The Daily COVID-19 Literature Surveillance Summary

July 2, 2020

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COVID-19 Daily Literature Surveillance

COVID19LST

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

LEVEL OF EVIDENCE

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

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

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

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

How to cite the Levels of Evidence Table

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

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

EXECUTIVE SUMMARY

Climate

- A review illustrates how African Americans are disproportionately infected and hospitalized due to COVID-19 infection and constitute over 1/3 of the reported COVID-19 related deaths in the United States – far exceeding those of other races. The authors discuss how disparities faced by African Americans are a result of structural racism and provide several recommendations to reduce disadvantageous health inequality moving forward.
- Public health experts in the United States indicate that communication regarding the COVID-19 pandemic must be improved by having a clear, singular communicator from the government, actively fighting the spread of misinformation, continuing to maintain peer-reviewed processes for research, and utilizing social media to address a wider demographic.

Understanding the Pathology

- Investigators found that the conjunctiva and cornea both express ACE2 at a low level and transmembrane serine protease 2 (TMPRSS2) at moderate levels. Since these proteins are known to interact with the spike proteins of SARS-CoV-2, these findings support the possibility that SARS-CoV-2 can transmit through the eyes, warranting further study on this mode of transmission.
- Single cell RNA sequencing of nasopharyngeal and bronchial samples from 24 patients found a 3-fold increase of ACE2 receptor expression in patients with COVID-19. Further, their findings suggest that the inhibition of chemokine receptors CCR1 and CCR5, which were found to be highly expressed in critical COVID-19 cases, may decrease immune hyperactivation and thus may serve as potential therapeutic targets.

Management:

- A retrospective cohort study in Italy found that the percent of compromised lung volume, as determined by a quantitative computer tomography (QCT) analysis, was an effective predictor of intubation and mortality risk among 222 hospitalized patients with COVID-19 adding to the existing literature that compromised lung volume and QCT can be used to triage COVID-19 patients upon arrival at a hospital.

Adjusting Practice During COVID-19:

- Physicians from Quebec, who have organized aeromedical transfers for 50 COVID-19 patients since March, discuss strategies to maximize patient and crew safety, enhance intubation protocols between facilities, establish protocols for early transfers, improve in-flight communications, and managing cross-contamination within aircraft.

R&D Diagnosis and Treatment:

- A study of 106 COVID-19 positive patients with pneumonia symptoms determined that C-reactive protein levels and lymphocyte percentage correlated with volume of disease measured by CT scan providing data to support the use of these values.
- A docking and molecular dynamics simulation found an 18 amino-acid inhibitory peptide that exhibits the theoretical capacity to interfere with the interaction between the SARS-CoV-2 S-glycoprotein and the ACE2 receptor, preventing viral entry into the cell. The authors suggest that inhibitory peptides may be developed as SARS-CoV-2 treatment and are continuing their investigation in this area with cell-based assays.

Mental Health and Resilience:

- A cross-sectional study (n=257) from Bahrain found that front line healthcare workers had poorer sleep quality and higher perceived stress than non-front-line healthcare workers (p=?), further highlighting the need for increased mental health resources to maintain a healthy workforce during the pandemic, especially amount female wokers.

TABLE OF CONTENTS

WHO COMPLIES WITH THE RESTRICTIONS TO REDUCE THE SPREAD OF COVID-19?: PERSONALITY AND PERCEPTIONS OF THE COVID-19 SITUATION

Zajenkowski M, Jonason PK, Leniarska M, Kozakiewicz Z.. Pers Individ Dif. 2020 Nov 1;166:110199. doi: 10.1016/j.paid.2020.110199. Epub 2020 Jun 16.
Level of Evidence: 3 - Local non-random sample

BLUF

A cohort study conducted by Polish researchers from April 14-30, 2020 surveyed 263 participants (71.5% female) to better understand compliance with protective measures based on various personality types (Big Five and Dark Triad) and perceptions ("DIAMONDS") of the pandemic (Table 1)(more details on these scales below). They found personality may alter individual perceptions that could affect compliance with government restrictions (7.4% variance, R=0.27, F[10,251] = 2.02, p less than 0.05) and Table 2 highlights which personality types are more or less likely to comply with preventive measures such as social distancing and mask-wearing.

SUMMARY

Personality traits and their measurements in the Polish version of scales:

1. The Big Five:
- Extraversion, neuroticism, agreeableness, conscientiousness, and openness/intellect.
- Measured by the 20-item International Personality Item Pool

2. The Dark Triad:
- Machiavellianism, measured by the MACH-IV
- Narcissism, measured by Narcissistic Admiration and Rivalry
- Psychopathy, measured by Levenson's Self-Report Psychopathy Scale

3. Individual Perception of COVID-19 situation measured by S8 scale:
- DIAMONDS: duty, intellect, adversity, mating, positivity, negativity, deception, sociality

