

# The Daily COVID-19 Literature Surveillance Summary

**June 26, 2020**



© 2020 | COVID19LST.org



## DISCLAIMER

This free and open source document represents a good faith effort to provide real time, distilled information for guiding best practices during the COVID-19 pandemic. This document is not intended to and cannot replace the original source documents and clinical decision making. These sources are explicitly cited for purposes of reference but do not imply endorsement, approval or validation.

This is not an official product or endorsement from the institutions affiliated with the authors, nor do the ideas and opinions described within this document represent the authors' or their affiliated institutions' values, opinions, ideas or beliefs. This is a good faith effort to share and disseminate accurate summaries of the current literature.

### NOW LIVE!

Daily audio summaries of the literature in 10 minutes or less.

<https://www.covid19lst.org/podcast/>



# COVID-19 Daily Literature Surveillance

COVID19LST



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

# LEVEL OF EVIDENCE

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

Question	Step 1 (Level 1*)	Step 2 (Level 2*)	Step 3 (Level 3*)	Step 4 (Level 4*)	Step 5 (Level 5)
<b>How common is the problem?</b>	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
<b>Is this diagnostic or monitoring test accurate? (Diagnosis)</b>	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
<b>What will happen if we do not add a therapy? (Prognosis)</b>	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
<b>Does this intervention help? (Treatment Benefits)</b>	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
<b>What are the COMMON harms? (Treatment Harms)</b>	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
<b>What are the RARE harms? (Treatment Harms)</b>	Systematic review of randomized trials or n-of-1 trial	Randomized trial or (exceptionally) observational study with dramatic effect			
<b>Is this (early detection) test worthwhile? (Screening)</b>	Systematic review of randomized trials	Randomized trial	Non-randomized controlled cohort/follow-up study**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning

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

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

## How to cite the Levels of Evidence Table

OCEBM Levels of Evidence Working Group\*. "The Oxford 2011 Levels of Evidence". Oxford Centre for Evidence-Based Medicine. <http://www.cebm.net/index.aspx?o=5653>

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

# EXECUTIVE SUMMARY

## Climate

- A survey of 426 emergency physicians from seven medical institutions in California, New Jersey, and Louisiana found inadequacy of PPE, inability to quickly and accurately diagnose COVID-19, and fear of infecting family members to be the [most salient stressors](#).

## Epidemiology

- A systematic review and meta-analysis, including 148 articles comprised of 24,410 COVID-19 positive adults from 9 countries, found that the [most common symptoms at presentation](#) were fever (78%), cough (57%), and fatigue (31%), with prevalence of dyspnea in only 23% of patients. The authors conclude that the most common symptoms are fever and cough, although it is noted that these prevalence findings are about 10% less than previously reported.
- A systematic review and meta-analysis of 18 studies ( $n = 14,558$  COVID-19 positive individuals) evaluating [severe infection and mortality risk in patients with comorbidities](#) found populations with diabetes, hypertension, cardiovascular disease, chronic obstructive pulmonary disease, and other comorbidities may have approximately double the risk of the general population and should take maximum preventive measures to protect themselves from infection with SARS-CoV-2.

## Understanding the Pathology

- A case series of 7 patients found that postmortem tissue samples from patients who died from COVID-19 pneumonia <7 days after onset of respiratory failure (RF) showed [acute diffuse alveolar damage \(DAD\)](#) while samples from those who died >14 days after onset of RF showed organizing DAD, with SARS-CoV-2 detected in tissues with acute DAD but not in tissues with organizing DAD.

## Management

- An analysis of 90 patients from the Affiliated Yueqing Hospital, Wenzhou Medical University to develop a [predictive model for rehabilitation time](#) for mild-moderate COVID-19 cases found that of 5 significant clinical predictors, increased partial pressure of carbon dioxide and decreased serum potassium correlated with increased rehabilitation duration. Sub-stratification of the patient group as a mild-moderate risk using a 3-tiered risk system, predicted a rehabilitation time of  $17.2 \pm 5.2$  days and suggested that the predictive tool may be used for personalized risk management.
- Analysis of three case series with conflicting data on [mechanically ventilated COVID-19 patients](#) indicated that: 1) low respiratory system compliance (Crs) may be associated with a higher gradient of arterial partial pressures of oxygen to alveolar partial pressures of oxygen (PaO<sub>2</sub>-PAO<sub>2</sub>) in COVID-19 respiratory failure, 2) positive end-expiratory pressure (PEEP) levels should be selected by measuring Crs, and 3) increasing tidal volume can reduce both serial dead space ventilation and parallel dead space ventilation. The authors suggest that clinicians focus on individual patient's needs when operating respirators given the heterogeneity in presentations of COVID-19 respiratory failure.

## Adjusting Practice During COVID-19

- An international group of physicians affiliated with the World Endoscopy Organization provide guideline on the [safe operation of endoscopy centers](#) during the COVID-19 pandemic that may help endoscopy centers continue to provide appropriate services during the different phases of the COVID-19 pandemic.

## R&D: Diagnosis & Treatments

- The Korea Centers for Disease Control and Prevention COVID-19 Diagnosis Test Management Committee provides [guidelines to supplement the "Guidelines for Laboratory Diagnosis of COVID-19 in Korea"](#) and provides technical support for common laboratory challenges in COVID-19 diagnostics.
- A cross-sectional study conducted by Tulane University School of Medicine using 29 nasal swab samples and found that COVID-19 could be diagnosed within 50 minutes via a [COVID-19 CRISPR fluorescent detection system](#)

[\(FDS\)](#) with 100% sensitivity and 71.4% specificity when compared to results obtained by a state testing laboratory via reverse transcriptase (RT)-PCR of the same samples

- A systematic review conducted among [clinical trials registered on ClinicalTrials.gov regarding hydroxychloroquine \(HCQ\) prophylaxis](#) for SARS-CoV-2 found that the range of HCQ loading dose across the studies was 400-1400 mg followed either by a daily dose (commonly 200mg or 400mg) or weekly dose (400 mg) with prophylaxis duration ranging from 4 to 180 days or 3 to 24 weeks. Based on this "high diversity in [HCQ] dosage and duration of prophylaxis," the authors suggest additional analysis of these trials' designs and results before determining the appropriate HCQ regimen.

### Mental Health & Resilience Needs

- Authors of the Department of Addictive Behavior and Addictive Medicine in Mannheim, Germany and the Department of Psychiatry and Psychotherapy in Paracelsus Medical University evaluated [the effect of social isolation on alcohol consumption during the pandemic](#) through an anonymous online survey of 2,102 participants and found that 34.7% of participants reported drinking more alcohol since the lockdown began, highlighting the need for healthcare providers to stay informed on this increased alcohol consumption during the lockdown and to be aware of its potential long-term effects.
- A systematic review conducted at the Galatea Care Programme for Sick Health Professionals in Barcelona, Spain analyzed 30 studies and found a [high prevalence of anxiety \(30-70%\) and depressive symptoms \(20-40%\) reported among healthcare professionals \(HPs\)](#), raising concerns that increased psychological support is needed in these population.

<b>EXECUTIVE SUMMARY .....</b>	<b>4</b>
<b>CLIMATE .....</b>	<b>8</b>
<b>GLOBAL.....</b>	<b>8</b>
Does culture matter social distancing under the COVID-19 pandemic?.....	8
<b>AFFECTING THE HEALTHCARE WORKFORCE.....</b>	<b>9</b>
Academic Emergency Medicine Physicians' Anxiety Levels, Stressors and Potential Stress Mitigation Measures during the Acceleration Phase of the COVID-19 Pandemic.....	9
<b>EPIDEMIOLOGY .....</b>	<b>13</b>
<b>SYMPTOMS AND CLINICAL PRESENTATION.....</b>	<b>13</b>
Temperature screening has negligible value for control of COVID-19.....	13
<b>Adults.....</b>	<b>14</b>
The prevalence of symptoms in 24,410 adults infected by the novel coronavirus (SARS-CoV-2; COVID-19): A systematic review and meta-analysis of 148 studies from 9 countries.....	14
Prevalence of comorbidities and their association with mortality in patients with COVID-19: A Systematic Review and Meta-analysis .....	15
Neurological involvement of coronavirus disease 2019: a systematic review.....	18
Asymptomatic SARS-CoV-2 Infection in Nursing Homes, Barcelona, Spain, April 2020.....	20
Laboratory predictors of death from coronavirus disease 2019 (COVID-19) in the area of Valcamonica, Italy .....	20
<b>UNDERSTANDING THE PATHOLOGY.....</b>	<b>23</b>
In situ detection of SARS-CoV-2 in lungs and airways of patients with COVID-19 .....	23
Insights into SARS-CoV-2, the Coronavirus Underlying COVID-19: Recent Genomic Data and the Development of Reverse Genetics Systems .....	24
<b>TRANSMISSION &amp; PREVENTION .....</b>	<b>26</b>
Examining the need for eye protection for COVID-19 prevention in the community .....	26
ACE2 and TMPRSS2 variation in savanna monkeys ( <i>Chlorocebus spp.</i> ): Potential risk for zoonotic/anthroponotic transmission of SARS-CoV-2 and a potential model for functional studies.....	26
<b>MANAGEMENT .....</b>	<b>28</b>
Improved Clinical Symptoms and Mortality on Severe/Critical COVID-19 Patients Utilizing Convalescent Plasma Transfusion.....	28
<b>ACUTE CARE .....</b>	<b>30</b>
Prediction of the rehabilitation duration and risk management for mild-moderate COVID-19.....	30
Heterogeneity of Acute Respiratory Distress Syndrome in COVID-19: "Typical" or Not?.....	31
<b>Critical Care .....</b>	<b>31</b>
Mechanics of Breathing and Gas Exchange in Mechanically Ventilated Patients with COVID-19 Associated Respiratory Failure.....	31
<b>MEDICAL SUBSPECIALTIES.....</b>	<b>32</b>
<b>Cardiology.....</b>	<b>32</b>
Spontaneous Coronary Artery Dissection in a Patient With COVID-19 .....	32
<b>Hematology and Oncology.....</b>	<b>33</b>
Consideration in the management of renal cell carcinoma during the COVID-19 Pandemic.....	33
<b>ADJUSTING PRACTICE DURING COVID-19.....</b>	<b>35</b>
<b>Gastroenterology .....</b>	<b>35</b>
Recommendations for the Operation of Endoscopy Centers in the setting of the COVID19 pandemic - A WEO guidance document... <td>35</td>	35
<b>R&amp;D: DIAGNOSIS &amp; TREATMENTS .....</b>	<b>37</b>
A sugar-coated strategy to treat a rare neurologic disease provides a blueprint for a decoy glycan therapeutic and a potential vaccine for CoViD-19: An Editorial Highlight for "Selective inhibition of anti-MAG IgM autoantibody binding to myelin by an antigen specific glycopolymer" on <a href="https://doi.org/10.1111/jnc.15021">https://doi.org/10.1111/jnc.15021</a> .....	37
<b>CURRENT DIAGNOSTICS .....</b>	<b>38</b>
COVID-19 Molecular Testing in Korea: Practical Essentials and Answers From Experts Based on Experiences of Emergency Use Authorization Assays .....	38
<b>DEVELOPMENTS IN DIAGNOSTICS .....</b>	<b>39</b>
Ultra-sensitive and high-throughput CRISPR-powered COVID-19 diagnosis .....	39
Mass Spectrometric Identification of SARS-CoV-2 Proteins from Gargle Solution Samples of COVID-19 Patients.....	41
<b>DEVELOPMENTS IN TREATMENTS.....</b>	<b>43</b>
Systematic review of registered trials of Hydroxychloroquine prophylaxis for COVID-19 health-care workers at the first third of 2020.....	43
In Vivo Expressed Biologics for Infectious Disease Prophylaxis: Rapid Delivery of DNA-Based Antiviral Antibodies .....	43

<b>MENTAL HEALTH &amp; RESILIENCE NEEDS .....</b>	<b>45</b>
Did the General Population in Germany Drink More Alcohol during the COVID-19 Pandemic Lockdown? .....	45
Psychiatric disorders and suicide in the COVID-19 era .....	45
<b>COVID-19'S IMPACT ON HEALTHCARE WORKFORCE .....</b>	<b>45</b>
The impact of the COVID-19 pandemic on the mental health of healthcare professionals.....	45
<b>IMPACT ON PUBLIC MENTAL HEALTH .....</b>	<b>46</b>
Emotional Distress in Young Adults During the COVID-19 Pandemic: Evidence of Risk and Resilience From a Longitudinal Cohort Study.....	46
The Coronavirus Disease 2019 (COVID-19) Outbreak and Mental Health: Current Risks and Recommended Actions .....	47
<b>ACKNOWLEDGEMENTS.....</b>	<b>48</b>

## DOES CULTURE MATTER SOCIAL DISTANCING UNDER THE COVID-19 PANDEMIC?

Huynh TLD.. Saf Sci. 2020 Oct;130:104872. doi: 10.1016/j.ssci.2020.104872. Epub 2020 Jun 10.

Level of Evidence: 3 - Local non-random sample

### BLUF

An observational study conducted at the University of Economics in Vietnam used Google COVID-19 community mobility reports data from February 16th, 2020 through March 29th, 2020 and found a correlation between nations with a high cultural preference for avoiding uncertainty and higher social distancing scores (Figures 2 and 3). This suggests that public health officials may be able to leverage concerns about uncertainty to encourage social distancing, though more research needs to be done to establish causation between these factors.

### ABSTRACT

This paper is the first to examine the role of the cultural dimension in practising social distancing across the world. By drawing the data from the Google COVID-19 community mobility reports and the Hofstede cultural factors for 58 countries over the period from 16 February to 29 March 2020, we find that countries with higher 'Uncertainty Avoidance Index' predict the lower proportion of people gathering in public such as retail and recreation, grocery and pharmacy, parks, transit stations, workplaces. However, we do not find any predictive factor in having a relationship with the percentage of citizens staying in their residential areas. Our results are robust by adding the control variable as the wealth status, GDP per capita. Hence, this paper suggests some effective communications to contain the COVID-19 pandemic by emphasizing the role of uncertainties.

### FIGURES

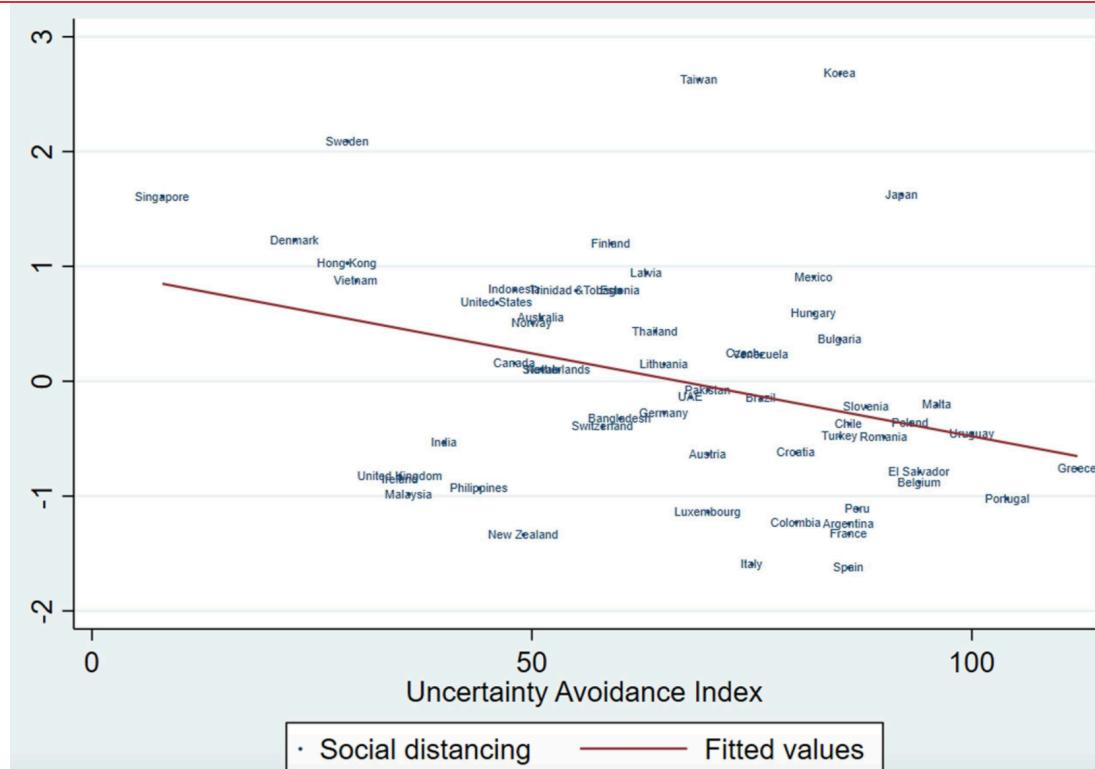


Figure 3. Uncertainty Avoidance Index and changes in proportion of social distancing at the public.

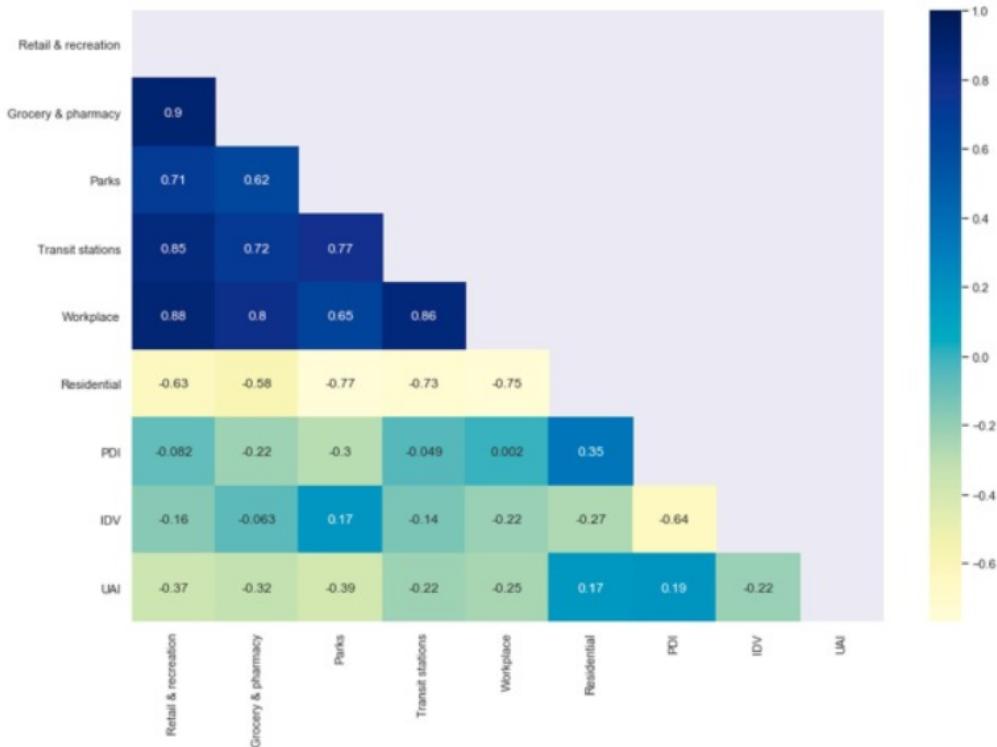


Figure 3. Uncertainty Avoidance Index and changes in proportion of social distancing at the public.

## AFFECTING THE HEALTHCARE WORKFORCE

### ACADEMIC EMERGENCY MEDICINE PHYSICIANS' ANXIETY LEVELS, STRESSORS AND POTENTIAL STRESS MITIGATION MEASURES DURING THE ACCELERATION PHASE OF THE COVID-19 PANDEMIC

Rodriguez RM, Medak AJ, Baumann BM, Lim S, Chinnock B, Frazier R, Cooper RJ.. Acad Emerg Med. 2020 Jun 22. doi: 10.1111/acem.14065. Online ahead of print.

