questionnaire-Revised (SBQ-R). This level of risk varied across social vulnerability groupings: Blacks, Native Americans, Hispanics, families with children, unmarried, and younger respondents reported higher SBQ-R scores than their counterparts (p < 0.000). Regression results confirm these bivariate differences, and also reveal that risk factors (food insecurity, physical symptoms, and CES-D symptomatology) are positive and significantly related to suicidality (p < 0.000). Additionally, resource measures are significant and negatively related to suicidality (p < 0.000). CONCLUSIONS: These results provide some insight on the impact COVID-19 is having on the general U.S. POPULATION: Practitioners should be prepared for what will likely be a significant mental health fall-out in the months and years ahead.

FIGURES

	SBQ-R Mean 4.6	*SBQ-R 0-5* (7,599)	SBQ-R 5-7 (949)	*SBQ-R 7+* (1,820)	*p*[1]
Social Vulnerabilities					
Gender (1 = Female)	4.5	74%	9%	17%	.244
(0 = Male)	4.8	73%	9%	18%	
Race (1 = Black)	5.0	71%	6%	23%	.000
(0 = Nonblack)	4.6	73%	10%	17%	
(1 = Asian)	4.6	74%	8%	18%	.369
(0 = Non-Asian)	4.6	74%	9%	17%	
(1 = Native American)	5.9	59%	5%	36%	.000
(0 = Non-Native American)	4.6	73%	9%	18%	
(1 = Other Races)	4.6	73%	13%	14%	.025
(0 = Non-Other Races)	4.6	73%	9%	18%	
Hispanic Status (1 = Hispanic)	5.4	67%	8%	25%	.000
(0 = Non-Hispanic)	4.5	75%	9%	16%	
Nativity (1 = Foreign Born)	4.7	75%	6%	19%	.003
(0 = Non-Foreign) Born)	4.5	73%	8%	19%	
Families w/Children (1 = Yes)	5.1	70%	8%	22%	.000
(0 = No)	4.5	74%	10%	16%	
Marital Status (1 = Unmarried)	4.9	67%	11%	22%	.000
(0 = Married)	4.3	80%	8%	12%	
Age[2]	-.28				.000
Individual Risks[3]					
CES-D Symptomatology	.56				.000
Food Insecurity (1 = Moderate to High)	5.9	59%	9%	32%	.000
(0 = No to Low)	3.8	83%	9%	8%	
Physical Symptoms	.32				.000
Social and Psychological Resources					
Strength of Social Ties	-.43				.000
Mastery of Fate	-.39				.000
Religion Important in Life	-.05				.000

* $p < 0.05$; ** $p < 0.01$
[1] X^2 analysis was used to test for differences between categorical variables and SBQ-R categories.
[2] Pearson correlations between SBQ-R scale and continuous level vulnerability, risk, and resource variables.
[3] One-way ANOVA tests for differences between SBQ-R categories and continuous vulnerability, risk, and resourc variables.

Table 2. Bivariate Measures with SBQ-R, Social Vulnerabilities, Risks, and Resources (n =10,368)

Model Variables	Model 1 b (B)	Model 2 b (B)	Model 3 b (B)
Social Vulnerabilities			
Gender (1 = Female)	-.30 (-.05)*****	-.49 (-.08)*****	-.44 (-.07)*****
Race (1 = Black)	-.01 (-.01)*	.27 (.03)** ***	.34 (.04)**
(1 = Asian)	-.28 (-.02)*	.18 (.01)	.10 (.01)
(1 = Native American)	1.1 (.03)**	1.1 (.03)**	1.2 (.03)**
(1 = Other Races)	.04 (.01)	.44 (.02)**	.47 (.02)**
Hispanic Status(1=Yes)	.26 (.03)*****	.20 (.02)**	.25 (.03)**
Nativity (1 = Foreign Born)	.17 (-.01)*	.12 (.01)	.10 (.01)
Families with Children (1 = Yes)	.08 (.01)	-.16 (-.02)**	-.16 (-.02)**
Marital Status (1= Unmarried)	.17 (.02)**	-.08 (-.01)	-.19 (-.03)**
Age	-.05 (-.27)**	-.01 (-.10)**	-.02 (-.09)**
Risks			
CES-D Symptomatology		- .09 (.45)**	- .07 (.36)**
Physical Symptoms		.19 (.15)**	-.18 (.14)**
Food Insecurity (1 = Moderate to High)		.37 (.06)**	-.22 (.04)**
Social and Psychological Resources			
Strength of Social Ties			-.09 (-.11)**
Mastery of Fate			-.05 (-.07)**
Religion Important in Life			-.06 (-.04)*****
Constant	6.90	3.76	6.46
Adjusted R^2	.09***	.35***	.37***