Level of Evidence: 3 - Local non-random sample

#### BLUF

A group of emergency physicians in California surveyed 426 emergency physicians via email at seven medical institutions in California, New Jersey, and Louisiana between 23 March and 10 April 2020 and found the following to be the most salient stressors for this population (Table 2, 3):

- Inadequacy of PPE
- Inability to quickly and accurately diagnose COVID-19
- Fear of infecting family members

The survey asked respondents to identify potentially helpful interventions (Table 4), which included increasing availability of PPE, increasing accessibility to tests with rapid turnaround, and assuring time off to be with family members.

#### ABSTRACT

**OBJECTIVE:** To assess anxiety and burnout levels, home life changes and measures to relieve stress of United States academic emergency medicine (EM) physicians during the COVID-19 pandemic acceleration phase. **METHODS:** We sent a cross-sectional email survey to all EM physicians at seven academic emergency departments. The survey incorporated items from validated stress scales and assessed perceptions and key elements in the following domains: numbers of suspected COVID-19 patients, availability of diagnostic testing, levels of home and workplace anxiety, severity of work burnout, identification of stressors, changes in home behaviors, and measures to decrease provider anxiety. **RESULTS:** 426 (56.7%) EM physicians responded. On a scale of 1-7 (1= not at all, 4 = somewhat, and 7=extremely), the median (interquartile range) reported effect of the pandemic

on both work and home stress levels was 5 (4,6). Reported levels of emotional exhaustion/burnout increased from pre-pandemic median 3 (2,4) to since the pandemic started median 4 (3,6); difference in medians = 1.8 (95% confidence interval 1.7-1.9). Most physicians (90.8%) reported changing their behavior towards family and friends, especially by decreasing signs of affection (76.8%). The most commonly cited measures cited to alleviate stress/anxiety were increasing personal protective equipment availability (PPE), offering rapid COVID-19 testing at physician discretion, providing clearer communication about COVID-19 protocol changes, and assuring that physicians can take leave for care of family and self. CONCLUSIONS: During the acceleration phase, the COVID-19 pandemic has induced substantial workplace and home anxiety in academic EM physicians and their exposure during work has had a major impact on their home lives. Measures cited to decrease stress include enhanced availability of PPE, rapid turnaround testing at provider discretion, and clear communication about COVID-19 protocol changes.

## FIGURES

**Table 2. Stratification for key response questions**

Characteristics	Effect of pandemic on workplace stress: median (IQR)	Effect of pandemic on home stress: median (IQR)	Pre-pandemic emotionally exhaustion and burnout: median (IQR)	Post-pandemic emotionally exhaustion and burnout: median (IQR)	Changed behavior with friends and family because of possible excess work exposure: n (%)	
					Yes	174 (90.6)
Female (n = 192)	6 (5,6)	6 (5,7)	3 (2,4)	4 (3,6)	No	13 (7.8)
					Unsure	3 (1.6)
					Yes	209 (91.3)
Male (n = 229)	5 (4,6)	5 (4,6)	2 (2,4)	4 (3,6)	No	17 (74.2)
					Unsure	2 (0.9)
					Yes	210 (89)
Faculty (n = 236)	5 (4,6)	5 (4,6)	3 (2,4)	5 (3,6)	No	21 (8.9)
					Unsure	3 (1.3)
					Yes	175 (93.6)
Resident or fellow (n = 187)	5 (4,6)	5 (4,6)	3 (2,4)	4 (3,6)	No	9 (4.8)
					Unsure	2 (1.1)
					Yes	149 (89.8)
Have children < 18 in home (n = 166)	5 (4,6)	5 (4,6)	3 (2,4)	4 (3,6)	No	13 (7.8)
					Unsure	2 (1.2)
					Yes	238 (91.9)
No children in home (n = 259)	5 (4,6)	5 (4,6)	3 (2,4)	4 (3,6)	No	18 (6.9)
					Unsure	3 (1.2)
					Yes	279 (91.2)
California sites (n = 306)	5 (4,6)	5 (4,6)	3 (2,4)	4 (3,6)	No	7 (2.3)
					Unsure	1 (0.3)
					Yes	109 (90.8)
Non-California sites (n = 120)	5 (4,6)	5 (4,6)	3 (2,4)	4 (3,6)	No	7 (5.8)
					Unsure	1 (0.8)

IQR = interquartile range

**Table 2. Stratification of key response questions**

**Table 3. Physicians' concerns relating to their work during the COVID-19 pandemic. Median and interquartile ranges to questions "I worry about or that..." on 1-7 scale, in which 1 = "not at all", 4 = "somewhat", and 7 = "extremely"**

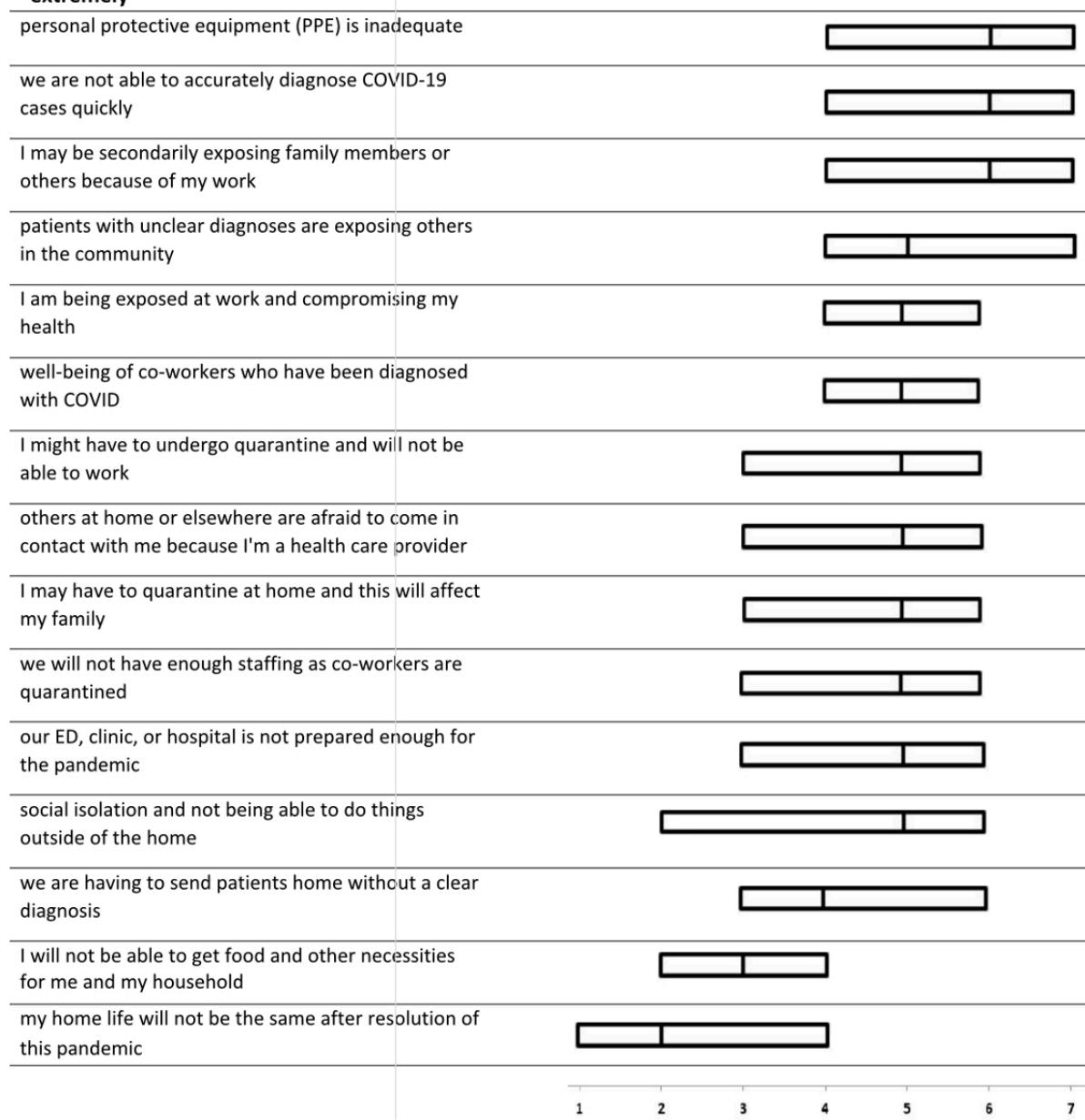


Table 3. Physicians' concerns relating to their work during the COVID-19 pandemic. Median and interquartile ranges to questions "I worry about or that..." on 1-7 scale, in which 1 = "not at all", 4 = "somewhat", and 7 = "extremely"

**Table 4. Rank summary of measures that emergency physicians believe would relieve their**

Measure	Aggregate Points	# (%) of Respondents Citing
		Measure (N = 426)
Enhanced availability of personal protective equipment	1637	410 (96.2)
Rapid turnaround (< 6 hours) testing	1362	392 (92.0)
Testing for COVID-19 for patients at my discretion (instead of as limited by current protocols)	1054	351 (82.4)
Clearer communication about changes in protocols	976	313 (73.5)
Assurances that I can take leave to care for myself and family members	933	306 (71.8)
Greater clarity regarding my risk for exposure	858	284 (66.7)
Assurances that my (and my dependents') medical care will be covered by my employer	799	270 (63.4)
Ability to request testing of myself for COVID-19 even if I do not have symptoms	787	295 (69.2)
Assurances about disability benefits	741	243 (57.0)
Easily available mental health consultations for myself and other health care providers	660	242 (56.8)
Departmental ZOOM or other video sessions to discuss COVID-19 response and changes	638	236 (55.4)

COVID – coronavirus disease

Respondents were asked: "From the list below, pick the top 5 measures (1 = highest priority) that you think would alleviate some of your anxiety/stress related to the COVID-19 pandemic". Aggregate Points are the sum of points in which 1 (highest priority) = 5 points, 2 = 4 points, 3 = 3 points, 4 = 2 points, 5 = 1 point.

**stress related to the COVID-19 pandemic.**

Table 3. Physicians' concerns relating to their work during the COVID-19 pandemic. Median and interquartile ranges to questions "I worry about or that..." on 1-7 scale, in which 1 = "not at all", 4 = "somewhat", and 7 = "extremely"

## EPIDEMIOLOGY

### SYMPTOMS AND CLINICAL PRESENTATION

#### TEMPERATURE SCREENING HAS NEGLIGIBLE VALUE FOR CONTROL OF COVID-19

Mitra B, Luckhoff C, Mitchell RD, O'Reilly G, Smit V, Cameron PA.. Emerg Med Australas. 2020 Jun 24. doi: 10.1111/1742-6723.13578. Online ahead of print.

Level of Evidence: 4 - Local non-random sample

#### BLUF

A retrospective analysis conducted at The Alfred Hospital in Melbourne, Victoria examined the presence of fever in SARS-CoV-2-positive patients (confirmed via RT-PCR) at the time of initial testing and again within 24 hours after initial presentation between 09 March and 13 May 2020 (Figure 1). They found that 16 of 86 patients (19%) with SARS-CoV-2 had a fever at presentation, with repeat temperature within 24 hours detecting fever in 18 of 75 cases (24%) (Figure 2). Though temperature collection methods were not standardized, these findings contribute to a growing body of evidence that suggests temperature may not be a reliable marker of SARS-CoV-2 infection.

#### ABSTRACT

OBJECTIVE: To report the incidence of fever among patients who tested positive for SARS-CoV-2.

METHODS: Retrospective cohort study of patients who tested positive for SARS-CoV-2 at a single centre. Temperature at time of testing and on repeat testing within 24 h were collected.

RESULTS: At the time of testing, fever was detected (sensitivity) in 16 of 86 (19%; 95% CI: 11-28) episodes of positive tests for SARS-CoV-2. With repeat testing, fever was detected in 18 of 75 (24%; 95% CI: 15-35) episodes.

CONCLUSIONS: In an Australian hospital, screening for fever lacked sensitivity for detection of people with SARS-CoV-2. This article is protected by copyright. All rights reserved.

#### FIGURES

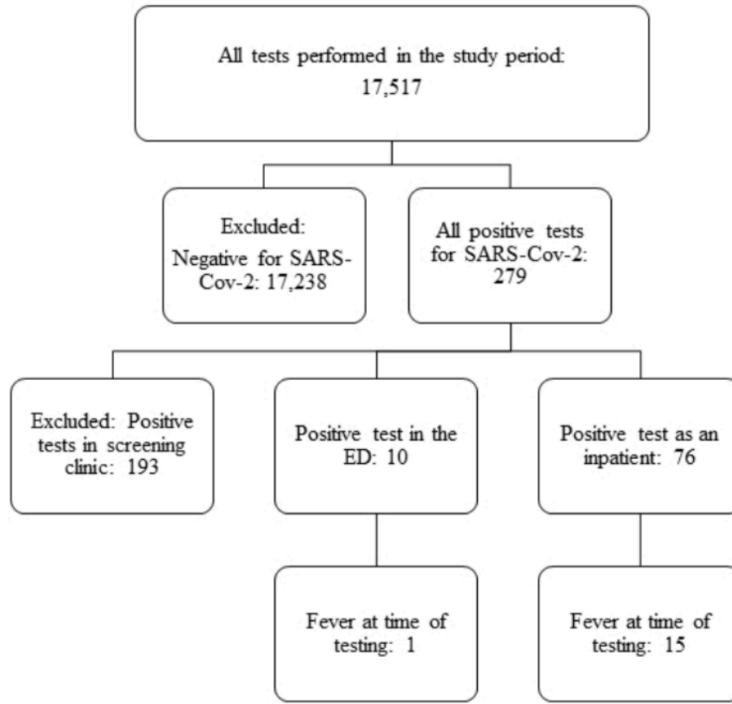


Figure 1. Selection of patients

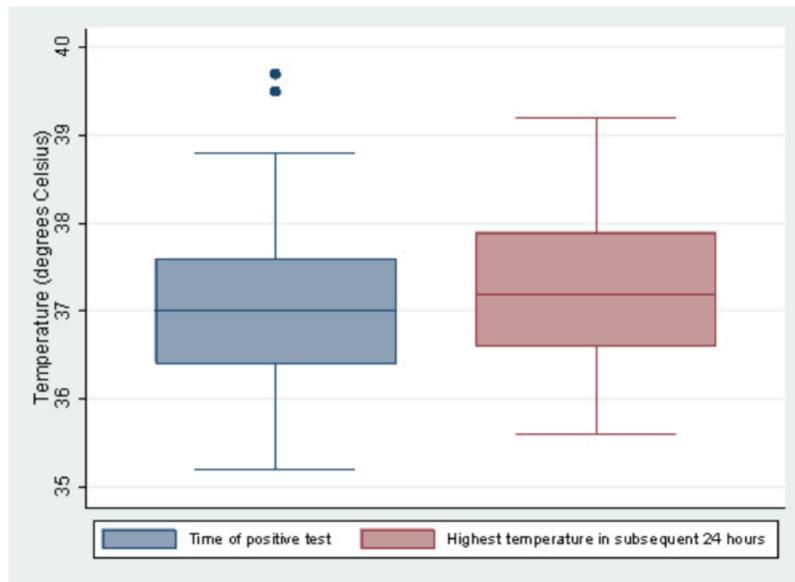


Figure 2. Body temperature at time of being tested positive for SARS-CoV-2 and highest temperature in subsequent 24 hours.

## ADULTS

### THE PREVALENCE OF SYMPTOMS IN 24,410 ADULTS INFECTED BY THE NOVEL CORONAVIRUS (SARS-COV-2; COVID-19): A SYSTEMATIC REVIEW AND META-ANALYSIS OF 148 STUDIES FROM 9 COUNTRIES

Grant MC, Geoghegan L, Arbyn M, Mohammed Z, McGuinness L, Clarke EL, Wade RG.. PLoS One. 2020 Jun 23;15(6):e0234765. doi: 10.1371/journal.pone.0234765. eCollection 2020.

Level of Evidence: 2 - Systematic review of surveys that allow matching to local circumstances

#### BLUF

A systematic review and meta-analysis, including 148 articles comprised of 24,410 COVID-19 positive adults from 9 countries, found that the most common symptoms at presentation were fever (78%; 95% CI 75%-81%), cough (57%; 95% CI 54%-60%), and fatigue (31%; 95% CI 27%-35%) with prevalence of dyspnea in only 23% of patients (CI 19%-28%; Table 1). The authors conclude that the most common symptoms are fever and cough, although it is noted that these prevalence findings are about 10% less than previously reported.

#### ABSTRACT

**BACKGROUND:** To limit the spread of SARS-CoV-2, an evidence-based understanding of the symptoms is critical to inform guidelines for quarantining and testing. The most common features are purported to be fever and a new persistent cough, although the global prevalence of these symptoms remains unclear. The aim of this systematic review is to determine the prevalence of symptoms associated with COVID-19 worldwide.

**METHODS:** We searched PubMed, Embase, CINAHL, AMED, medRxiv and bioRxiv on 5th April 2020 for studies of adults (>16 years) with laboratory test confirmed COVID-19. No language or publication status restrictions were applied. Data were independently extracted by two review authors into standardised forms. All datapoints were independently checked by three other review authors. A random-effects model for pooling of binomial data was applied to estimate the prevalence of symptoms, subgrouping estimates by country. I<sup>2</sup> was used to assess inter-study heterogeneity.

**RESULTS:** Of 851 unique citations, 148 articles were included which comprised 24,410 adults with confirmed COVID-19 from 9 countries. The most prevalent symptoms were fever (78% [95% CI 75%-81%]; 138 studies, 21,701 patients; I<sup>2</sup> 94%), a cough (57% [95% CI 54%-60%]; 138 studies, 21,682 patients; I<sup>2</sup> 94%) and fatigue (31% [95% CI 27%-35%]; 78 studies, 13,385 patients; I<sup>2</sup> 95%). Overall, 19% of hospitalised patients required non-invasive ventilation (44 studies, 6,513 patients),

17% required intensive care (33 studies, 7504 patients), 9% required invasive ventilation (45 studies, 6933 patients) and 2% required extra-corporeal membrane oxygenation (12 studies, 1,486 patients). The mortality rate was 7% (73 studies, 10,402 patients).

**CONCLUSIONS:** We confirm that fever and cough are the most prevalent symptoms of adults infected by SARS-CoV-2. However, there is a large proportion of infected adults which symptoms-alone do not identify.

## FIGURES

**Table 1. Meta-analysis of the prevalence of symptoms in adults with laboratory test confirmed COVID-19.**

System	Symptom	Number of studies	Number of people	Prevalence (95% CI)	I <sup>2</sup>
Systemic	Fever	138	21,701	78 (75, 81)	94%
	Fatigue	78	13,385	31 (27, 35)	95%
	Myalgia	72	11,389	17 (14, 19)	88%
	Rigors	17	2834	18 (13, 22)	88%
	Arthralgia	2	401	11 (8, 14)	/
	Rash	1	1099	0 (0, 1)	/
Respiratory	Any cough (dry or productive)	138	21,682	57 (54, 60)	94%
	Dry (non-productive) cough	136	17,380	58 (54, 61)	93%
	Productive cough	70	10,017	25 (22, 28)	90%
	Dyspnoea	94	12,713	23 (19, 28)	97%
	Chest pain	30	3510	7, (4, 10)	92%
	Haemoptysis	21	4698	2 (1, 2)	42%
	Wheeze	16	2013	17 (9, 26)	96%
Ear, nose and throat	Sore throat	78	11,721	12 (10, 14)	88%
	Rhinorrhoea	36	10,656	8 (5, 12)	97%
	Vertigo / dizziness	16	1972	11 (6, 16)	90%
	Nasal congestion	10	2584	5 (3, 7)	78%
	Hyposmia	3	317	25 (4, 55)	/
	Hypogeusia	2	220	4 (1, 8)	/
	Otalgia	1	68	4 (1, 11)	/
Gastrointestinal	Diarrhoea	93	11,707	10 (8, 12)	93%
	Nausea	27	4584	6 (3, 10)	95%
	Vomiting	26	4959	4 (2, 8)	94%
	Abdominal pain	19	3331	4 (2, 7)	88%
Central nervous system	Headache	65	15,958	13 (10, 16)	97%
	Confusion	6	869	11 (7, 15)	67%
	Ataxia	1	214	0 (0, 2)	/
Eyes	Conjunctivitis	9	2715	2 (1, 4)	80%
	Ophthalmalgia	1	534	4 (3, 6)	/
	Photophobia	1	534	3 (2, 4)	/

## PREVALENCE OF COMORBIDITIES AND THEIR ASSOCIATION WITH MORTALITY IN PATIENTS WITH COVID-19: A SYSTEMATIC REVIEW AND META-ANALYSIS

Singh AK, Gillies CL, Singh R, Singh A, Chudasama Y, Coles B, Seidu S, Zaccardi F, Davies MJ, Khunti K.. Diabetes Obes Metab. 2020 Jun 23. doi: 10.1111/dom.14124. Online ahead of print.

Level of Evidence: 2 - Systematic review of surveys that allow matching to local circumstances

### BLUF

A systematic review and meta-analysis of 18 studies from December 2019-March 2020 (N studies = 18; 16 in China, 1 in US, 1 in Italy; n = 14,558 COVID-19 positive individuals) evaluated severe infection and mortality risk in patients with comorbidities (Table 2). Their results (summarized below) suggest populations with diabetes, hypertension, cardiovascular disease, chronic obstructive pulmonary disease, and other comorbidities may have approximately double the risk of the general population and should take maximum preventive measures to protect themselves from infection with SARS-CoV-2.

### SUMMARY

1. The study found that hypertension, diabetes, cardiovascular disease (CVD), chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), and cancer were risk factors for severe COVID-19 infection:

"The meta-analyses showed that hypertension (RR 1.66 [95% CI: 1.32, 2.09]), diabetes (2.11 [1.40, 3.19], CVD (2.55 [1.85,

3.51], COPD [2.62 [2.31, 2.97], CKD [3.86 [2.32, 6.40]], and cancer [2.48 [1.46, 4.19]] were all significantly associated with a higher risk of severe COVID-19, compared to patients without comorbidities (figure 2[sic], table 2[sic])."

2. Additionally CVD, COPD, CKD, cerebrovascular disease, and cancer carried significant mortality risk in COVID-19 patients: "Compared to individuals without comorbidities, the risk of death was significantly increased in those with CVD (RR 1.88 [95% CI: 1.41, 2.51], COPD (1.53 [1.03, 2.28]), CKD (1.84 [1.03, 3.30]), cerebrovascular disease (2.48 [2.14, 2.86]), and cancer (1.77 [1.08, 2.88]) (figure 3[sic], table 2[sic])."

## ABSTRACT

**AIMS:** COVID-19 is a global pandemic that as of the 4th May has registered over 3 585 711 confirmed cases and 248 780 deaths. This review aims to estimate the prevalence of both cardiometabolic and other co-morbidities in patients with COVID-19 infection, and to estimate the increased risk of severity and mortality in people with co-morbidities.

**MATERIALS AND METHODS:** Medline, Scopus and the World Health Organisation (WHO) website for Global research on COVID-19 were searched from January 2019 up to April 23, 2020. Study inclusion was restricted to English language publications, original articles that reported prevalence of co-morbidities in individuals with COVID-19 disease, and case-series >10 patients. 18 studies were selected for inclusion. Data were analysed using random effects meta-analysis models.

**RESULTS:** Eighteen studies with a total of 14 558 individuals were identified. The pooled prevalence for co-morbidities in patients with COVID-19 disease was 22.9% (95% CI: 15.8 to 29.9) for hypertension; 11.5% (9.7 to 13.4) for diabetes; and 9.7% (6.8 to 12.6) for cardiovascular disease (CVD). For chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), cerebrovascular disease, and cancer, the pooled prevalences were all less than 4%. With the exception of cerebrovascular disease, all other co-morbidities had a significantly increased risk for having severe COVID-19. In addition, the risk of mortality was significantly increased in individuals with CVD, COPD, CKD, cerebrovascular disease, and cancer.

**CONCLUSIONS:** In individuals with COVID-19, the presence of co-morbidities (both cardiometabolic and other) is associated with a higher risk of severe COVID-19 and mortality. These findings have important implications for the public health with regards to risk stratification and future planning. This article is protected by copyright. All rights reserved.

## FIGURES

Comorbidities	N studies	Pooled effect size (95% CI), p-value	I <sup>2</sup> (%), p-value	Egger's (p-value)
<i>Estimated pooled prevalences (%) of co-morbidities in COVID-19 patients</i>				
Hypertension	13	22.9 (15.8, 29.9), <0.001	97.3, <0.001	0.524
Diabetes	14	11.5 (9.7, 13.4), <0.001	81.2, <0.001	0.573
CVD	14	9.7 (6.8, 12.6), <0.001	96.6, <0.001	0.724
COPD	13	3.1 (1.0, 5.2), <0.004	97.4, <0.001	0.018*
CKD	10	2.4 (1.5, 3.2), <0.001	81.8, <0.001	0.996
Cerebrovascular disease	7	3.0 (1.8, 4.2), <0.001	56.3, 0.033	0.114
Cancer	13	3.9 (2.5, 5.4), <0.001	88.2, 0.001	0.400
<i>Estimated pooled RR of suffering severe COVID-19 if you have a comorbidity compared to if you do not</i>				
Hypertension	6	1.66 (1.32, 2.09), <0.001	30.9, 0.204	0.819
Diabetes	7	2.11 (1.40, 3.19), <0.001	84.6, 0.001	0.030*
CVD	7	2.55 (1.85, 3.51), <0.001	72.5, 0.001	0.031*
COPD	6	2.62 (2.31, 2.97), <0.001	0.0, 0.830	0.015*
CKD	2	3.86 (2.32, 6.40), <0.001	38.5, 0.202	-
Cerebrovascular disease	1	1.73 (0.74, 4.05), 0.208	-	-
Cancer	2	2.48 (1.46, 4.19), 0.001	0.0, 0.544	-
<i>Estimated pooled RR of mortality from COVID-19 if you have a comorbidity compared to if you do not</i>				
Hypertension	3	1.52 (0.86, 2.71), 0.151	92.2, 0.001	0.251
Diabetes	2	1.83 (0.89, 3.73), 0.100	81.9, 0.019	-
CVD	2	1.88 (1.41, 2.51), <0.001	0.0, 0.478	-
COPD	1	1.53 (1.03, 2.28), 0.035	-	-
CKD	1	1.84 (1.03, 3.30), 0.040	-	-
Cerebrovascular disease	1	2.48 (2.14, 2.86), <0.001	-	-
Cancer	1	1.77 (1.08, 2.88), 0.023	-	-

\*Where publication bias was significant trim and fill analyses were carried out (details reported in supplementary material)

Table 2: Summary of meta-analyses results for prevalence of co-morbidities, and increased risk of mortality and severity of disease by co-morbidities, in COVID-19 patients.

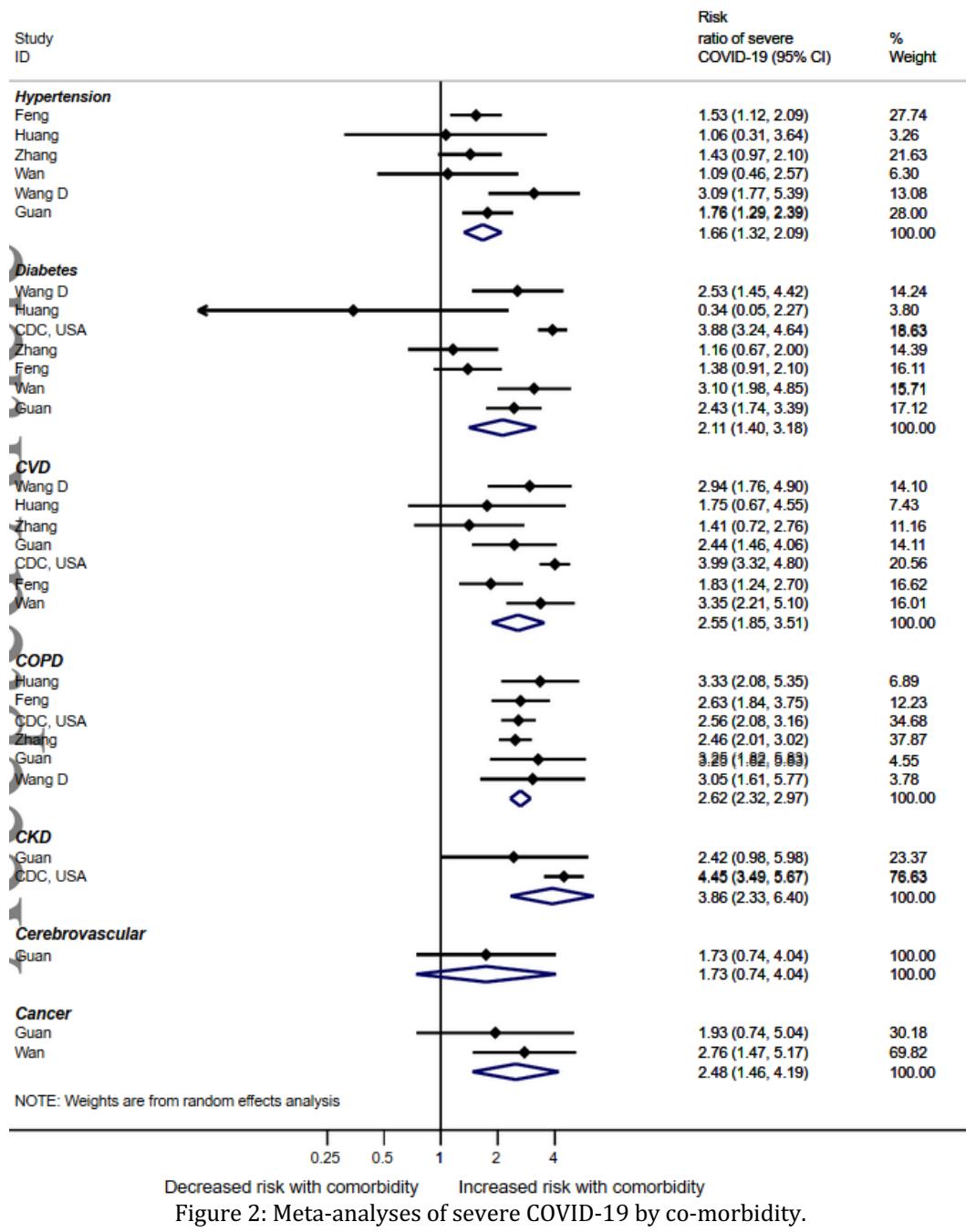


Figure 2: Meta-analyses of severe COVID-19 by co-morbidity.

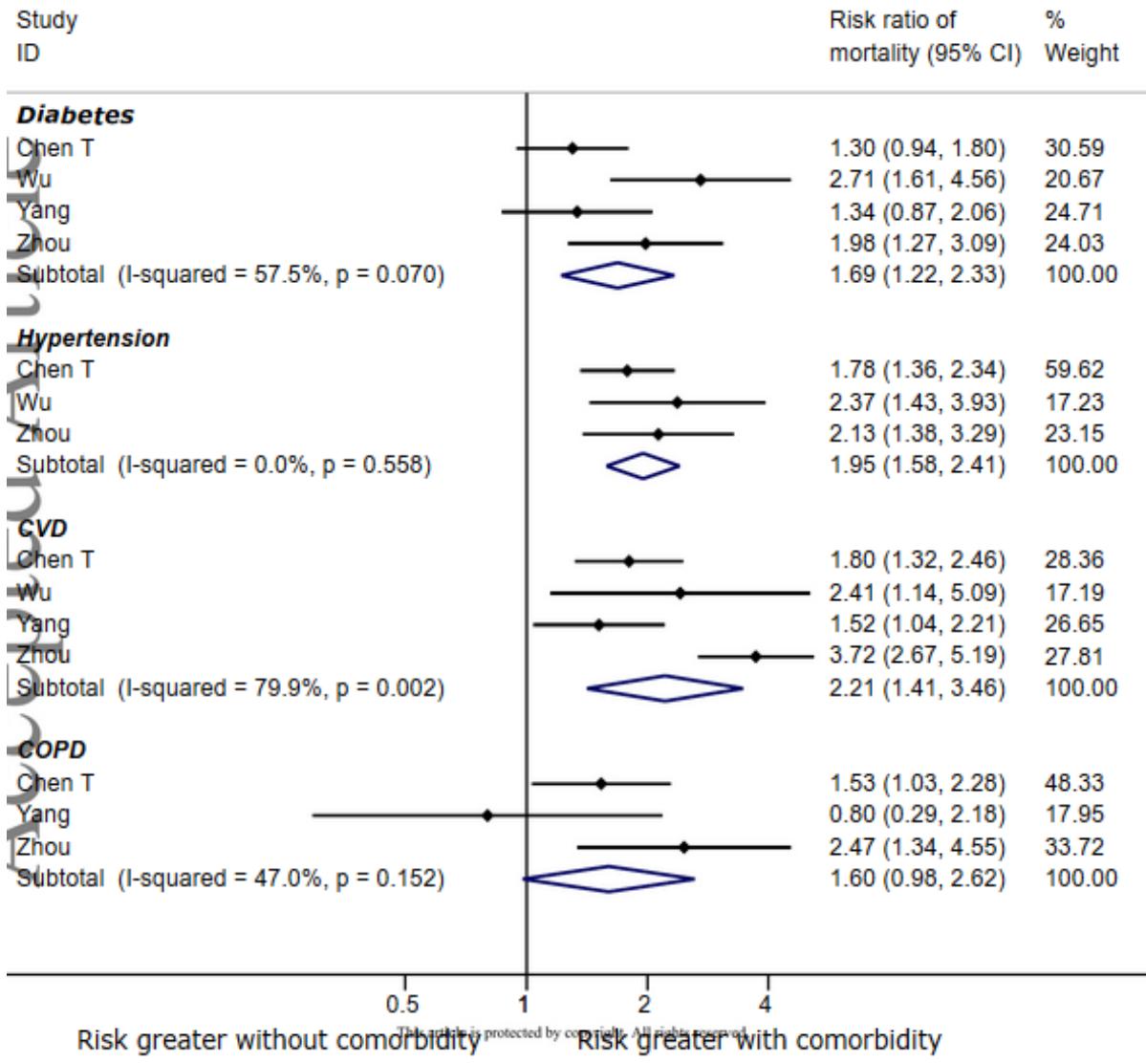


Figure 2: Meta-analyses of severe COVID-19 by co-morbidity.

## NEUROLOGICAL INVOLVEMENT OF CORONAVIRUS DISEASE 2019: A SYSTEMATIC REVIEW

Ghannam M, Alshaer Q, Al-Chalabi M, Zakarna L, Robertson J, Manousakis G.. J Neurol. 2020 Jun 19. doi: 10.1007/s00415-020-09990-2. Online ahead of print.

Level of Evidence: 2 - Systematic review of surveys that allow matching to local circumstances

### BLUF

A systematic review conducted by the Department of Neurology at the University of Minnesota of articles published December 1, 2019 to May 12, 2020. Researchers ultimately identified 42 articles and 82 cases of neurologic manifestations in COVID-19 (Figure 1). The most common CNS complications and outcomes were analyzed and are reported in Figure 2 and additional details are summarized below. The authors recommend further studies aim to clarify the prevalence and mechanisms of neurological symptoms and explore treatment options.

### SUMMARY

Results suggest ischemic stroke, Guillain-Barre syndrome, and meningoencephalitis are common neurological manifestations of COVID-19.

Ischemic stroke was the most common cause of cerebrovascular complications:

- 77% large vessel occlusion stroke.
- 14% small vessel stroke.

- 9% cardioembolic stroke.
- 80% had elevated D-dimer.
- 57% had elevated C-reactive protein.
- Thrombolytic treatment is reasonable in the appropriate time-frame.

Guillain-Barre syndrome was the most common neuromuscular disorder:

- GBS developed 3-24 days after onset of flu-like symptoms in 14 of the patients.
- 7 out of 17 had facial weakness.
- IVIG was used as a treatment.
- Proposed mechanisms include a para-infectious process from cytokine release syndrome and a post-infectious process from molecular mimicry production of anti-ganglioside antibodies.

Meningoencephalitis was the most common cause of CNS inflammation/infections:

- 4 out of 13 CSF samples showed lymphocytic pleocytosis.
- 2 of those CSF samples were positive for SARS-CoV-2 RT-PCR.
- 6 patients received plasmapheresis as treatment.
- Cases without the virus in the CSF could have suffered from immune-mediated encephalitis, thrombotic microangiopathy-like state, or false-negative PCR.
- SARS-CoV-2 may enter the CNS hematogenously or through retrograde synaptic transmission via olfactory nerve.

## ABSTRACT

**BACKGROUND:** In December 2019, unexplained cases of pneumonia emerged in Wuhan, China, which were found to be secondary to the novel coronavirus SARS-CoV-2. On March 11, 2020, the WHO declared the Coronavirus Disease 2019 (COVID-2019) outbreak, a pandemic.

**OBJECTIVE:** To clarify the neurological complications of SARS-CoV-2 infection including the potential mechanisms and therapeutic options.

**METHODS:** We conducted a systematic literature search from December 01, 2019 to May 14, 2020 using multiple combinations of keywords from PubMed and Ovid Medline databases according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. We included articles with cases of COVID-19 where neurological involvement was evident.

**RESULTS:** We were able to identify 82 cases of COVID-19 with neurological complications. The mean age was 62.3 years. 37.8% of the patients were women ( $n = 31$ ). 48.8% of the patients ( $n = 40$ ) had cerebrovascular insults, 28% ( $n = 23$ ) had neuromuscular disorders, and 23% of the patients ( $n = 19$ ) had encephalitis or encephalopathy.

**CONCLUSIONS:** Neurological manifestations of COVID-19 are not rare, especially large vessel stroke, Guillain-Barre syndrome, and meningoencephalitis. Moving forward, further studies are needed to clarify the prevalence of the neurological complications of SARS-CoV-2 infection, investigate their biological backgrounds, and test treatment options. Physicians should be cautious not to overlook other neurological diagnoses that can mimic COVID-19 during the pandemic.

## FIGURES

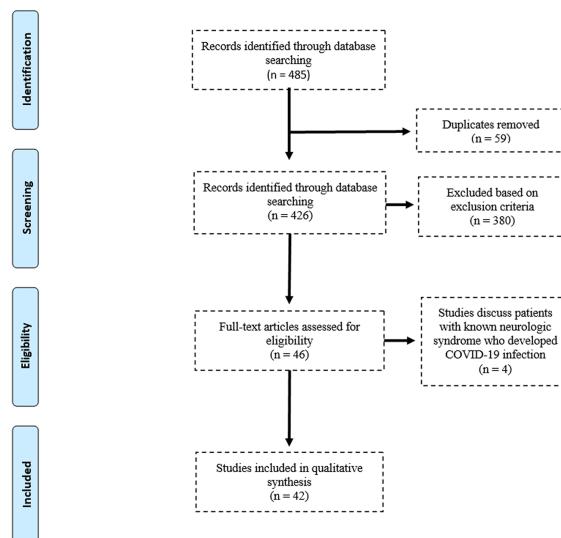


Figure 1. PRISMA flowchart of the selection of the studies for this review

## **ASYMPTOMATIC SARS-COV-2 INFECTION IN NURSING HOMES, BARCELONA, SPAIN, APRIL 2020**

Borras-Bermejo B, Martínez-Gómez X, San Miguel MG, Esperalba J, Antón A, Martin E, Selvi M, Abadías MJ, Román A, Pumarola T, Campins M, Almirante B.. Emerg Infect Dis. 2020 Jun 23;26(9). doi: 10.3201/eid2609.202603. Online ahead of print.

Level of Evidence: 3 - Local non-random sample

### **BLUF**

A Spanish research team performed a cross-sectional assessment of SARS-CoV-2 prevalence in residents and staff at 69 nursing homes in Catalonia, Spain during the week of April 10-24, 2020. They collected 5,869 samples (3,214 residents and 2,655 staff) and found 23.9% of residents and 15.2% of staff tested positive via RT-PCR, the majority of whom reported no symptoms in the preceding 14 days (69.7% and 55.8%, respectively)(Table). The researchers suggest SARS-CoV-2 is prevalent in nursing homes and laboratory-based surveillance may be necessary to identify infected individuals without symptoms.