One-tailed t-tests p < 0.05*, p < 0.01**; R^2 change p < 0.001*** (two-tailed)

Table 3. Suicidality Multiple Regressions (n=10,368)

COVID-19'S IMPACT ON HEALTHCARE WORKFORCE

FACTORS ASSOCIATED WITH POST-TRAUMATIC STRESS DISORDER OF NURSES EXPOSED TO CORONA VIRUS DISEASE 2019 IN CHINA

Wang YX, Guo HT, Du XW, Song W, Lu C, Hao WN.. Medicine (Baltimore). 2020 Jun 26;99(26):e20965. doi: 10.1097/MD.0000000000020965.

Level of Evidence: 3 - Local non-random sample

BLUF

A group of researchers at Inner Mongolia Medical University in China conducted a survey of 202 nurses from tertiary hospitals in the Hubei province who were exposed to COVID-19 to evaluate factors that may contribute to the development of post-traumatic stress disorder (PTSD). Between February and March 2020, nurses (Table 1) were assessed via simplified coping style questionnaire (SCSQ) to evaluate coping styles and the PTSD checklist-civilian (PCL-C) to evaluate PTSD symptoms. Authors found an overall 16.83% PTSD incidence rate based on PCL-C scores (Table 2) and note that lower levels of PTSD symptoms were associated with higher job satisfaction (P<.001), positive (adaptive) coping mechanisms (P=.032), and being male (P<.001). The authors suggest that nurses exposed to COVID-19 could benefit from empowerment via education and training, while receiving sustainable counseling to reduce risk of psychological impairment.

ABSTRACT

Quantitative studies using validated questionnaires on post-traumatic stress disorder (PTSD) of Nurses exposed to corona virus disease 2019 (COVID-19) in China are rare and the baseline PTSD must first be evaluated before prevention. This study aimed to investigate the factors potentially involved in the level of PTSD of Nurses exposed to COVID-19 in China.In this cross-sectional study, male and female Nurses (n = 202) exposed to COVID-19 from HuBei China were included in the final sample. The PTSD Checklist-Civilian (PCL-C) questionnaire and Simplified Coping Style Questionnaire (SCSQ) were used for evaluation. Multivariate stepwise linear regression analysis and spearman correlation test were performed to assess the association between various factors associated with PTSD.The incidence of PTSD in Nurses exposed to COVID-19 was 16.83%, the PCL-C score was 27.00 (21.00-34.00), and the highest score in the three dimensions was avoidance dimension 9.50 (7.00-13.25); multivariable stepwise linear regression analysis showed that job satisfaction and gender were independently associated with lower PCL-C scores (both P < .001); PCL-C scores were correlated with positive coping (r = -0.151, P = .032), negative coping (r = 0.154, P = .029).Nurses exposed to COVID-19 from HuBei China with job satisfaction, male and positive coping had low PCL-C scores which necessitate reducing the PTSD level by ways of improving job satisfaction, positive response, and strengthening the psychological counseling of female nurses in order to reduce the risk of psychological impairment.