### **ABSTRACT**

During the coronavirus disease pandemic in Spain, from April 10-24, 2020, a total of 5,869 persons were screened for severe acute respiratory syndrome coronavirus 2 at nursing homes. Among residents, 768 (23.9%) tested positive; among staff, 403 (15.2%). Of those testing positive, 69.7% of residents and 55.8% of staff were asymptomatic.

### **FIGURES**

Residents		Staff	
Positive, N = 768	Negative, N = 2,446	Positive, N = 403	Negative, N = 2,252
Asymptomatic	486 (69.7)	1,727 (89.6)	144 (55.8) 1,311 (86.6)
Symptomatic*	211 (30.3)	200 (10.4)	114 (44.2) 203 (13.4)

Table. SARS-CoV-2 test results for residents and staff of 69 nursing homes, Barcelona, Spain, April 2020\* \*Results include all residents and staff who were in the facility the day of screening intervention. Testing was by reverse transcription PCR. SARS-CoV-2, severe acute respiratory syndrome coronavirus 2. †Percentage calculated over those with symptom information available; it was missing for 590 (18.4%) residents and 883 (33.3%) staff members.‡A person was considered symptomatic if fever or respiratory symptoms were present at time of assessment, or at any moment in the preceding 14 days.

## **LABORATORY PREDICTORS OF DEATH FROM CORONAVIRUS DISEASE 2019 (COVID-19) IN THE AREA OF VALCAMONICA, ITALY**

Bonetti G, Manelli F, Patroni A, Bettinardi A, Borrelli G, Fiordalisi G, Marino A, Menolfi A, Saggini S, Volpi R, Anesi A, Lippi G.. Clin Chem Lab Med. 2020 Jun 25;58(7):1100-1105. doi: 10.1515/cclm-2020-0459.

Level of Evidence: 3 - Local non-random sample

### **BLUF**

Between March 1 and March 30, 2020, Italian researchers performed a retrospective study of 230 hospitalized COVID-19 patients at Valcamonica Hospital. They divided this group into two cohorts; discharged (n=74) and expired (n=70) (Table 1). Increased age, LDH, C-reactive protein, neutrophils, activated prothrombin time, decreased lymphocytes, and albumin were independent predictors of worse outcomes (i.e. death) (Table 2 for p-values). The researchers suggest these variables may be useful to include in clinical and laboratory algorithms to identify patients at increased risk of developing severe COVID-19.

### **ABSTRACT**

Background Comprehensive information has been published on laboratory tests which may predict worse outcome in Asian populations with coronavirus disease 2019 (COVID-19). The aim of this study is to describe laboratory findings in a group of

Italian COVID-19 patients in the area of Valcamonica, and correlate abnormalities with disease severity. Methods The final study population consisted of 144 patients diagnosed with COVID-19 (70 who died during hospital stay and 74 who survived and could be discharged) between March 1 and 30, 2020, in Valcamonica Hospital. Demographical, clinical and laboratory data were collected upon hospital admission and were then correlated with outcome (i.e. in-hospital death vs. discharge). Results Compared to patients who could be finally discharged, those who died during hospital stay displayed significantly higher values of serum glucose, aspartate aminotransferase (AST), creatine kinase (CK), lactate dehydrogenase (LDH), urea, creatinine, high-sensitivity cardiac troponin I (hsCTnI), prothrombin time/international normalized ratio (PT/INR), activated partial thromboplastin time (APTT), D-dimer, C reactive protein (CRP), ferritin and leukocytes (especially neutrophils), whilst values of albumin, hemoglobin and lymphocytes were significantly decreased. In multiple regression analysis, LDH, CRP, neutrophils, lymphocytes, albumin, APTT and age remained significant predictors of in-hospital death. A regression model incorporating these variables explained 80% of overall variance of in-hospital death. Conclusions The most important laboratory abnormalities described here in a subset of European COVID-19 patients residing in Valcamonica are highly predictive of in-hospital death and may be useful for guiding risk assessment and clinical decision-making.

## FIGURES

Clinical and demographical characteristics	In-hospital death (n=70)	Discharged (n=74)	p-Value
Age, years	78.0 (64.2–84.0)	62.1 (53.0–72.8)	<0.001
Males, %	45 (64.3%)	51 (68.9%)	0.383
Females, %	25 (35.7%)	24 (31.1%)	
Days from symptoms onset to hospital admission	4	7	
Days from hospital admission to outcome	6	2	
Chronic diseases	49 (70%)	43 (57.3%)	0.114
Cancer	9 (12.9%)	6 (8.0%)	0.335
Diabetes	21 (30%)	16 (21.3%)	0.231
Cardiovascular disease	38 (54.3%)	33 (44.0%)	0.217
Immunodeficiencies	2 (2.8%)	0 (0.0%)	0.146
Chronic respiratory diseases	14 (20.5%)	6 (8.0%)	0.031
Chronic kidney diseases	9 (12.9%)	3 (4.0%)	0.053
Metabolic diseases	10 (14.3%)	7 (9.3%)	0.351
BMI 30–40	11 (15.7%)	5 (6.7%)	0.085
BMI >40	1 (1.4%)	0 (0.0%)	0.306

Results are shown as median and interquartile range (between brackets). BMI, body mass index.

Table 1. Clinical and demographical characteristics of coronavirus disease 2019 (COVID-19) patients who died during hospital stay and those who survived and could be discharged.

Parameters	In-hospital death (n=70)	Discharged (n=74)	p-Value
Glucose, mmol/L	7.63 (6.44–10.60)	6.10 (5.61–6.77)	<0.001
Albumin, g/L	34.6 (31.8–35.9)	36.5 (33.8–39.3)	<0.001
ALT, U/L	34 (23–49)	31.5 (21–46)	0.516
AST, U/L	61.5 (44–83)	45 (25–59)	0.001
Bilirubin total, µmol/L	11.7 (8.7–19.5)	10.6 (8.7–13.9)	0.109
GGT, U/L	56 (31.25–105.0)	45 (28.0–86.75)	0.232
Lipase, U/L	33 (25.0–41.25)	38 (31.0–45.0)	0.013
CK, U/L	168 (92.0–350.5)	92.5 (60.0–198.0)	0.001
LDH, U/L	521 (416–636)	316 (247–397.25)	<0.001
Sodium, mmol/L	138 (135–141)	137 (135–140)	0.655
Potassium, mmol/L	4.0 (3.6–4.55)	3.9 (3.45–4.20)	0.165
Chloride, mmol/L	101 (98.5–103.5)	101 (98.0–104.0)	0.722
Urea, mmol/L	23.4 (16.1–33.6)	12.1 (10.4–19.3)	<0.001
Creatinine, µmol/L	124 (85–155)	91 (73–104)	<0.001
hsCTnI, ng/L	47.5 (2.0–290.0)	8.0 (5.1–15.0)	<0.001
PT/INR	1.12 (1.03–1.28)	1.04 (1.00–1.10)	0.001
APTT, s	34 (29–37)	31 (29–34)	0.014
D-dimer, g/L	1.99 (1.27–3.63)	0.91 (0.60–2.03)	<0.001
CRP, g/L	165.65 (82.45–241.4)	60.3 (23.6–154.4)	<0.001
Ferritin, ng/mL	1285 (431–2409)	701.5 (382–1475)	0.01
Hb, g/L	130 (114–144)	137 (125–150)	0.024
WBC, ×10 <sup>9</sup> /L	6.64 (5.63–12.16)	5.605 (4.38–7.60)	0.002
Neutrophils, ×10 <sup>9</sup> /L	5.59 (4.45–9.72)	4.13 (2.72–5.79)	<0.001
Lymphocytes, ×10 <sup>9</sup> /L	0.75 (0.56–1.01)	1.04 (0.81–1.30)	<0.001
Platelets, ×10 <sup>9</sup> /L	178 (132–216)	189 (148–230)	0.237

Results are shown as median and interquartile range (between brackets). The parameters were compared using the Mann-Whitney test for independent samples. APTT, activated partial thromboplastin time; AST, aspartate aminotransferase; ALT, alanine aminotransferase; CK, creatine kinase; CRP, C reactive protein; GGT, gamma-glutamyltransferase; Hb, hemoglobin; hsCTnI, high-sensitive cardiac troponin I; LDH, lactate dehydrogenase; PT/INR, prothrombin time/international normalized ratio; WBC, white blood cells.

Table 2. Comparison of laboratory parameters between coronavirus disease 2019 (COVID-19) patients who died during hospital stay and those who survived and could be discharged.



# UNDERSTANDING THE PATHOLOGY

## IN SITU DETECTION OF SARS-COV-2 IN LUNGS AND AIRWAYS OF PATIENTS WITH COVID-19

Schaefer IM, Padera RF, Solomon IH, Kanjilal S, Hammer MM, Hornick JL, Sholl LM.. Mod Pathol. 2020 Jun 19. doi: 10.1038/s41379-020-0595-z. Online ahead of print.

Level of Evidence: 4 - Case-series

### BLUF

This case series of 7 patients found that postmortem tissue samples from patients who died from COVID-19 pneumonia <7 days after onset of respiratory failure (RF) showed acute diffuse alveolar damage (DAD) while samples from those who died >14 days after onset of RF showed organizing DAD (Table 2). Furthermore, SARS-CoV-2 was detected in tissues with acute DAD but not in tissues with organizing DAD (Table 3), suggesting that SARS-CoV-2 "can be detected during the acute phase of lung injury and is absent in the organizing phase."

### ABSTRACT

Coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2 has led to a global public health crisis. In elderly individuals and those with comorbidities, COVID-19 is associated with high mortality, frequently caused by acute respiratory distress syndrome. We examine in situ expression of SARS-CoV-2 in airways and lung obtained at autopsy of individuals with confirmed COVID-19 infection. Seven autopsy cases (male, N = 5; female, N = 2) with reverse transcriptase-polymerase chain reaction (RT-PCR)-confirmed SARS-CoV-2 infection and a median age of 66 years (range, 50-77 years) were evaluated using a rabbit polyclonal antibody against SARS Nucleocapsid protein in correlation with clinical parameters. The median time from symptom onset to death was 9 days (range, 6-31 days), from hospitalization 7 days (range, 1-21 days), from positive RT-PCR 7 days (range, 0-18 days), and from intensive care unit admission defining onset of respiratory failure 3 days (range, 1-18 days). Chest imaging identified diffuse airspace disease in all patients corresponding to acute and (N = 5) or organizing (N = 2) diffuse alveolar damage (DAD) on histologic examination. Among five patients with acute-phase DAD (<=7 days from onset of respiratory failure), SARS-CoV-2 was detected in pulmonary pneumocytes and ciliated airway cells (N = 5), and in upper airway epithelium (N = 2). In two patients with organizing DAD (>14 days from onset of respiratory failure), no virus was detected in lungs or airways. No endothelial cell infection was observed. The findings suggest that SARS-CoV-2 infection of epithelial cells in lungs and airways of patients with COVID-19 who developed respiratory failure can be detected during the acute phase of lung injury and is absent in the organizing phase.

### FIGURES

Table 2 Radiologic findings, treatment, and disease course in seven patients with COVID-19 who underwent autopsy.

Case No.	Radiologic findings	Treatment	Time to death (Days)					Cause of death
			Symptom onset	Hospitalization	ICU admission	RT-PCR	Postmortem interval	
1	CT: lower lobe and peripheral patchy GGO X-ray: bilateral peripheral-predominant airspace opacities	Hydroxychloroquine (SLE)	21	7	3	7	2	SARS-CoV-2 pneumonia
2	X-ray: diffuse bilateral pulmonary airspace disease	None	Several	1	1	0	1	SARS-CoV-2 pneumonia
3	X-ray: diffuse interstitial and airspace disease	None	6	3	3	3	2	SARS-CoV-2 pneumonia
4	X-ray: diffuse bilateral airspace disease	None	9	11	7	8	2	SARS-CoV-2 pneumonia
5	CT: extensive bilateral GGO with subpleural sparing and organization X-ray: diffuse bilateral interstitial and airspace disease	None	8	1	1	1	1	SARS-CoV-2 pneumonia complicating a recent myocardial infarction
6	X-ray: bilateral peripheral-predominant airspace opacities	Hydroxychloroquine	23	16	15	16	1	SARS-CoV-2 pneumonia
7	X-ray: diffuse bilateral airspace disease, pneumo-mediastinum	Remdesivir	31	21	18	18	2	SARS-CoV-2 pneumonia

DAD diffuse alveolar damage, GGO ground-glass opacities, SLE systemic lupus erythematosus.

**Table 3** SARS-CoV-2 immunohistochemical findings and histologic correlates in seven patients with COVID-19 who underwent autopsy.

Case No.	Lung histology	Pulmonary thromboembolism	SARS-CoV-2 IHC on trachea			SARS-CoV-2 IHC on lung		
			Extent of staining	Cell type staining positive	Histology corresponding to areas with positive staining	Extent of Staining	Cell type staining positive	Histology corresponding to areas with positive staining
1	Acute DAD (with scattered foci of organizing DAD) Interstitial lung disease with bronchiectasis	+	-	N/A	N/A	+	Pneumocytes	Acute DAD
2	Acute DAD (with scattered foci of organizing DAD)	+	-	N/A	N/A	+	Pneumocytes	Acute DAD
3	Acute DAD (with scattered foci of organizing DAD) Superimposed bacterial lobar pneumonia	+	-	N/A	N/A	+	Pneumocytes	Acute DAD
4	Acute DAD (with scattered foci of organizing DAD) Prominent reactive pneumocyte hyperplasia Superimposed bacterial lobar pneumonia Aspergillus abscess	-	+	Ciliated airways cells, rare epithelial cells in submucous glands	Focally denuded airway mucosa with focal squamous metaplasia	++	Pneumocytes	Acute DAD
5	Acute DAD Prominent reactive pneumocyte hyperplasia	+	++	Ciliated airways cells, epithelial cells in submucous glands	Focally denuded airway mucosa with focal squamous metaplasia	+++	Pneumocytes, few macrophages	Acute DAD
6	Organizing lung injury/ DAD	-	-	N/A	N/A	-	N/A	N/A
7	Organizing lung injury/ DAD Superimposed bacterial lobar pneumonia	+	-	N/A	N/A	-	N/A	N/A

DAD diffuse alveolar damage, N/A not applicable.

## INSIGHTS INTO SARS-COV-2, THE CORONAVIRUS UNDERLYING COVID-19: RECENT GENOMIC DATA AND THE DEVELOPMENT OF REVERSE GENETICS SYSTEMS

Silva SJRD, Germano Mendes RP, Alves da Silva CT, Lorusso A, Kohl A, Pena L.. J Gen Virol. 2020 Jun 24. doi: 10.1099/jgv.0.001458. Online ahead of print.

Level of Evidence: Other - Mechanism-based reasoning

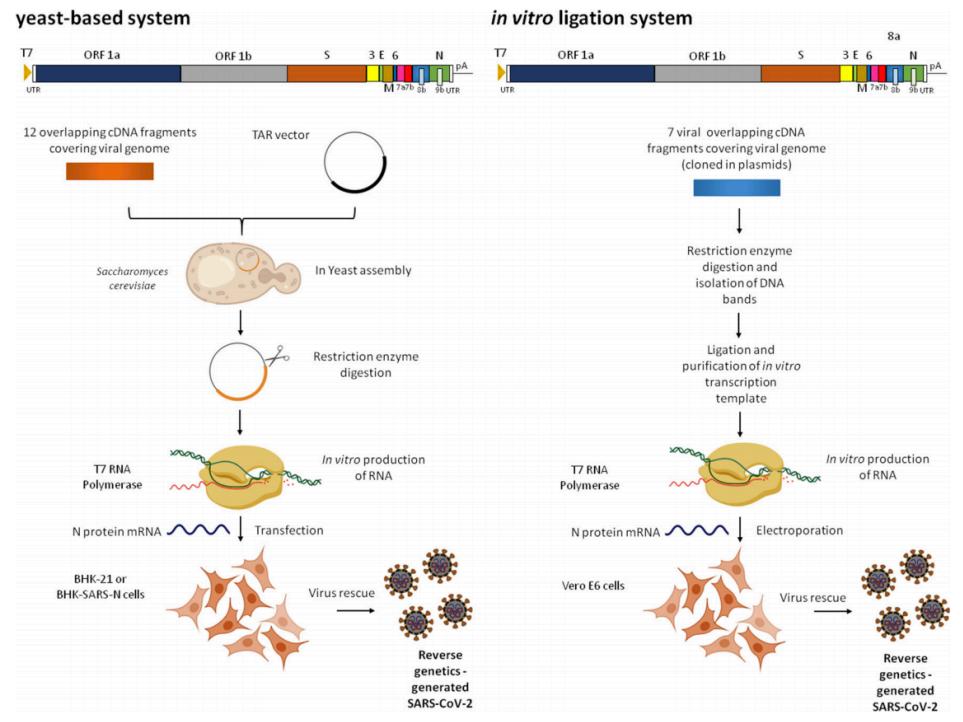
### BLUF

In this study, authors pooled various genomic analyses from over 200 SARS-CoV-2 strains. Notable findings and their roles include: D614G mutation in the S glycoprotein (transmissibility), genome termini (replication/transcription), and spike (S) protein with furin-like cleavage site (virulence). The authors promote reverse genetic systems to allow simulated manipulation of SARS-CoV-2 to elucidate viral mechanisms and potentially aid in the development of vaccines and targeted therapeutics (Figure 1).

### ABSTRACT

The emergence and rapid worldwide spread of a novel pandemic of acute respiratory disease - eventually named coronavirus disease 2019 (COVID-19) by the World Health Organization (WHO) - across the human population has raised great concerns. It prompted a mobilization around the globe to study the underlying pathogen, a close relative of severe acute respiratory syndrome coronavirus (SARS-CoV) called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Numerous genome sequences of SARS-CoV-2 are now available and in-depth analyses are advancing. These will allow detailed characterization of sequence and protein functions, including comparative studies. Care should be taken when inferring function from sequence information alone, and reverse genetics systems can be used to unequivocally identify key features. For example, the molecular markers of virulence, host range and transmissibility of SARS-CoV-2 can be compared to those of related viruses in order to shed light on the biology of this emerging pathogen. Here, we summarize some recent insights from genomic studies and strategies for reverse genetics systems to generate recombinant viruses, which will be useful to investigate viral genome properties and evolution.

## FIGURES



**Fig. 1.** Reverse genetics systems for SARS-CoV-2. Viral genome and organization are shown at the top of each panel. (a) Description of yeast-based assembly and rescue system. Twelve viral subgenomic cDNA fragments were assembled in *Saccharomyces cerevisiae* using transformation-associated recombination (TAR) cloning to maintain the genome as a yeast artificial chromosome (YAC). *In vitro*-transcribed (by T7 RNA polymerase) viral genome RNAs were electroporated into BHK-21 cells (or BHK-SARS-N) together with an mRNA encoding the SARS-CoV-2 N protein to rescue viable virus. (b) Description of *in vitro* ligation system. In this approach, seven contiguous cDNA fragments covering the entire viral genome were isolated from plasmid vectors and directionally ligated to assemble the full-length viral genome. *In vitro*-transcribed (by T7 RNA polymerase) genome RNA was transfected into Vero E6 cells along with mRNA encoding N protein to recover infectious SARS-CoV-2. A schematic representation of the SARS-CoV-2 genome organization is shown in the upper part of the panels. T7, T7 RNA polymerase promoter; UTR, untranslated region; pA, poly (A) tail. Created with Biorender.com

## TRANSMISSION & PREVENTION

### EXAMINING THE NEED FOR EYE PROTECTION FOR COVID-19 PREVENTION IN THE COMMUNITY

Marra AR, Edmond MB, Popescu SV, Perencevich EN.. Infect Control Hosp Epidemiol. 2020 Jun 24:1-6. doi: 10.1017/ice.2020.314. Online ahead of print.

Level of Evidence: Other - Expert Opinion

#### **BLUF**

This professional opinion piece indicates that since SARS-CoV-1 was presumed to be transmitted through the mucous membranes of the conjunctiva, and there is also some evidence from recent studies showing similar transmission of SARS-CoV-2 in macaques, it is likely that SARS-CoV-2 can be transmitted to humans through the eyes. They suggest that medical professionals and the public should employ face shields that guard this possible route of infection until more is known about this mechanism of disease spread in humans.

### ACE2 AND TMPRSS2 VARIATION IN SAVANNA MONKEYS (CHLOROCEBUS spp.): POTENTIAL RISK FOR ZOONOTIC/ANTHROPONOTIC TRANSMISSION OF SARS-COV-2 AND A POTENTIAL MODEL FOR FUNCTIONAL STUDIES

Schmitt CA, Bergey CM, Jasinska AJ, Ramensky V, Burt F, Svardal H, Jorgensen MJ, Freimer NB, Grobler JP, Turner TR.. PLoS One. 2020 Jun 23;15(6):e0235106. doi: 10.1371/journal.pone.0235106. eCollection 2020.

Level of Evidence: Other - Modeling

#### **BLUF**

This study analyzed genomic data from 245 savanna monkeys (*Chlorocebus* spp.) to assess functional variation in the main receptors associated with SARS-CoV-2 infectivity (ACE2 and TMPRSS2). The authors report that, except for one missense variation in ACE2 (X:14,077,550; Asp30Gly) among *Chlorocebus sabaeus* which prevents adequate binding between the receptor and its viral counterpart, the majority of variants are unlikely to significantly alter susceptibility to SARS-CoV-2 (Table 1), rendering the animals potentially susceptible to infection. The findings of this study suggest that bi-directional transfer between humans and savanna monkeys may be an important factor in controlling the COVID-19 pandemic.

#### **ABSTRACT**

The COVID-19 pandemic, caused by the coronavirus SARS-CoV-2, has devastated health infrastructure around the world. Both ACE2 (an entry receptor) and TMPRSS2 (used by the virus for spike protein priming) are key proteins to SARS-CoV-2 cell entry, enabling progression to COVID-19 in humans. Comparative genomic research into critical ACE2 binding sites, associated with the spike receptor binding domain, has suggested that African and Asian primates may also be susceptible to disease from SARS-CoV-2 infection. Savanna monkeys (*Chlorocebus* spp.) are a widespread non-human primate with well-established potential as a bi-directional zoonotic/anthroponotic agent due to high levels of human interaction throughout their range in sub-Saharan Africa and the Caribbean. To characterize potential functional variation in savanna monkey ACE2 and TMPRSS2, we inspected recently published genomic data from 245 savanna monkeys, including 163 wild monkeys from Africa and the Caribbean and 82 captive monkeys from the Vervet Research Colony (VRC). We found several missense variants. One missense variant in ACE2 (X:14,077,550; Asp30Gly), common in *Ch. sabaeus*, causes a change in amino acid residue that has been inferred to reduce binding efficiency of SARS-CoV-2, suggesting potentially reduced susceptibility. The remaining populations appear as susceptible as humans, based on these criteria for receptor usage. All missense variants observed in wild *Ch. sabaeus* populations are also present in the VRC, along with two splice acceptor variants (at X:14,065,076) not observed in the wild sample that are potentially disruptive to ACE2 function. The presence of these variants in the VRC suggests a promising model for SARS-CoV-2 infection and vaccine and therapy development. In keeping with a One Health approach, characterizing actual susceptibility and potential for bi-directional zoonotic/anthroponotic transfer in savanna monkey populations may be an important consideration for controlling COVID-19 epidemics in communities with frequent human/non-human primate interactions that, in many cases, may have limited health infrastructure.

#### **FIGURES**

Table 1. Potential functional variants in ACE2 gene region sequence among wild savanna monkeys.

Position	Variant	Consequence	AAF <sup>a</sup>	AA	Pos <sub>AA</sub>	Notes
X:14035311	T/C	Missense	0.09	I/V	753	Alt. allele prevalent in Ethiopia (AAF = 0.94); absent in all others
X:14035353*	C/T	Missense	0.33	V/I	739	Alt. allele only in <i>Ch. sabaeus</i> (AAF = 0.75–1; AAF <sub>VRC</sub> = 0.84).
X:14035354	G/A	Synonymous	0.09	P	738	Alt. allele prevalent in Ethiopia (AAF = 0.94); absent in all others
X:14035357	G/A	Synonymous	0.02	S	737	Alt. allele only found in Ethiopia (AAF = 0.16)
X:14035374*	T/C	Missense	0.97	I/V	732	Ref. allele only found in St. Kitts (AAF = 0.75; AAF <sub>VRC</sub> = 0.85).
X:14041898	T/C	Synonymous	0.13	G	629	Alt. allele only found in southern Africa (AAF = 0.36–1.00)
X:14043283	G/C	Synonymous	0.04	L	585	Alt. allele predominantly found in Central African Republic (AAF = 0.36)
X:14043289*	T/G	Synonymous	0.06	P	583	AAF <sub>VRC</sub> = 0.01
X:14043304	G/A	Synonymous	0.03	N	578	Alt. allele only found in South Africa (AAF = 0.10)
X:14043773	T/A	Intronic SRV	0.45	-	-	Fixation of minor allele in <i>Ch. sabaeus</i>
X:14043797	T/A	Missense	0.02	E/V	549	Alt. allele only found in Ethiopia (AAF = 0.19)
X:14045023*	C/G	Missense	0.62	E/D	483	Ref. allele near fixation in <i>Ch. sabaeus</i> (AAF = 0.00–0.50; AAF <sub>VRC</sub> = 0.01).
X:14049928	G/A	Synonymous	0.01	I	358	
X:14052949	A/G	Synonymous	0.18	F	315	Alt. allele only found in southern Africa (AAF = 0.22–0.52)
X:14061092	C/T	Intronic SRV	0.02	-	-	Alt. allele only present in The Gambia (AAF = 0.14)
X:14063390	A/G	Synonymous	0.02	L	266	Alt. allele only found in Ethiopia (AAF = 0.22)
X:14064963	C/T	Synonymous; SRV	0.02	E	232	Alt. allele only present in The Gambia (AAF = 0.14)
X:14065002	G/A	Synonymous	0.01	R	219	Alt. allele only present in East Africa (AAF = 0.13–0.25)
<b>X:10465076</b>	<b>C/CT CT/C</b>	<b>Splice Acceptor</b>	<b>0.08 0.34</b>	<b>-</b>	<b>-</b>	<b>Only present in the VRC, expected to be deleterious.</b>
X:14067819	T/C	Intronic SRV	0.04	-	-	Alt. allele only found in southern Africa (AAF = 0.03–0.13)
X:14077504	A/G	Synonymous	0.02	L	45	Alt. allele only present in Ethiopia (AAF = 0.25)
X:14077524*	A/G	Synonymous	0.61	L	39	Fixation of reference allele in <i>Ch. sabaeus</i> (AAF <sub>VRC</sub> = 0.01)
X:14077531	G/A	Synonymous	0.01	A	36	Alt. allele only present in Zambia (AAF = 0.06)
X:14077550*	T/C	Missense	0.13	D/G	30	Alt. allele only found in <i>Ch. sabaeus</i> (AAF = 0.01–1.00; AAF <sub>VRC</sub> = 0.36)

Emboldened, shaded text indicates coding regions or residues critical to SARS-CoV-2 binding. AAF = alternative allele frequency for the full sample. AA = change in amino acid residue predicted to accompany sequence variation. Pos<sub>AA</sub> = amino acid position in the protein. SRV = splice region variant. Asterisks (\*) = variant also present in the Vervet Research Colony at Wake Forest School of Medicine. AAF<sub>VRC</sub> = alternative allele frequency in the VRC.

<sup>a</sup>For population-specific values of AAF see S1 Table.

<https://doi.org/10.1371/journal.pone.0235106.t001>

## MANAGEMENT

### IMPROVED CLINICAL SYMPTOMS AND MORTALITY ON SEVERE/CRITICAL COVID-19 PATIENTS UTILIZING CONVALESCENT PLASMA TRANSFUSION

Xia X, Li K, Wu L, Wang Z, Zhu M, Huang B, Li J, Wang Z, Wu W, Wu M, Li W, Li L, Cai Y, Bosco B, Zhong A, Liu X, Lv T, Gan Z, Chen G, Pan Y, Liu C, Zhang K, Xu X, Wang C, Wang Q.. Blood. 2020 Jun 23:blood.2020007079. doi: 10.1182/blood.2020007079. Online ahead of print.

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

#### BLUF

This is a retrospective cohort study of severe and critical COVID-19 patients (admitted between February 4 to March 30, 2020) who either received convalescent plasma transfusions (CCP, 200-1200 mL; n=138) or standard treatment (n=1,430) at Wuhan Huoshenshan Hospital, China. Their findings (summarized below) suggest CCP has potential as a therapy for severe/critical COVID-19 patients and may assist research in monoclonal antibody development.

#### SUMMARY

Summary of findings:

- The CCP group had a lower mortality than the standard-treated group (2.2 vs 4.1%), although this finding was not statistically significant.
- A significant increase in lymphocyte percentage within 3 days of treatment ( $p=0.0009$ ) with a significant decline in neutrophil percentage when analyzing the CCP group before and after therapy.
- Among the CCP group, "responders" to treatment had a significantly lower C-reactive protein (CRP), lower neutrophil percentage prior to treatment, and higher lymphocyte percentage than "non-responders."

#### ABSTRACT

Coronavirus disease 2019 (COVID-19) is causing worldwide pandemic with no specific therapeutic agents, especially for severe or critical patients. To comprehensively evaluate the effectiveness, safety, and indications of convalescent plasma transfusion (CPT) therapy for severe or critical COVID-19 patients, we analyzed the clinical, laboratory, and radiologic characteristics of 1,568 patients from a single center, in which 138 patients received ABO-compatible CPT. The median time from the first symptom to CPT was 45 days. 2.2% and 4.1% of cases died in the CPT group and in the standard-treatment group, respectively. 2.4% and 5.1% of patients in the CPT and the standard-treatment group have been admitted to ICU eventually. 70% of the patients who had severe respiratory symptoms got improved and removed oxygen supports within 7 days after CPT. The viral loads and C-reactive protein (CRP) concentration significantly decreased ( $P<0.001$ ), and the percentage of lymphocytes increased ( $P=0.006$ ), 76.8% of cases received radiological improvements within 14 days after CPT. Patients with a higher percentage of lymphocytes and a lower percentage of neutrophils and CRP concentration respond better to CPT ( $P<0.05$ ). Notably, for the patients who received CPT within 7 weeks after symptom onset, the median time from CPT to clinical improvements was approximately 10 days. But the time to clinical improvements was significantly prolonged for patients who received CPT later than 7 weeks after onset. Our study will provide important information for the clinical practice in COVID-19 treatment, as well as provide real-world observations and clinical data for the development of monoclonal antibodies.

## FIGURES

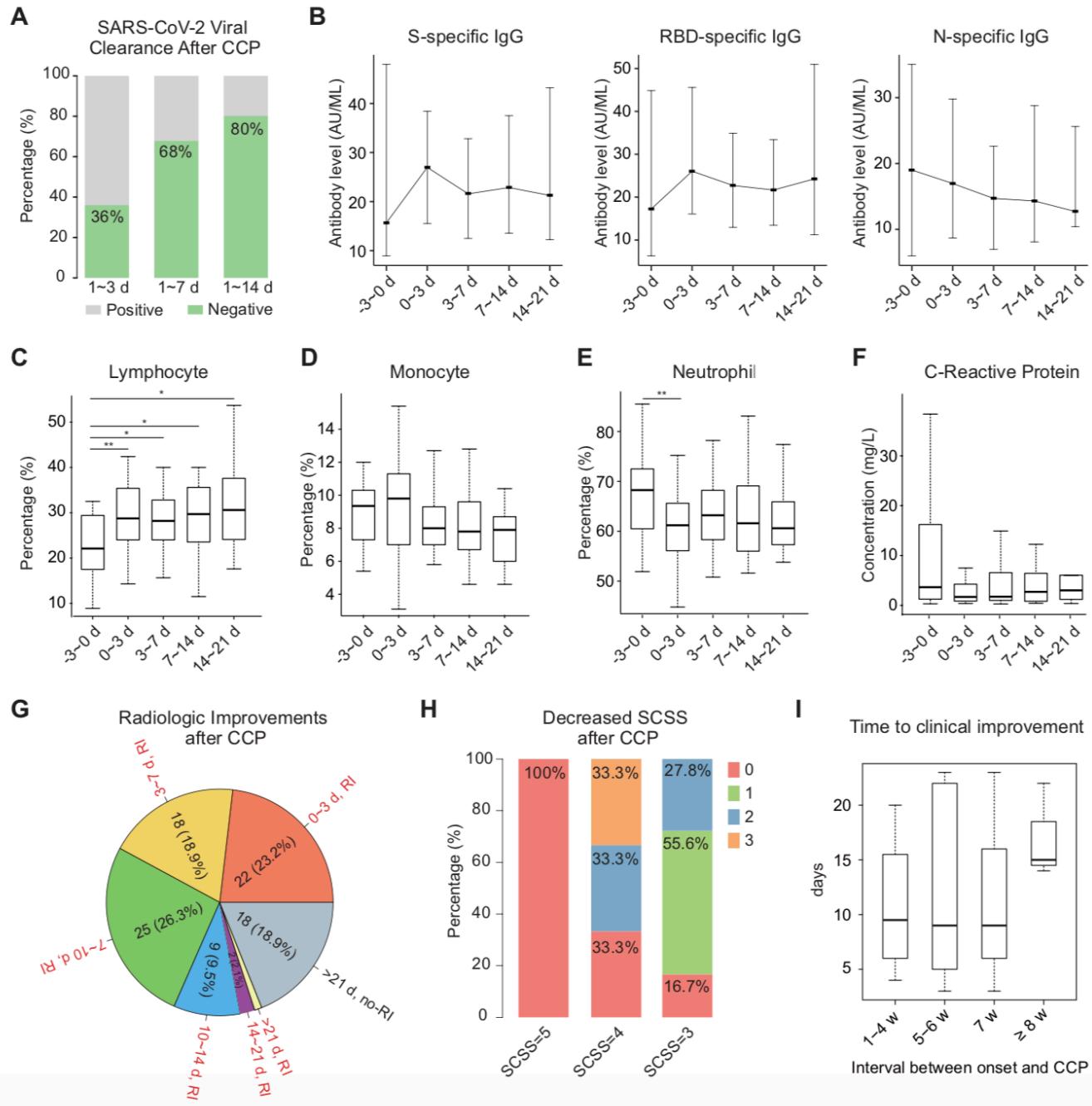


Figure 1. Laboratory, radiological, and clinical changes after COVID-19 convalescent plasma (CCP) therapy. (A) Proportion of patients who became virus-free after 1-3 days, 1-7 days, and 1-14 days of CCP therapy. (B) Dynamic changes in spike (S)-, receptor-binding domain (RBD)-, and N-specific IgG levels before and after CCP therapy. (C-E) Dynamic changes in lymphocyte, monocyte, and neutrophil percentages before and after CCP therapy. \* p < 0.05, \*\* p < 0.01. (F) Dynamic changes in CRP concentration before and after CCP therapy. (G) Number and proportion of patients with radiological improvement after 1-3 days, 3-7 days, 7-10 days, 10-14 days, and 14-21 days after CCP therapy. RI indicates radiological improvements, and no-RI indicates no radiological improvements were observed after CCP therapy. (H) Proportion of patients whose six-category scale score (SCSS) decreased within one week after CCP therapy. (I) Time to clinical improvement after CCP therapy in patients with different therapy timings. The x-axis represents the number of weeks from symptom onset to CCP therapy. The y-axis represents the number of days from CCP therapy to a 2-point decrease in SCSS. The number of patients in 1-4 weeks, 5-6 weeks, 7 weeks, and ≥8 weeks.

## PREDICTION OF THE REHABILITATION DURATION AND RISK MANAGEMENT FOR MILD-MODERATE COVID-19

Zheng QN, Xu MY, Zheng YL, Wang XY, Zhao H.. Disaster Med Public Health Prep. 2020 Jun 24:1-27. doi: 10.1017/dmp.2020.214. Online ahead of print.

Level of Evidence: 3 - Cohort study or control arm of randomized trial

### BLUF

This retrospective study analyzed 90 patients from the Affiliated Yueqing Hospital, Wenzhou Medical University from January to February 2020 to develop a predictive model for rehabilitation time for mild-moderate COVID-19 cases. Of the 5 significant clinical predictors (Table 2), increased partial pressure of carbon dioxide and decreased serum potassium correlated with increased rehabilitation duration. When the authors sub-stratified their patient group as a mild-moderate risk using a 3-tiered risk system, they predicted a rehabilitation time of  $17.2 \pm 5.2$  days and suggest that their predictive tool may be used for personalized risk management.

### ABSTRACT

**BACKGROUND:** More than 80% COVID-19 cases are mild or moderate. In this study, a risk model was developed for predicting rehabilitation duration of the mild-moderate COVID-19 cases, thereby conducting refined risk management for different risk population.

**METHODS:** 90 consecutive mild-moderate COVID-19 cases were enrolled. Large-scale datasets were extracted from clinical practices. Through the multivariable linear regression analysis, the model was based on significant risk factors and was developed for predicting the rehabilitation duration of mild-moderate COVID-19. According to the local epidemic situation, risk management was conducted by weighing the risk assessment for different risk populations.

**RESULTS:** Ten risk factors from 44 high-dimensional clinical datasets were significantly correlated to rehabilitation duration ( $P < 0.05$ ). Among these, five risk predictors were incorporated into a risk model. Individual rehabilitation durations were effectively calculated. Weighing the local epidemic situation, threshold probability was classified for low risk, intermediate risk, and high risk. According to this classification, risk management was based on a treatment flowchart for tailored clinical decisions-making.

**CONCLUSIONS:** The proposed model is a useful tool for the individualized risk management of mild-moderate COVID-19 cases for the first time, and it may readily facilitate dynamic clinical decision-making for different risk populations.

### FIGURES

Table 2 Multiple linear regression analysis of predictors parameters with respect

	to rehabilitation duration				
	df	SS	MS	F	p
Regression	5	968.156	193.631	11.055	< 0.001
Residual	84	1471.335	17.516		
Total	89	2439.491			

Multiple Linear Regression					
	Coefficient	Std. Error	Beta	95% CI	P
Constant	-21.696	7.198		-36.010 – -7.382	0.003
WBC	0.908	0.277	0.297	0.358 – 1.458	0.001
PaCO <sub>2</sub>	0.428	0.120	0.312	0.189 – 0.667	0.001
K	4.209	1.014	0.372	2.192 – 6.226	< 0.001
TBIL	0.251	0.082	0.282	0.087 – 0.415	0.005
AST	-0.086	0.036	-0.217	-0.157 – -0.015	0.018

Table 2. Multiple linear regression analysis of predictors parameters with respect to rehabilitation duration

Note: R<sup>2</sup> = 0.397; Adjusted R<sup>2</sup> = 0.361.

Abbreviations: df: degrees of freedom; SS: sum of squares; MS: mean squares; CI: confidence interval; WBC: white blood cell; PaCO<sub>2</sub>: partial pressure of carbon dioxide in artery; K: serum potassium; TBIL: total serum bilirubin; AST: aspartate aminotransaminase.

## HETEROGENEITY OF ACUTE RESPIRATORY DISTRESS SYNDROME IN COVID-19: "TYPICAL" OR NOT?

Maley JH, Winkler T, Hardin CC.. Am J Respir Crit Care Med. 2020 Jun 24. doi: 10.1164/rccm.202004-1106LE. Online ahead of print.

Level of Evidence: Other - Expert Opinion

### BLUF

Authors from Massachusetts General Hospital critique Gattinoni et. al. paper 'Covid-19 Does Not Lead to a "Typical" Acute Respiratory Distress Syndrome [ARDS]," specifically noting the following: a small and heterogeneous sample size, not using respiratory compliance to determine prone positioning eligibility, and the potential of COVID-19 disease to progress to ARDS following mechanical ventilation. The authors suggest that low tidal volume ventilation and prone positioning, which were not supported in the Gattinoni et. al. paper, are the best evidence-based care recommendations for ARDS, typical or not.