Variable	n (%)	PCL-C scores M (IQR)	Z/H	P
Age (years)		32.00 (29.00–40.00)	2.157	.000***
Gender				
Male	25 (12.4)	19.00 (17.00–26.00)	−3.874	.000***
Female	177 (87.6)	28.00 (22.50–34.50)		
Ethnic group				
Han	167 (82.7)	28.00 (21.00–34.00)	0.446	.800
Mongolian	23 (11.4)	24.00 (19.00–31.00)		
Others	12 (5.9)	29.00 (20.25–42.25)		
Professional title				
Staff nurse	10 (5.0)	25.50 (22.00–32.50)	0.435	.933
Nurse practitioner	104 (51.5)	27.50 (21.00–34.00)		
Chief nurse	59 (29.2)	28.00 (21.00–35.00)		
Deputy director	29 (14.3)	25.00 (20.00–34.00)		
Work experience (years)		10.00 (6.00–19.00)	2.064	.000***
Education				
Junior college	27 (13.4)	22.00 (19.00–34.00)	3.422	.181
Undergraduate	166 (82.2)	28.00 (21.00–34.00)		
Master	9 (4.4)	26.00 (23.50–34.00)		
Average monthly income (RMB)				
1000–3000	5 (2.5)	30.00 (19.00–31.00)	0.595	.898
3001–5000	63 (31.2)	26.00 (21.00–21.00)		
5001–7000	65 (32.2)	26.00 (20.50–34.50)		
>7000	69 (34.1)	28.00 (21.00–37.00)		
Marital status				
Married	148 (73.3)	26.00 (20.25–34.00)	4.498	.106
Unmarried	46 (22.8)	29.00 (21.00–35.50)		
Divorced	8 (3.9)	35.50 (28.00–47.75)		
Degree of family support				
Yes	199 (98.5)	27.00 (21.00–34.00)	3.795	.051
No opinion	3 (1.5)	37.00 (34.00–)		
Degree of job satisfaction				
Very satisfied	95 (47.0)	23.00 (19.00–30.00)	36.101	.000***
Satisfied	79 (39.1)	30.00 (26.00–39.00)		
Neutral	28 (13.9)	30.00 (21.50–38.75)		
Training or learning methods				
Protection knowledge				
Live lecture	26 (12.9)	26.00 (20.75–30.25)	2.952	.707
Online teaching	33 (16.3)	27.00 (21.00–34.00)		
Distribute ppt lecture notes, videos, and video materials	48 (23.8)	28.00 (23.00–37.00)		
Putting on and taking off protective equipment exercises	39 (19.3)	30.00 (21.00–37.00)		
Combat drill	48 (23.8)	26.00 (20.00–33.50)		
Others	8 (3.9)	33.50 (17.50–40.25)		
Have you participated in SARS prevention and control				
Yes	47 (23.3)	28.00 (21.00–37.00)	−0.983	.326
No	155 (76.7)	27.00 (21.00–34.00)		

M (IQR) = median (inter quartile range), PCL-C = PTSD checklist-civilian, RMB = renminbi (Chinese currency).
*** $P < .001$.

Table 1: Socio-demographic data, job characteristics and PCL-C Scores of nurses (n = 202) exposed to COVID-19 in Tertiary Hospitals in China.

PCL-C score	Frequency	Composition ratio (%)
PTSD (17–37 分)	168	83.17
some degree of PTSD (38–49 分)	15	7.42
definitively diagnosed PTSD (50–85 分)	19	9.41

Table 2: PCL-C score distribution (N = 202).

IMPACT ON PUBLIC MENTAL HEALTH

ASSOCIATIONS AMONG STATE-LEVEL PHYSICAL DISTANCING MEASURES AND SUICIDAL THOUGHTS AND BEHAVIORS AMONG U.S. ADULTS DURING THE EARLY COVID-19 PANDEMIC

Bryan CJ, Bryan AO, Baker JC.. Suicide Life Threat Behav. 2020 Jun 26. doi: 10.1111/sltb.12653. Online ahead of print.
Level of Evidence: 1 - Local and current random sample surveys (or censuses)

BLUF

A cross-sectional survey of 10,625 United States adults (Table 1) conducted by authors at The University of Utah assessed the relationship between state-imposed COVID-19 physical distancing measures and mental health outcomes between 18 March and 4 April 2020. They found that rates of poor mental health (distress, depression, and suicidal thoughts/behaviors) were generally unrelated to state-imposed physical distancing measures (Table 4), rather there was evidence for better mental health outcomes among participants subject to physical distancing measures. Although people in states with stay-at-home orders were significantly less likely to report depression (odds ratio [OR]=0.75, 95% CI=0.57-0.99, p=0.044) and participants with past-month suicidal ideation that were subject to large gathering bans were significantly less likely to report a suicide attempt in the prior month (OR=0.39, 95% CI=0.17-0.88, p=0.024), the overall likelihood of depression and past-month suicidal ideation/attempt was significantly increased in those with past-month stressors (Table 5). This suggests that depression and suicide risk is decreased due to stay-at-home orders but increased as a result of other life stressors, which can inform resource allocation and global readiness for future public health crises.

ABSTRACT

PURPOSE: The purpose of this study was to identify leading sources of stress, describe rates of mental health outcomes, and examine their associations among U.S. adults during the first months of the COVID-19 pandemic.
METHOD: In a cross-sectional, general population survey conducted from March 18 to April 4, 2020, U.S. adults (n=10,625) were recruited through Qualtrics Panels using quota sampling methods.
RESULTS: Life stressors, probable depression, past-month suicide ideation, and past-month suicide attempts were not elevated among participants subject to state-level stay-at-home orders and/or large gatherings bans. Multiple life stressors were associated with increased rates of probable depression. Past-month suicide ideation was significantly higher among participants reporting ongoing arguments with a partner and serious legal problems. Past-month suicide attempt was significantly higher among participants reporting concerns about a life-threatening illness or injury, but was significantly lower among participants reporting an unexpected bill or expense.
CONCLUSIONS: Results failed to support the conclusion that physical distancing measures are correlated with worse mental health outcomes. Concerns about life-threatening illness or injury was uniquely associated with increased risk of suicide attempt.