## CRITICAL CARE

### MECHANICS OF BREATHING AND GAS EXCHANGE IN MECHANICALLY VENTILATED PATIENTS WITH COVID-19 ASSOCIATED RESPIRATORY FAILURE

Haouzi P, Zamir A, Villarreal-Fernandez E, Stauffer D, Ventola L, Ahmad D, Dewaters A, Khalid M, Wojnar M.. Am J Respir Crit Care Med. 2020 Jun 24. doi: 10.1164/rccm.202004-1041LE. Online ahead of print.

Level of Evidence: 4 – Case Series

### BLUF

In a critical analysis of three recently published case series with conflicting data on mechanically ventilated COVID-19 patients (Figure 1), Pennsylvania State University researchers found that:

1. Low respiratory system compliance (Crs) may be associated with a higher gradient of arterial partial pressures of oxygen to alveolar partial pressures of oxygen (PaO<sub>2</sub>-PAO<sub>2</sub>) in COVID-19 respiratory failure,
2. Positive end-expiratory pressure (PEEP) levels should be selected by measuring Crs to compensate for lack of lung compliance while minimizing risk, and
3. Increasing tidal volume can reduce both serial dead space ventilation and parallel dead space ventilation.

The authors suggest that clinicians focus on individual patient's needs when operating respirators given the heterogeneity in presentations of COVID-19 respiratory failure.

### FIGURES

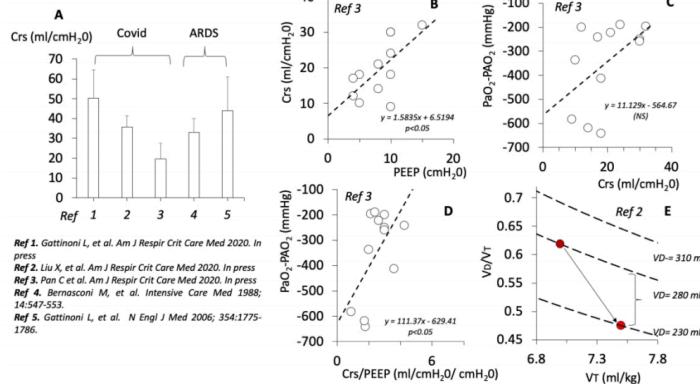


Figure 1. A: Values of Crs collected in mechanically ventilated COVID-19 patients compared to data reported in acute respiratory distress syndrome (ARDS) (the references of the selected studies are given in the figure). Although data were not obtained at the same time of the disease, alterations of the elastic properties of the respiratory system can be significant in all these patients and are not dramatically different between COVID and ARDS patients. B: Relationship between PEEP and Crs, showing that when low levels of PEEP were used, low Crs were always present. C: Crs vs PAO<sub>2</sub>-PaO<sub>2</sub> gradient. Extreme deterioration of PAO<sub>2</sub>-PaO<sub>2</sub> gradient was observed in many patients; yet, the patients with the lowest Crs have the greatest gradient, the correlation remains weak in this limited population. D: relationship between Crs/PEEP ratio vs PAO<sub>2</sub>-PaO<sub>2</sub> gradient, the ratio was used as an indicator of the effects of PEEP applied at any given Crs. The patients with the lowest ratio had the highest gradient with a significant correlation between the two variables. E: IsoVD (dead space ventilation) curves showing the relationship between VT (tidal volume) and VD/VT ratio. By minimally increasing VT, the change in VD/VT ratio and thus in alveolar gas composition improves out of proportion of the changes in serial dead space.

## MEDICAL SUBSPECIALTIES

### CARDIOLOGY

#### SPONTANEOUS CORONARY ARTERY DISSECTION IN A PATIENT WITH COVID-19

32553344. Spontaneous Coronary Artery Dissection in a Patient With COVID-19

Level of Evidence: Other - Case Report

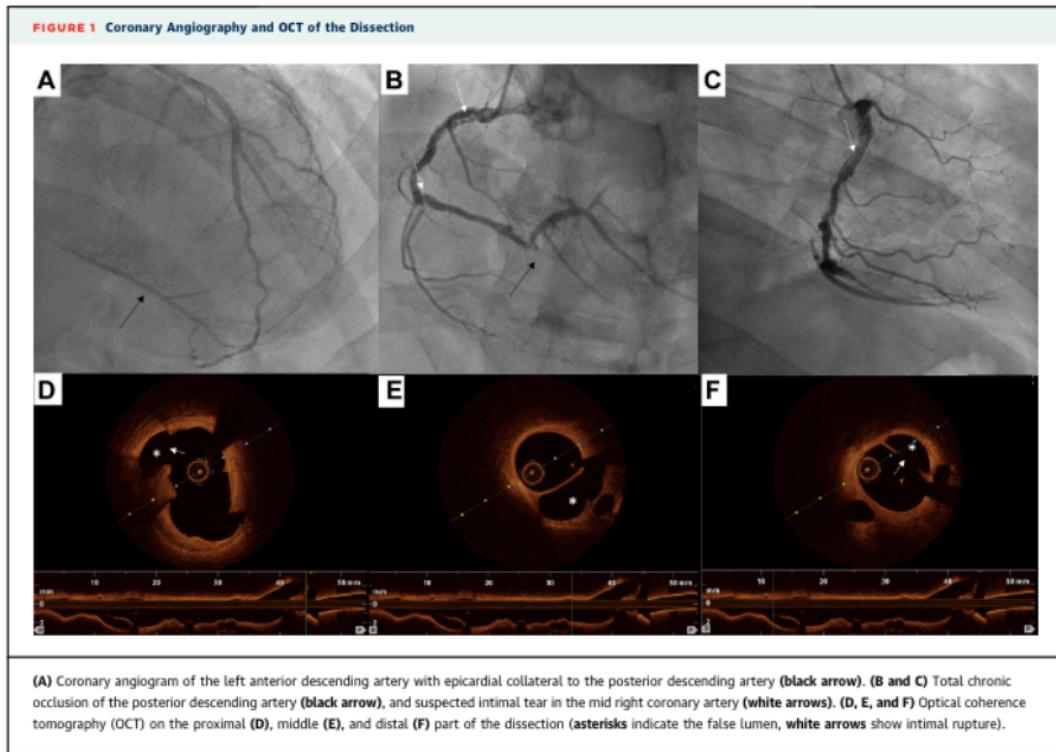
#### BLUF

In this case report from Lyon, France, a 55-year-old male presented with fever, cough, dyspnea, and was subsequently confirmed to have COVID-19; he then developed chest pain, and was found to have a spontaneous coronary artery dissection. This was the first case report of an acute coronary dissection in the setting of COVID-19 infection, and suggests further investigation into the mechanisms of COVID-19 and acute coronary syndrome.

#### SUMMARY

A 55-year-old male with history of peripheral artery disease presented to a hospital in Lyon, France with fever, cough and dyspnea. COVID-19 suspicion was confirmed by PCR, and he was admitted for treatment; 48 hours later, he developed chest pain. Subsequent workup revealed EKG with inferior T-wave inversions and grossly normal echocardiogram. He was then taken to cardiac catheterization lab where he was found to have a chronic total occlusion of the posterior descending artery filled by collaterals of the LAD (Figure 1A) and a spontaneous dissection in the mid right coronary artery (Figure 1B and 1C), which was then confirmed by optical coherence tomography (Figure 1D-F). It was decided to treat the patient conservatively with medical therapy of aspirin, statin, and a beta blocker, with a plan to repeat angiogram in the future. Previous viral outbreaks have been known to trigger acute coronary syndrome, and this case represents the first COVID-19 positive patient with a concurrent spontaneous coronary artery dissection. Further investigation is needed to determine if dissections in the setting of associated COVID-19 infections are from a systemic inflammatory process and general inflammation, or direct damage from the virus.

## FIGURES



## HEMATOLOGY AND ONCOLOGY

### CONSIDERATION IN THE MANAGEMENT OF RENAL CELL CARCINOMA DURING THE COVID-19 PANDEMIC

Zequi SC, Abreu D.. Int Braz J Urol. 2020 Jun 17;46. doi: 10.1590/S1677-5538.IBJU.2020.S108. Online ahead of print.  
Level of Evidence: Other - Review / Literature Review

#### BLUF

A review of literature through April 30, 2020 by urologists in São Paulo, Brasil provides risk-based recommendations for patients with renal cell cancer during the COVID-19 pandemic (Table 1) and analyzes data of COVID-19 infection risk with systemic therapy. Results suggest there is no current evidence to support withholding chemotherapy or immunotherapy for non-infected patients.

#### SUMMARY

Risk-based renal cell carcinoma management recommendations are summarized in Table 1. Per the authors, current evidence of increased COVID-19 risk in cancer patients is limited and inconclusive. Additionally, it is unknown how systemic treatment of renal cancer such as tyrosine kinase inhibitors (TKI) or immune checkpoint inhibitors (ICI) affects risks of COVID-19 infection. The two main concerns are the potential for overlap of coronavirus intersstitial pneumonia with pulmonary toxicity of anti-PD-1/PD-L1 agents or a synergistic immune hyper-reactivation. However, at this time, there is no evidence to support withholding chemotherapy or immunotherapy. The authors make the following recommendations:

1. Discussion between patient and doctor of pros and cons for delaying systemic treatment due to COVID-19 risks.
2. Patients undergoing systemic treatment should be extra cautious to avoid COVID-19 infection.
3. Less frequent dosing intervals may be reasonable if indicated.

#### ABSTRACT

**INTRODUCTION:** Recently the COVID-19 pandemic became the main global priority; main efforts and health infrastructures have been prioritized in favor of COVID-19 battle and the treatment of benign diseases has been postponed. Renal cell cancer

(RCC) patients configure a heterogenous populations: some of them present indolent cases which can safely have postponed their treatments, others present aggressive tumors, deserving immediate care. These scenarios must be properly identified before a tailored therapeutic choice.

**OBJECTIVES:** We propose a risk- based approach for patients with RCC, to be used during this unprecedented viral infection time.

**MATERIALS AND METHODS:** After a literature review focused in COVID-19 and current RCC treatments, we suggest therapeutic strategies of RCC in two sections: surgical approach and systemic therapy, in all stages of this malignancy.

**RESULTS:** Patients with cT1a tumors (and complex cysts, Bosniak III/IV), must be put under active surveillance and delayed intervention. cT1b-T2a/b cases must be managed by partial or radical nephrectomy, some selected T1b-T2a ( $\leq 7\text{cm}$ ) cases can have the surgery postponed by 60-90 days). Locally advanced tumors ( $\geq \text{cT3}$  and or N+) must be promptly resected. As possible, minimally invasive surgery and early hospital discharge are encouraged. Upfront cytoreduction, is not recommendable for low risk oligometastatic patients, which must start systemic treatment or even could be put under surveillance and delayed therapy. Intermediate and poor risk metastatic patients must start target therapy and/or immunotherapy (few good responders intermediate cases can have postponed cytoreduction). The recommendation about hereditary RCC syndromes are lacking, thus we recommend its usual care. Local or loco regional recurrence must have individualized approaches. For all cases, we suggest the application of a specific informed consent and a shared therapeutic choice.

**CONCLUSION:** In the pandemic COVID -19 times, a tailored risk-based approach must be used for a safe management of RCC, aiming to not compromise the oncological outcomes of the patients.

## FIGURES

Stage/clinical presentation	Suggestion (s)	Alternative(s)
cT1aNOMO ( $<4.0\text{cm}$ ) and complex renal cysts (Bosniak III/IV)	Active Surveillance and postponed Surgery <sup>Ψ</sup>	Thermal ablation <i>Obs.:</i> For patients refractory or unavailable for surveillance.
cT1b-T2 NOMO	Surgery <sup>Ψ</sup>	Surveillance and delayed surgery <sup>Ψ</sup> (only for selected cT1b and cT2a $< 7.0\text{ cm}$ ) <i>Obs.:</i> CT* ou MRI* after 90 days in recommendable) <i>Obs.:</i> A renal biopsy could be discussed before decision between surgery or surveillance.
$\geq \text{cT3}$ and or N+, venous thrombus	Upfront Surgery <sup>Ψ</sup>	Individualized discussion or tumor board discussion
Low Risk Metastatic	Systemic Therapy (TKI or TKI+ICI) and postponed cytoreduction <sup>Ψ</sup>	Active surveillance for selected cases
Intermediate and poor Risk Metastatic	Systemic Therapy (ICI+ICIC, or ICI+ TKI)	Alternative drugs doses or scheduling intervals between applications. For selected intermediate risks patients with satisfactory response after systemic therapy delayed cytoreduction <sup>Ψ</sup> can be discussed.
<b>Special conditions</b>		
Local Recurrences (small asymptomatic lesion)	Surveillance	Thermal ablation
Local Recurrences (symptomatic or locally invasive lesion)	Wide surgery <sup>Ψ</sup>	Systemic Therapy and delayed postponed surgery. Individualized discussion or tumor board
Hereditary RCC	Follow usual guidelines (surgery <sup>Ψ</sup> if $>3.0\text{ cm}$ , except for HLRCC syndrome (prompt resection))	Individualized discussion or tumor board discussion

\*CT-Computerized Tomography; \*\* MR -Magnetic Resonance

Table 1. Summarized risk-based suggested approaches ( and alternative options) for renal cell carcinoma during the COVID-19 pandemic.

# ADJUSTING PRACTICE DURING COVID-19

## GASTROENTEROLOGY

### RECOMMENDATIONS FOR THE OPERATION OF ENDOSCOPY CENTERS IN THE SETTING OF THE COVID19 PANDEMIC - A WEO GUIDANCE DOCUMENT

Guda NM, Emura F, Reddy DN, Rey JF, Seo DW, Gyokeres T, Tajiri H, Faigel D.. Dig Endosc. 2020 Jun 22. doi: 10.1111/den.13777. Online ahead of print.

Level of Evidence: Other - Guidelines and Recommendations

#### BLUF

An international group of physicians affiliated with the World Endoscopy Organization provide guidance on the safe operation of endoscopy centers during the COVID-19 pandemic. These guidelines may help endoscopy centers continue to provide appropriate services during the different phases of the COVID-19 pandemic.

#### SUMMARY

The specific recommendations include:

- During a peak or resurgence phase of COVID-19, avoid routine procedures (Table 1).
- Complete urgent and emergent procedures while making sure to screen patients for COVID-19 and to test those with symptoms by rapid RT-PCR tests.
- Perform endoscopy on high-risk or infected patients in a negative pressure room in a hospital setting with all providers in full, appropriate PPE to avoid transmission.
- Perform endoscopy on low-risk or asymptomatic patients with standard PPE and respirator masks if available.
- After the peak or resurgence phase is over, open endoscopy services two weeks after no surge in cases is noted and do so according to local regulations. During re-opening, adequately prepare facilities and personnel and have appropriate PPE available.

#### ABSTRACT

SARS-CoV-2 (Severe Acute Respiratory Syndrome Corona Virus 2) is the etiologic agent causing the disease COVID-19(Corona Virus Disease 19), resulting in a worldwide pandemic. Non emergent endoscopy services have been disrupted as incidence and hospitalizations were rising. It is anticipated that the peak incidence may be leveling off in many parts of the world, but there is a concern for resurgence of the virus activity. Thus, it is important for endoscopy units to have plans in place during peak times of the epidemic and when resuming endoscopic services as the pandemic wanes. The global endoscopy community is faced with the challenge of providing care during this time. The WEO-COVID guidance task force has provided this resource document based on the current evidence and consensus opinion. These WEO recommendations are meant to guide endoscopists worldwide, should be interpreted in light of specific clinical conditions and resource availability and may not apply in all situations. This guidance document does not supersede the need to check for all local regulations and legislations.

## FIGURES

Procedures to be done	Informed decision	Procedures to be delayed
Upper and lower GI bleeding - Symptomatic	HGD/CiS -esophagus/stomach	Screening and Surveillance colonoscopy (asymptomatic)
Dysphagia – Foreign body/malignancy	Large colon polyps with dysplasia- delay may result in inoperability	Screening, Surveillance (post bleed) of esophageal varices
Cholangitis or suspected cholangitis	Enteral nutrition	EGD for non-alarm symptoms
Symptomatic pancreaticobiliary disease – drainage procedures	Closure of fistula/leakage	pH and motility procedures
<b>Palliative procedure for luminal obstruction</b>	Dysphagia/dyspepsia without alarm symptoms	EUS for evaluation of low/intermediate risk cyst surveillance
Patients with a time-sensitive diagnosis – endoscopy effects treatment change - malignant/premalignant/IBD	Stable GI bleed/anemia	Bariatric procedures
	Non urgent evaluation of radiological abnormalities/tissue acquisition	Screening or surveillance for Barrett's esophagus
		Gastric cancer screening (no symptoms)

Table 1. Prioritization of endoscopic procedures during peak pandemic prevalence. HGD = high grade dysplasia. CiS = carcinoma in situ.

## R&D: DIAGNOSIS & TREATMENTS

### A SUGAR-COATED STRATEGY TO TREAT A RARE NEUROLOGIC DISEASE PROVIDES A BLUEPRINT FOR A DECOY GLYCAN THERAPEUTIC AND A POTENTIAL VACCINE FOR COVID-19: AN EDITORIAL HIGHLIGHT FOR "SELECTIVE INHIBITION OF ANTI-MAG IgM AUTOANTIBODY BINDING TO MYELIN BY AN ANTIGEN SPECIFIC GLYCOPOLYMER" ON [HTTPS://DOI.ORG/10.1111/JNC.15021](https://doi.org/10.1111/jnc.15021)

Steinman L.. J Neurochem. 2020 Jun 23. doi: 10.1111/jnc.15098. Online ahead of print.

Level of Evidence: Other - Mechanism-based reasoning

#### BLUF

A pediatric neurologist at Stanford University highlights a study recently published in the Journal of Neurochemistry, wherein researchers constructed a decoy glycopolymers to block and remove IgM autoantibodies against a myelin-associated glycoprotein in a mouse model for IgM monoclonal gammopathy, a rare autoimmune demyelinating neuropathy. They propose that similar strategies could be utilized to develop decoy carbohydrates that mimic the glycans associated with the spike protein of SARS-CoV-2, which could potentially block the virus from binding to the angiotensin converting enzyme-2 (ACE-2) receptor and provide a basis for a polysaccharide-based vaccine (Figure 1).

#### ABSTRACT

In a rare neurologic disease known as IgM monoclonal gammopathy the immune system targets a sulfated trisaccharide known as the Human Natural Killer-1 (HNK-1) epitope that comprises a constituent of the myelin sheath known as MAG (myelin-associated glycoprotein). This Editorial highlights a study by Aliu and colleagues in the current issue of the Journal of Neurochemistry, in which the investigators constructed a biodegradable poly-l-lysine backbone with multiple copies of this sulfated HNK-1 trisaccharide. This decoy, poly(phenyl disodium 3-O-sulfo-beta-d-glucopyranuronate)-(1 3)-beta-d-galactopyranoside, known as PPSGG, removed anti-MAG IgM autoantibodies from the blood, while not activating the immune system. These findings provide a path for the selective removal of a pathogenic set of antibodies that target the myelin sheath resulting in neuropathy. These findings are applicable to a parallel strategy for the generation of polysaccharides similar to those present in the receptor-binding domain of CoViD-19, which might inhibit viral adhesion to its receptor, the angiotensin-converting enzyme-2 (ACE2) protein, thereby impairing cellular uptake of the virus itself. The deployment of complex polysaccharides that mimic actual COVID19 polysaccharides on the spike protein may also provide a feasible structural basis for a vaccine. Carbohydrate mimics, if conjugated to a carrier or backbone, might provoke an immune response to the spike protein. A vaccine that targets critical carbohydrates on COVID19, and then neutralizes the virus would recapitulate a successful strategy employed in other microbial vaccines, like the pneumococcal vaccines and the meningococcal vaccines. These vaccines direct an immune response to complex carbohydrates and successfully prevent life-threatening disease. This paper provides lessons from a rare neurologic disease that may teach us strategies applicable to a global pandemic.