FIGURES

	None	SAH Only	LGB Only	Both	Stay-at-Home Order			Large Gatherings Ban			Both		
Mental health outcome	%	%	%	%	OR	(95% CI)	p	OR	(95% CI)	p	OR	(95% CI)	p
Probable depression	23.4	14.4	18.6	19.2	0.75	(0.57-0.99)	.044	0.91	(0.78-1.06)	.211	1.32	(0.98-1.79)	.071
Past-month suicide ideation	5.9	3.0	4.2	4.5	0.70	(0.41-1.21)	.201	0.86	(0.64-1.14)	.279	1.50	(0.83-2.71)	.180
Past-month suicide attempt	1.5	0.4	1.1	1.2	0.35	(0.08-1.49)	.155	0.85	(0.49-1.45)	.547	2.70	(0.59-12.30)	.201
Among those with past-month ideation	22.6	6.3	11.5	15.3	0.29	(0.03-2.49)	.258	0.39	(0.17-0.88)	.024	4.59	(0.47-44.75)	.190

Table 4: Percentage of participants with probable depression, past-month suicide ideation, and past-month suicide attempt, by state-level physical distancing measures in effect at the time of survey completion.

							Past-Month Suicide Attempt					
	Probable Depression			Past-Month Suicide Ideation			Full Sample			Among those with Past-Month Ideation		
Past-month stressors	OR	(95% CI)	p	OR	(95% CI)	p	OR	(95% CI)	p	OR	(95% CI)	p
Life-threatening illness/injury of friend/family	1.81	(1.59-2.05)	<.001	0.96	(0.75-1.22)	.740	2.26	(1.48-3.46)	<.001	3.87	(2.14-6.99)	<.001
Death of close friend or family	1.12	(0.99-1.27)	.073	0.88	(0.70-1.11)	.278	0.89	(0.58-1.39)	.616	1.07	(0.58-1.99)	.830
Separation or divorce from spouse/partner	1.81	(1.51-2.17)	<.001	1.36	(1.00-1.84)	.049	1.45	(0.91-2.33)	.120	1.18	(0.57-2.44)	.659
Serious arguments with spouse/partner	1.83	(1.59-2.09)	<.001	1.46	(1.16-1.83)	.001	1.64	(1.08-2.48)	.020	1.06	(0.56-2.03)	.855
Spouse/partner infidelity	1.43	(1.19-1.71)	<.001	0.95	(0.70-1.29)	.725	1.83	(1.10-3.04)	.020	1.57	(0.74-3.35)	.244
Serious betrayal by someone else	1.52	(1.32-1.76)	<.001	1.25	(0.97-1.60)	.086	1.18	(0.74-1.89)	.495	0.91	(0.45-1.84)	.801
Unexpected bill or expense	1.15	(1.03-1.29)	.018	1.05	(0.84-1.32)	.657	0.41	(0.24-0.70)	.001	0.38	(0.17-0.85)	.019
Did not get promoted	1.12	(0.91-1.38)	.273	0.96	(0.67-1.39)	.843	0.93	(0.49-1.78)	.825	1.16	(0.46-2.94)	.750
Lower score than expected on assignment	0.85	(0.71-1.02)	.086	1.27	(0.95-1.72)	.112	1.30	(0.76-2.22)	.335	1.19	(0.56-2.50)	.656
Disciplined or punished at work	1.07	(0.86-1.32)	.555	1.28	(0.89-1.83)	.183	0.87	(0.47-1.60)	.648	0.56	(0.18-1.820	.337
Trouble with police	1.17	(0.91-1.52)	.220	0.63	(0.39-1.01)	.053	1.45	(0.72-2.94)	.297	1.08	(0.38-3.09)	.888
Spent time in jail or prison	1.01	(0.75-1.35)	.959	1.15	(0.70-1.91)	.577	1.07	(0.50-2.27)	.865	1.46	(0.52-4.07)	.474
Other serious legal problem	1.88	(1.49-2.36)	<.001	1.85	(1.31-2.62)	<.001	1.29	(0.65-2.55)	.462	0.78	(0.35-1.77)	.559

Table 5: Association of past-month stressors with probable depression, past-month suicide ideation, and past-month suicide attempt.

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