#### FIGURES

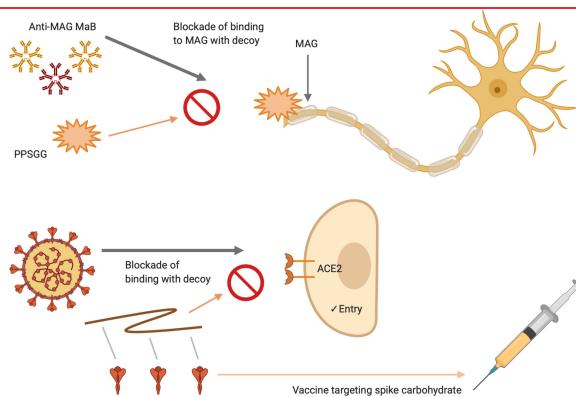


Figure 1. The strategy employed by Aliu et al. provides a basis for a passive immune therapy with a decoy carbohydrate preventing the virus from docking on its receptor, and also provides a foundation for a carbohydrate-based active immunization when coupled to a suitable carrier.

## CURRENT DIAGNOSTICS

### COVID-19 MOLECULAR TESTING IN KOREA: PRACTICAL ESSENTIALS AND ANSWERS FROM EXPERTS BASED ON EXPERIENCES OF EMERGENCY USE AUTHORIZATION ASSAYS

Sung H, Roh KH, Hong KH, Seong MW, Ryoo N, Kim HS, Lee J, Kim SY, Yoo S, Kim MN, Han MG, Lee SW, Lee H, Yoo CK.. Ann Lab Med. 2020 Nov;40(6):439-447. doi: 10.3343/alm.2020.40.6.439. Epub 2020 Nov 1.

Level of Evidence: Other - Guidelines and Recommendations

#### BLUF

These guidelines (summarized below) from the Korea Centers for Disease Control and Prevention COVID-19 Diagnosis Test Management Committee are a supplement to the "Guidelines for Laboratory Diagnosis of COVID-19 in Korea." They provide technical support for common laboratory challenges in COVID-19 diagnostics.

#### SUMMARY

Practical and Technical Supplementary Guidelines to "Guidelines for Laboratory Diagnosis of COVID-19 in Korea:"

1. Both upper respiratory and lower respiratory tract samples should be collected, in the same universal transport medium (UTM). If only one sample can be accessed, nasopharyngeal sample is preferred.
2. Available flocked swabs in Korea can be seen in Figure 1.
3. For sputum samples, it is recommended that 500ul sputum is mixed in a 1:1 ratio with PBS or UTM and glass beads. After sufficient vortexing and centrifugation, supernatant can be used for nucleic acid extraction.
4. When validating extraction methods, the QIAamp Viral RNA Mini Kit should be used as a gold standard.
5. The six approved RT-PCR assays for COVID-19 diagnosis can be found in Table 2.
6. "To change or add EUA [emergency use authorization] assays, parallel tests using at least 10 positive and 10 negative samples should be performed, and the results should be reviewed by the person in charge of the laboratory."
7. For assays that involve an internal, positive control in each sample, if internal control is not detected, retesting is recommended. If there is not enough sample for re-extraction, a 10-fold dilution of the RNA can be used.
8. Increasing input RNA for increased testing sensitivity is not recommended.
9. If upper and lower respiratory tract samples reveal conflicting results, tests can be considered positive, as long as positive testing criteria are met.
10. For newly diagnosed patients, E-positive/RdRp-negative test results should be re-run for the possibility of contamination.
11. Amplification signal in the negative control may be due to workspace contamination, nonspecific amplification, or probe instability.
12. Manufacturer-provided Ct values should be used with caution.
13. Follow-up testing should be reported as "positive" if all tested genes are detectable, "indeterminate" if more than one but not all genes are detectable, and "negative" only if all clinical symptoms are gone and there have been two consecutive tests with no detectable genes.

#### ABSTRACT

Coronavirus disease 2019 (COVID-19) is a respiratory disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Early detection of COVID-19 and immediate isolation of infected patients from the naive population are important to prevent further pandemic spread of the infection. Real-time reverse transcription (RT)-PCR to detect SARS-CoV-2 RNA is currently the most reliable diagnostic method for confirming COVID-19 worldwide. Guidelines for clinical laboratories on the COVID-19 diagnosis have been recently published by Korean Society for Laboratory Medicine and the Korea Centers for Disease Control and Prevention. However, these formal guidelines do not address common practical laboratory issues related to COVID-19 real-time RT-PCR testing and their solutions. Therefore, this guideline is intended as a practical and technical supplement to the "Guidelines for Laboratory Diagnosis of COVID-19 in Korea".

## FIGURES

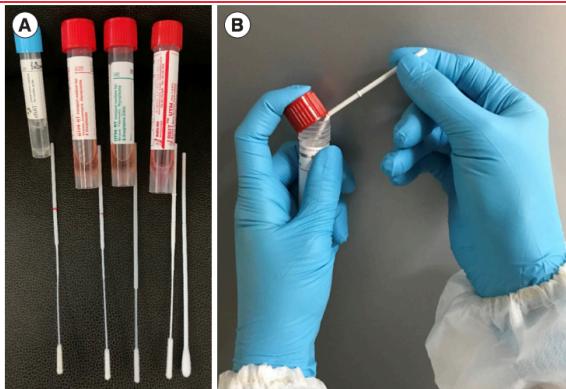


Figure 1. Swab products available in Korea and how to use them. (A) Commercial flocked swabs and universal transport media (UTM). eNAT and FLOQSwab (Copán, Brescia, Italy), UTM and FLOQSwab (Copán), UTM (Copán) and HydraFlocked (Diagnostic Hybrids, Athens, OH, USA), and REST UTM and NFS-Swab Applicator (Noble Bio, Hwaseong, Korea) (left to right). (B) Breaking swab shaft between lid and upper rim of UTM. Abbreviation: UTM, universal transport medium.

EUA assay	Target gene	Tubes/sample	RNA/each tube ( $\mu$ L)	IC	IC addition to	Instrument used	Indicating COVID-19
PowerChek 2019-nCoV (Kogenebiotech, Seoul, Korea)	<i>E, RdRp</i>	2	5	Recombinant plasmid DNA	PCR mixture	Applied Biosystems 7500 FAST and 7500 Real-Time PCR System (Thermo Fisher Scientific, Waltham, MA, USA), CFX96 Real-Time Detection System (Bio-Rad, Hercules, CA, USA)*	<i>E Ct</i> $\leq$ 35 and <i>RdRp Ct</i> $\leq$ 35
Allplex 2019-nCoV (Seegene, Seoul, Korea)	<i>E, RdRp, N</i>	1	8	Bacteriophage	Sample	CFX96 Real-Time Detection System	<i>E Ct</i> $\leq$ 40, <i>RdRp Ct</i> $\leq$ 40, and <i>N Ct</i> $\leq$ 40
Standard M nCoV Real-Time Detection (SD Biosensors, Suwon, Korea)	<i>E, ORF1ab (RdRp)</i>	1	10	Lentivirus	PCR mixture (0.5 $\mu$ L) or sample (5 $\mu$ L)	Applied Biosystems 7500 FAST and 7500 Real-Time PCR System, CFX96 Real-Time Detection System†	<i>E Ct</i> $\leq$ 36 and <i>ORF1ab Ct</i> $\leq$ 36
DiaPlexQ 2019-nCoV (Solgent, Daejeon, Korea)	<i>N, ORF1a</i>	1	5	Rice phosphoglycerate kinase gene, mRNA	PCR mixture	Applied Biosystems 7500 FAST and 7500 Real-Time PCR System, CFX96 Real-Time Detection System	<i>N Ct</i> $\leq$ 40 or <i>ORF1a Ct</i> $\leq$ 40
Real-Q 2019-nCoV (BioSewoom, Seoul, Korea)	<i>E, RdRp</i>	1	5	Human <i>RNase P</i> gene (intrinsic)	-	Applied Biosystems 7500 FAST and 7500 Real-Time PCR System, CFX96 Real-Time Detection System	<i>E Ct</i> $<$ 38 and <i>RdRp Ct</i> $<$ 38
BioCore 2019-nCoV Real Time PCR (BioCore, Seoul, Korea)	<i>N, RdRp</i>	1	5	Human <i><math>\beta</math>-globin</i> gene (intrinsic)	-	Applied Biosystems 7500 FAST and 7500 Real-Time PCR System, CFX96 Real-Time Detection System‡	<i>N Ct</i> $\leq$ 40 and <i>RdRp Ct</i> $\leq$ 40

Table 2. The characteristics of six EUA real-time RT-PCR assays for COVID-19 diagnosis

This table was modified from Table 1 by Hong, et al. [3] with permission from Annals of Laboratory Medicine. Manufacturer claimed \*Gentier 96E Real-Time PCR System (Tianlong Science & Technology, Xi'an, China), † LightCycler 480 Instrument (Roche, Pleasanton, CA, USA), and ‡ SLAN 96P Real Time PCR System (Sansure Biotech, Hunan, China) can be used.

Abbreviations: IC, internal control; Ct, cycle threshold.

## DEVELOPMENTS IN DIAGNOSTICS

### ULTRA-SENSITIVE AND HIGH-THROUGHPUT CRISPR-P OWERED COVID-19 DIAGNOSIS

32553350. Ultra-sensitive and high-throughput CRISPR-powered COVID-19 diagnosis

Level of Evidence: 3 - Non-consecutive studies, or studies without consistently applied reference standards

#### BLUF

A cross-sectional study conducted by Tulane University School of Medicine collected 29 nasal swab samples between 1 April and 10 April 2020 and found that COVID-19 could be diagnosed within 50 minutes via a COVID-19 CRISPR fluorescent

detection system (FDS) with 100% sensitivity and 71.4% specificity when compared to results obtained by a state testing laboratory via reverse transcriptase (RT)-PCR of the same samples (Figure 3). Overall, these findings suggest the CRISPR-FDS assay may be easier and faster to use than RT-PCR, though additional studies are needed to assess its overall reliability.

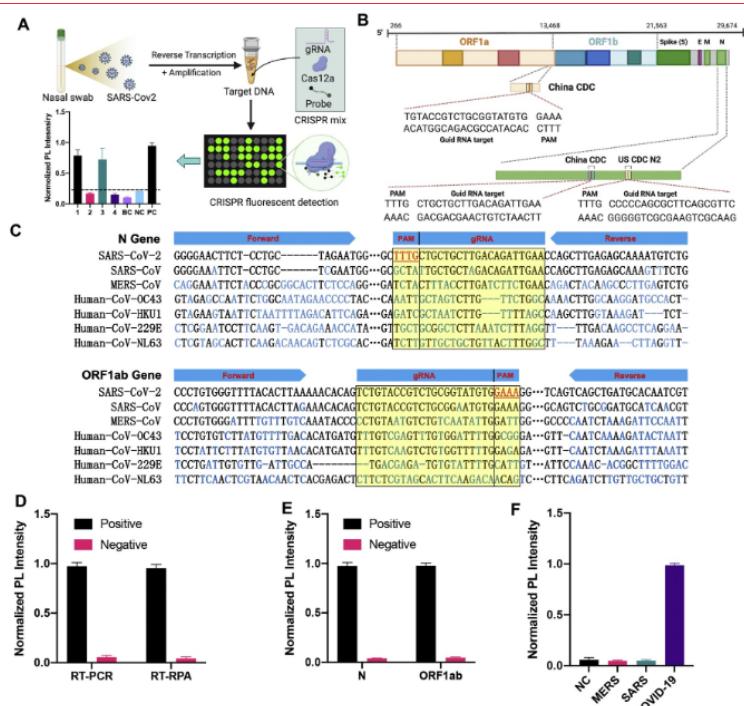
## SUMMARY

A cross-sectional study conducted in New Orleans, Louisiana by Tulane University School of Medicine collected 29 nasal swab samples from 1 April to 10 April 2020 and found that COVID-19 could be diagnosed within 50 minutes via a COVID-19 CRISPR fluorescent detection system (FDS) with 100% sensitivity and 71.4% specificity when compared to results obtained by a state testing laboratory via reverse transcriptase (RT)-PCR of the same samples (Figure 3). The authors emphasize that it is unclear whether the samples noted as positive by the CRISPR-FDS assay but not the RT-PCR method represent false positives, or are true positives missed by the latter test. Overall, these findings suggest that the CRISPR-FDS assay may be more efficient and easier to use than RT-PCR in terms of required equipment and expertise, though additional studies are needed to assess its overall reliability and scalability.

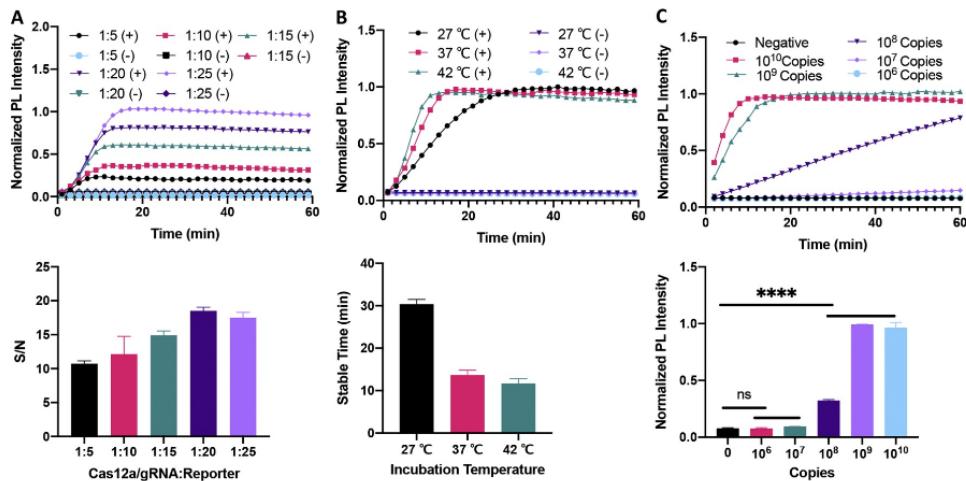
## ABSTRACT

Recent research suggests that SARS-CoV-2-infected individuals can be highly infectious while asymptomatic or pre-symptomatic, and that an infected person may infect 5.6 other individuals on average. This situation highlights the need for rapid, sensitive SARS-CoV-2 diagnostic assays capable of high-throughput operation that can preferably utilize existing equipment to facilitate broad, large-scale screening efforts. We have developed a CRISPR-based assay that can meet all these criteria. This assay utilizes a custom CRISPR Cas12a/gRNA complex and a fluorescent probe to detect target amplicons produced by standard RT-PCR or isothermal recombinase polymerase amplification (RPA), to allow sensitive detection at sites not equipped with real-time PCR systems required for qPCR diagnostics. We found this approach allowed sensitive and robust detection of SARS-CoV-2 positive samples, with a sample-to-answer time of ~50 min, and a limit of detection of 2 copies per sample. CRISPR assay diagnostic results obtained nasal swab samples of individuals with suspected COVID-19 cases were comparable to paired results from a CDC-approved quantitative RT-PCR (RT-qPCR) assay performed in a state testing lab, and superior to those produced by same assay in a clinical lab, where the RT-qPCR assay exhibited multiple invalid or inconclusive results. Our assay also demonstrated greater analytical sensitivity and more robust diagnostic performance than other recently reported CRISPR-based assays. Based on these findings, we believe that a CRISPR-based fluorescent application has potential to improve current COVID-19 screening efforts.

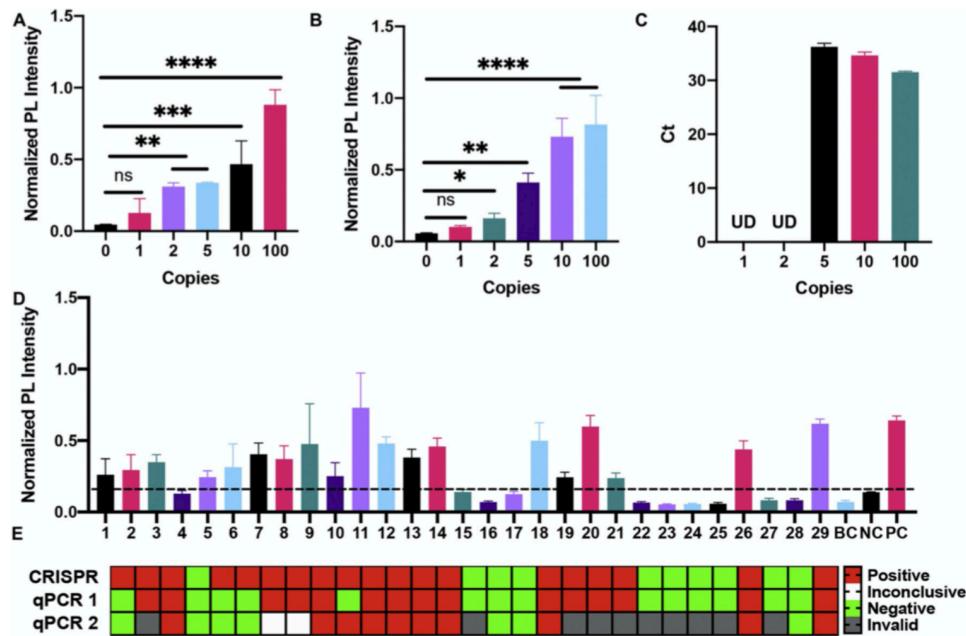
## FIGURES



**Fig. 1. A CRISPR-based Fluorescent Diagnosis System for COVID-19 (COVID-19 CRISPR-FDS).** (A) Schematic illustration of a CRISPR-FDS assay for detection of SARS-CoV-2 RNA in clinical samples. (B) SARS-CoV-2 genome map of COVID-19 CRISPR-FDS target sequences, and (C) sites in ORF1ab gene and the N protein gene that are detected COVID-19 CRISPR-FDS. Normalized CRISPR-FDS photoluminescent (PL) signal from SARS-CoV-2 RNA positive ( $10^9$  copies/sample) and negative control (polyA carrier RNA) samples following (D) target amplification by RT-PCR or RPA, (E) by RT-PCR for each assay target, and (F) by RT-PCR for related beta coronavirus species ( $10^9$  copies/sample). Bar graph data represents the mean  $\pm$  SD, of three experimental replicates.



**Fig. 2. COVID-19 CRISPR-FDS assay optimization.** (A) Substrate-dependent, (B) temperature-dependent, and (C) target-dependent effects on CRISPR-FDS signal. An aliquot containing  $10^9$  target amplicon copies, or an equivalent amount of poly A carrier RNA were analyzed as positive (+) and negative (-) control samples, respectively. Data presented in the top rows of each panel and the bottom row of (C) are normalized to the highest signal intensity detected in the corresponding experiment. Bar graph data represents the mean  $\pm$  SD, of three experimental replicates. (ns,  $P > 0.05$ ; \*\*\*\*,  $P < 0.0001$ ).



**Fig. 3. COVID-19 CRISPR-FDS analytical and diagnostic performance.** Limit of detection (LOD) samples containing the indicated number of viral genomes after amplification by (A) RT-PCR and (B) RT-RPA for COVID-19 CRISPR-FDS analysis or by (C) RT-qPCR, indicated significant differences and undetermined (UD) results. (D) RT-PCR COVID-19 CRISPR-FDS results for a cohort of 29 individuals with suspected COVID-19 cases, run in parallel with blank (BC; nuclease free water), negative (NC; carrier RNA) and positive (PC;  $10^9$  target amplicon copies) control samples, where the dashed line indicates the threshold for a positive result. Results depict the mean  $\pm$  SD of three experimental replicates. (E) Comparison of SARS-CoV-2 test results for matching patient samples analyzed by CRISPR-FDS, or by RT-qPCR by a state (qPCR 1) and a clinical testing laboratory (qPCR 2). (ns,  $P > 0.05$ ; \*,  $P < 0.05$ ; \*\*,  $P < 0.01$ ; \*\*\*,  $P < 0.001$ ; \*\*\*\*,  $P < 0.0001$ ).

## MASS SPECTROMETRIC IDENTIFICATION OF SARS-COV-2 PROTEINS FROM GARGLE SOLUTION SAMPLES OF COVID-19 PATIENTS

Ihling C, Tänzler D, Hagemann S, Kehlen A, Hüttelmaier S, Arlt C, Sinz A.. J Proteome Res. 2020 Jun 22. doi: 10.1021/acs.jproteome.0c00280. Online ahead of print.  
Level of Evidence: 5 - Mechanism-based reasoning

## BLUF

German researchers at the Martin Luther University developed a mass spectrometry (MS) method to detect SARS-CoV-2 proteins from highly diluted gargled samples of three COVID-19 patients and found unique peptides originating from SARS-CoV-2 nucleoprotein in two samples (Figure 1 and 2). The researchers anticipate with improvement of the MS-based method, testing of bronchoalveolar lavage may become routine in the diagnosis of COVID-19 patients.

## ABSTRACT

Mass spectrometry (MS) can deliver valuable diagnostic data that complements genomic information and allows us to increase our current knowledge of the COVID-19 disease caused by the SARS-CoV-2 virus. We developed a simple, MS-based method to specifically detect SARS-CoV-2 proteins from gargle solution samples of COVID-19 patients. The protocol consists of an acetone precipitation and tryptic digestion of proteins contained within the gargle solution, followed by a targeted MS analysis. Our methodology identifies unique peptides originating from SARS-CoV-2 nucleoprotein. Building on these promising initial results, faster MS protocols can now be developed as routine diagnostic tools for COVID-19 patients. Data are available via ProteomeXchange with identifier PXD019423.

## FIGURES

**A**

MSDNGPQNQR NAPRITFGGP SDSTGSNQNG ERSGARSKQR RPQGLPNNTA SWFTALTQHG KEDLKFPKG  
GVPINTNSSP DDQIGYYRRA TRRIRGGDGK MKDLSPRWYF YYLGTGPEAG LPYGANKDGI IIVVATEGALN  
TPKDHIGHTRN PANNAAIVLQ LPQGTTLPKG FYAEGSRGGG QASSRSSRS RNSSRNSTPG SSRGTPARM  
AGNGGDAALA LLLLDRINQL ESKMSGKGQQ QQGQTVTKKS AAEASKKPRQ KRTATKAYNV TQAFGRRGPE  
QTQGNFGDQE LIRQGTDYKH WPQIAQFAPS ASAFFGMSR I GMEVTPSGTW LTYTGAIKLD DKDPNFKDQV  
ILLNKHIDAY KTFPPTEPKK DKKKADETQ ALPQRQKKQQ TVTLLPAADL DDFSKQLQQS MSSADSTQA

**B**

MSDNGPQNQR NAPRITFGGP SDSTGSNQNG ERSGARSKQR RPQGLPNNTA SWFTALTQHG KEDLKFPKG  
GVPINTNSSP DDQIGYYRRA TRRIRGGDGK MKDLSPRWYF YYLGTGPEAG LPYGANKDGI IIVVATEGALN  
TPKDHIGHTRN PANNAAIVLQ LPQGTTLPKG FYAEGSRGGG QASSRSSRS RNSSRNSTPG SSRGTPARM  
AGNGGDAALA LLLLDRINQL ESKMSGKGQQ QQGQTVTKKS AAEASKKPRQ KRTATKAYNV TQAFGRRGPE  
QTQGNFGDQE LIRQGTDYKH WPQIAQFAPS ASAFFGMSR I GMEVTPSGTW LTYTGAIKLD DKDPNFKDQV  
ILLNKHIDAY KTFPPTEPKK DKKKADETQ ALPQRQKKOO TVTLLPAADL DDFSKQLQQS MSSADSTQA

Figure 1. Sequence coverage of SARS-CoV-2 nucleoprotein in gargle samples (A, B) of two COVID-19 patients. Identified peptides are shown in green. The peptide (aa 41–61) identified in both samples is highlighted in gray.

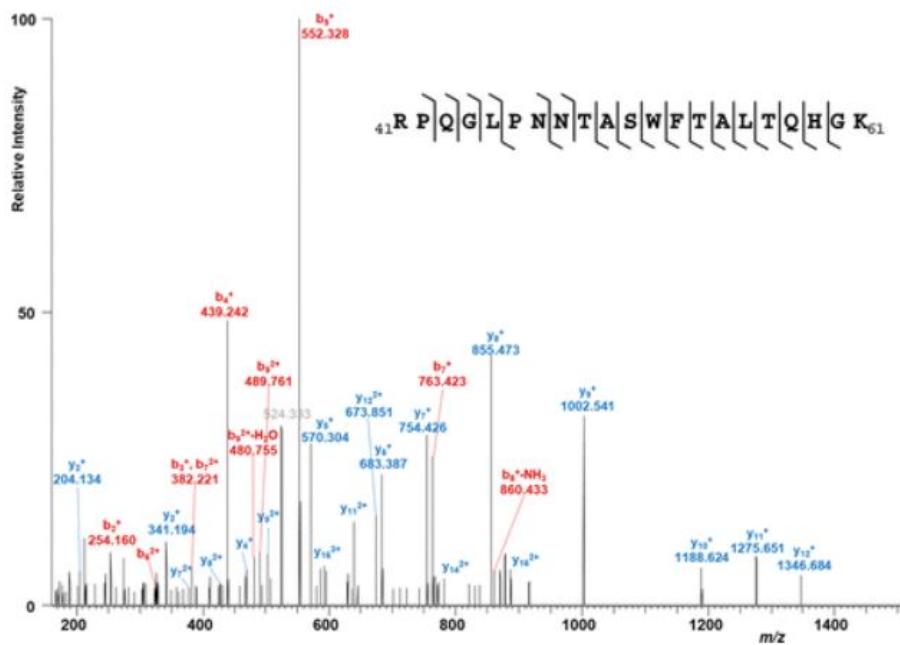


Figure 2. Fragment-ion mass spectrum (HCD-MS/MS) of the 4+ charged signal of peptide RPQGLPNNTASWFTALTQHGK (amino acids 41–61) from SARS-CoV-2 nucleoprotein.

## DEVELOPMENTS IN TREATMENTS

### SYSTEMATIC REVIEW OF REGISTERED TRIALS OF HYDROXYCHLOROQUINE PROPHYLAXIS FOR COVID-19 HEALTH-CARE WORKERS AT THE FIRST THIRD OF 2020

Bienvenu AL, Marty AM, Jones MK, Picot S.. One Health. 2020 Dec;10:100141. doi: 10.1016/j.onehlt.2020.100141. Epub 2020 May 19.

Level of Evidence: 1 - Systematic review of randomized trials or n-of-1 trials

#### BLUF

A systematic review conducted among clinical trials registered on ClinicalTrials.gov from March 17 to April 24, 2020 regarding hydroxychloroquine (HCQ) prophylaxis for SARS-CoV-2 found that the range of HCQ loading dose across the studies was 400-1400 mg followed either by a daily dose (commonly 200mg or 400mg) or weekly dose (400 mg) with prophylaxis duration ranging from 4 to 180 days or 3 to 24 weeks. Based on this "high diversity in [HCQ] dosage and duration of prophylaxis," the authors suggest additional analysis of these trials' designs and results before determining the appropriate HCQ regimen.

#### ABSTRACT

In the absence of a vaccine the medical and scientific community is looking intensely at utilizing a pre or post exposure drug that could decrease viremia. The search for a medication that could reduce risk of serious disease, and ideally of any manifestation of disease from SARS-CoV2, and of asymptomatic shedding of SARS-CoV2 is of urgent interest. Repurposing existing pharmaceuticals is among the approaches to achieve these ends. We performed a systematic review of all interventional studies registered in ClinicalTrials.gov with a focus on one repurposed drug, Hydroxychloroquine (HCQ). The detailed analysis of these studies, some of them already recruiting, provide an overall picture of HCQ use as a COVID-19 prophylaxis around the world. Among the included studies, all but three were randomized and parallel and most of them (74%, 23/31) were double-blinded to quadruple-blinded studies. We found a great diversity in dosing and nearly all the possible scientifically reasonable regimens are under evaluation. This diversity offers benefits as well as challenges. Importantly, the final analysis of these trials should be done through an extensive reading of the results in regard to the clinical design, it will be crucial to carefully read and evaluate the results of each study in regards to the clinical design rather than quickly glancing a 140 characters-based social media message announcing the failure or success of a drug against a disease.

### IN VIVO EXPRESSED BIOLOGICS FOR INFECTIOUS DISEASE PROPHYLAXIS: RAPID DELIVERY OF DNA-BASED ANTIVIRAL ANTIBODIES

Andrews CD, Huang Y, Ho DD, Liberatore RA.. Emerg Microbes Infect. 2020 Jun 24:1-32. doi: 10.1080/22221751.2020.1787108. Online ahead of print.

Level of Evidence: Other - Expert Opinion

#### BLUF

Authors associated with RenBio, an antibody gene therapy company, discuss the potential use and repurposing of monoclonal antibodies (mAbs) for the treatment of infectious viral diseases such as COVID-19. Advantages include invoking a natural B-cell response and rapid sequencing capacity, and disadvantages include significant cost and time to develop. They also discuss nucleic acid based neutralizing antibody (NAb) delivery with Adeno-associated virus vectors, lipid nanoparticle (LNP)-formulated mRNA, and in vivo transfection of naked DNA facilitated by electroporation (DNA/EP) to enhance the efficacy of mAbs. Authors suggest that nucleic acid based technologies offer the most potential in treating viral outbreaks.

#### ABSTRACT

With increasing frequency, humans are facing outbreaks of emerging infectious diseases (EIDs) with the potential to cause significant morbidity and mortality. In the most extreme instances, such outbreaks can become pandemics, as we are now witnessing with COVID-19. According to the World Health Organization, this new disease, caused by the novel coronavirus SARS-CoV-2, has already infected more than 8 million people worldwide and led to 461,715 deaths as of 21 June, 2020. How high these numbers will eventually go depends on many factors, including policies on travel and movement, availability of medical support, and, because there is no vaccine or highly effective treatment, the pace of biomedical research. Other than an approved antiviral drug that can be repurposed, monoclonal antibodies (mAbs) hold the most promise for providing a stopgap

measure to lessen the impact of an outbreak while vaccines are in development. Technical advances in mAb identification, combined with the flexibility and clinical experience of mAbs in general, make them ideal candidates for rapid deployment. Furthermore, the development of mAb cocktails can provide a faster route to developing a robust medical intervention than searching for a single, outstanding mAb. In addition, mAbs are well-suited for integration into platform technologies for delivery, in which minimal components need to be changed in order to be redirected against a novel pathogen. In particular, utilizing the manufacturing and logistical benefits of DNA-based platform technologies in order to deliver one or more antiviral mAbs has the potential to revolutionize EID responses. Trial registration: ClinicalTrials.gov identifier: NCT03374202.. Trial registration: ClinicalTrials.gov identifier: NCT03829384..

## MENTAL HEALTH & RESILIENCE NEEDS

### DID THE GENERAL POPULATION IN GERMANY DRINK MORE ALCOHOL DURING THE COVID-19 PANDEMIC LOCKDOWN?

32556079. Did the General Population in Germany Drink More Alcohol during the COVID-19 Pandemic Lockdown?  
Level of Evidence: 1 - Local and current random sample surveys (or censuses)

#### BLUF

This letter to the editor written by authors of the Department of Addictive Behavior and Addictive Medicine in Mannheim Germany and the Department of Psychiatry and Psychotherapy in Paracelsus Medical University evaluates the effect of social isolation on alcohol consumption during the pandemic through an anonymous online survey of 2,102 participants. They found that 34.7% of participants reported drinking more alcohol since the lockdown began. These findings highlight the need for healthcare providers to stay informed on this increased alcohol consumption during the lockdown and to be aware of its potential long-term effects.

### PSYCHIATRIC DISORDERS AND SUICIDE IN THE COVID-19 ERA

Sher L.. QJM. 2020 Jun 22:hcaa204. doi: 10.1093/qjmed/hcaa204. Online ahead of print.  
Level of Evidence: Other - Opinion

#### BLUF

An opinion letter by a New York psychiatrist summarizes research related to psychiatric consequences of the COVID-19 pandemic, namely how higher rates of associated anxiety and depression may lead to increased suicide risk. The author's intention is to raise awareness and as a call to action for proactive planning to minimize negative mental health impacts from the pandemic.

## COVID-19'S IMPACT ON HEALTHCARE WORKFORCE

### THE IMPACT OF THE COVID-19 PANDEMIC ON THE MENTAL HEALTH OF HEALTHCARE PROFESSIONALS

Braquehais MD, Vargas-Cáceres S, Gómez-Durán E, Nieva G, Valero S, Casas M, Bruguera E.. QJM. 2020 Jun 22:hcaa207. doi: 10.1093/qjmed/hcaa207. Online ahead of print.  
Level of Evidence: 2 - Systematic review of surveys that allow matching to local circumstances

#### BLUF

This systematic review conducted at the Galatea Care Programme for Sick Health Professionals in Barcelona, Spain looked at articles published between December 2019 and May 2020 to determine the impact of COVID-19 on the mental health of healthcare professionals (HPs). The authors analyzed 30 studies and found a high prevalence of anxiety (30-70%) and depressive symptoms (20-40%) reported, raising concerns that increased psychological support is needed in these populations.

#### SUMMARY

"Most studies report a high prevalence of anxiety (ranging from 30-70%) and depressive symptoms (20-40%). Insomnia, burnout, emotional exhaustion or somatic symptoms were also similarly reported." Factors potentially related to HPs mental distress can be found in Table 1. The authors hypothesize that while HPs may be used to witnessing traumatic experiences the high morbidity and mortality in patients affected by the pandemic, shortage of PPE, and fear of infection or transmission to family members has led to an increase in mental health disorders among HPs. They recommend psychological support be provided to address these issues during and after the pandemic.

## ABSTRACT

INTRODUCTION: Healthcare professionals (HPs) have been confronted by unprecedented traumatic experiences during the COVID-19 pandemic, especially in countries that had not experienced similar epidemic outbreaks in recent years. AIM: To analyze the impact of the COVID-19 pandemic on the mental health of HPs.

METHOD: We comprehensively reviewed the studies published in MEDLINE (PubMed), Web of Science and Google Scholar between December 2019 and May 2020.

RESULTS: Most studies report a high prevalence of anxiety and depressive symptoms among HPs that can be associated with: a) COVID-19 exposure; b) epidemiological issues; c) material resources; d) human resources; and e) personal factors. The role of certain variables, before, during and after the pandemic, remains unexplored. Longitudinal studies will help elucidate which factors are associated with a higher risk of developing long-lasting negative effects. Qualitative studies may contribute to understanding the influence of individual and social narratives in HPs' distress.

CONCLUSION: A deeper analysis on the individual, institutional, political and socio-cultural factors, meanings and values influencing HPs distress and resilience during the COVID-19 pandemic is needed.

## FIGURES

COVID-19 EXPOSURE	EPIDEMIOLOGY	HEALTH POLICIES	MATERIAL RESOURCES	HUMAN RESOURCES	PERSONAL FACTORS
<ul style="list-style-type: none"><li>• First line of care (Emergency/ Intensive Care Units/ Primary Care/ COVID-19 hospitals)</li><li>• COVID + (quarantined)</li><li>• Peer infection/ deaths</li><li>• Vicarious trauma (type).</li><li>• Hospitalized for COVID-19</li><li>• End-of-life decisions</li><li>• Degree of responsibility</li><li>• Second line of clinical care</li><li>• Remote tele-working</li></ul>	<ul style="list-style-type: none"><li>• Previous epidemics</li><li>• Incidence (country/ region)</li><li>• Pandemic stage</li></ul>	<ul style="list-style-type: none"><li>• Public data transparency</li><li>• Government global action plan</li><li>• Public health strategy</li><li>• Public health system coverage</li></ul>	<ul style="list-style-type: none"><li>• Personal protection equipment availability</li><li>• Time/place to rest</li><li>• Health system capacity (hospitals, intensive care units)</li><li>• Treatment resources availability</li></ul>	<ul style="list-style-type: none"><li>• Psychological support resources</li><li>• Hours on ward</li><li>• "Converted" medical professionals</li><li>• Internal residents</li><li>• New teams formation</li><li>• Reinforcement staff</li></ul>	<ul style="list-style-type: none"><li>• Sex</li><li>• Age</li><li>• Social support</li><li>• Coping strategies</li><li>• Personality traits</li><li>• Attachment style</li><li>• Having children</li><li>• Pre-morbid mental disorders</li><li>• Recent physical symptoms</li><li>• Ageing family members</li><li>• Deaths of relatives</li><li>• Legal/illegal drug misuse</li><li>• Alcohol use</li></ul>

Table 1. Factors related to the impact of the COVID-19 pandemic on healthcare professionals.

## IMPACT ON PUBLIC MENTAL HEALTH

### EMOTIONAL DISTRESS IN YOUNG ADULTS DURING THE COVID-19 PANDEMIC: EVIDENCE OF RISK AND RESILIENCE FROM A LONGITUDINAL COHORT STUDY

Shanahan L, Steinhoff A, Bechtiger L, Murray AL, Nivette A, Hepp U, Ribeaud D, Eisner M.. Psychol Med. 2020 Jun 23:1-32. doi: 10.1017/S003329172000241X. Online ahead of print.

Level of Evidence: 3 - Local non-random sample

## BLUF

Authors from Switzerland surveyed 786 young adults to evaluate their emotional distress before and during COVID-19, measured by perceived stress, internalizing symptoms, anger, social isolation, victimization, and stressful events. They found that participants had higher levels of perceived stress and anger during the pandemic compared to pre-pandemic ( $p<0.001$ ), and that keeping a daily routine, exercise, and reframing were associated with less stress among young adults. They suggest that although young adults report higher levels of stress during the pandemic, this is likely due to lifestyle and economic effects of COVID-19 rather than the health related effects.

## **THE CORONAVIRUS DISEASE 2019 (COVID-19) OUTBREAK AND MENTAL HEALTH: CURRENT RISKS AND RECOMMENDED ACTIONS**

Amsalem D, Dixon LB, Neria Y.. JAMA Psychiatry. 2020 Jun 24. doi: 10.1001/jamapsychiatry.2020.1730. Online ahead of print.  
Level of Evidence: Other - Expert Opinion

### **BLUF**

Experts from Columbia University in New York highlight the potential for social media and various websites to mitigate fear-related behaviors and anxiety due to the COVID-19 pandemic by improving social connections, offering mental health telemedicine services, directing the public to reliable resources, and delivering information while minimizing time on social media. Overall, they suggest that the potential of online platforms should be maximized to effectively deal with increased mental health and psychiatric needs.

### **SUMMARY**

The authors state, "... mass quarantine and social isolation lead to increased use of social media and other information-based websites, which in turn increases fear, stress, and the risk of fear-related disorders. In times of rapidly spreading infectious diseases and mass exposure to trauma, online platforms can be used to guide effective consumption of information, facilitate social support, continue mental health care delivery, and develop and test innovative, personalized contact-based interventions that, if found effective, can be disseminated to address emerging mental health needs."

# ACKNOWLEDGEMENTS

## CONTRIBUTORS

---

Alvin Rafou  
Amanda Nguyen  
Ben Showalter  
Carter Butuk  
Diep Nguyen  
Eva Shelton  
Jonathan Baker  
Julia Ghering  
Krithika Kumarasan  
Maresa Woodfield  
Maryam Naushab  
Mitchell Dumais  
Rechel Geiger  
Renate Meckl  
Ryan Wertz  
Shayan Ebrahimian  
Sokena Zaidi  
Tasha Ramparas  
Tina Samsamshariat  
Tyler Gallagher  
Veronica Graham

## EDITORS

---

Allen Doan  
Daniel Lee  
Julie Tran  
Luke Johnson  
Maggie Donovan  
Michelle Arnold  
Taylor Bozich

## SENIOR EDITORS

---

Avery Forrow  
Charlotte Archuleta  
Kyle Ellingsen  
Sangeetha Thevuthasan

## CHIEF EDITOR

---

Jasmine Rah

## ADVISOR

---

Will Smith