ABSTRACT

In 2020, many countries around the world created and enforced heavy restrictions geared towards reducing the spread of the coronavirus (i.e., COVID-19). In this study (N = 263), we examined the role of personality traits (i.e., Big Five and Dark Triad) and individual differences in perceptions of the COVID-19 pandemic situation (the situational eight: Duty, Intellect, Adversity, Mating, Positivity, Negativity, Deception, and Sociality) in accounting for individual differences in compliance with the governmental restrictions in Poland. We found that the way people perceived the situation explained more variance in compliance than personality traits which is in accordance with the hypothesis that strong situations, such as the COVID-19 pandemic, leave less room for dispositional tendencies in predicting behaviors than situational cues. Moreover, people scoring low on agreeableness and high on aspects of the Dark Triad traits (i.e., Machiavellianism, psychopathy Factor 1, and narcissistic rivalry) were less likely to comply with the restrictions. Additionally, we replicated and extended what is known about the associations between personality and individual differences in the perception of situations when the latter were assessed in relation to a strong situation and the former were assessed with long and multidimensional measures.

FIGURES

	1	2	3	4	5	6	7	8	9
1. Extraversion									
2. Neuroticism	−0.08								
3. Agreeableness	0.31**	0.10							
4. Conscientiousness	0.06	−0.16*	−0.07						
5. Openness/Intellect	0.26**	0.03	0.04	−0.02					
6. Machiavellianism	−0.05	0.20**	−0.26**	−0.09	0.06				
7. Narcissism-A	0.43**	−0.24**	0.08	0.08	0.31**	0.05			
8. Narcissism-R	−0.10	0.18**	−0.35**	−0.08	−0.11	0.58**	0.14*		
9. Psychopathy F1	0.04	−0.08	−0.40**	0.06	−0.01	0.57**	0.22**	0.48**	
10. Psychopathy F2	−0.06	0.32**	−0.17**	−0.37**	−0.16*	0.33**	−0.09	0.36**	0.26**
11. Duty	0.20**	−0.04	0.25**	0.23**	0.10	−0.09	0.22**	−0.06	−0.02
12. Intellect	0.15*	0.00	0.14*	0.10	0.20**	0.11	0.30**	0.02	0.05
13. Adversity	0.01	0.41**	0.01	−0.11	0.02	0.11	−0.07	0.18**	0.03
14. Mating	0.21**	−0.13*	0.07	0.03	−0.05	0.08	0.12	0.09	0.15*
15. pOsitivity	0.07	−0.16**	−0.11	0.03	0.12	0.20**	0.17**	0.19**	0.28**
16. Negativity	0.01	0.30**	0.20**	−0.06	−0.07	−0.04	−0.16*	−0.07	−0.19**
17. Deception	−0.04	0.11	0.02	−0.03	0.02	0.11	−0.01	0.07	−0.04
18. Sociality	0.26**	−0.02	0.33**	−0.04	0.07	−0.07	0.22**	−0.10	−0.12
19. Compliance %	−0.05	0.04	0.17**	0.00	0.04	−0.19**	−0.05	−0.18**	−0.16**
Cronbach's α	0.85	0.79	0.69	0.78	0.62	0.74	0.81	0.75	0.78
M (SD)	3.07 (0.99)	3.32 (0.92)	4.07 (0.65)	3.08 (0.94)	4.05 (0.61)	3.40 (0.65)	3.31 (0.85)	2.50 (0.76)	1.57 (0.37)

	10	11	12	13	14	15	16	17	18	19
1. Extraversion										
2. Neuroticism										
3. Agreeableness										
4. Conscientiousness										
5. Openness/Intellect										
6. Machiavellianism										
7. Narcissism-A										
8. Narcissism-R										
9. Psychopathy F1										
10. Psychopathy F2										
11. Duty	−0.22**									
12. Intellect	−0.16*	0.48**								
13. Adversity	0.30**	−0.05	0.03							
14. Mating	−0.07	0.20**	0.20**	−0.04						
15. pOsitivity	0.03	0.03	0.08	−0.14*	0.21**					
16. Negativity	0.09	0.04	0.11	0.37**	0.01	−0.55**				
17. Deception	0.06	0.07	0.17**	0.23**	−0.01	−33**	0.53**			
18. Sociality	−0.03	0.22**	0.33**	−0.01	0.26**	0.00	0.18**	0.16*		
19. Compliance %	−0.11	0.08	−0.02	−0.03	−0.19**	0.11	0.14*	0.03	−0.03	
Cronbach's α	0.53	0.77	0.76	0.69	0.77	0.84	0.90	0.92	0.74	
M (SD)	2.08 (0.40)	5.51 (1.04)	5.19 (1.16)	3.14 (1.21)	3.11 (1.46)	2.50 (1.32)	5.46 (1.31)	5.01 (1.60)	5.04 (1.17)	85.37 (16.91)

Note. Narcissism-A = Narcissistic Admiration; Narcissism-R = Narcissistic Rivalry; F1 = Factor 1; F2 = Factor 2.
* $p < .05$
** $p < .01$.

Table 1. Correlations between personality, perceptions of the COVID-19 situation, and compliance with restrictions along with descriptive statistics and internal consistency.

		β
Model 1. Big Five as predictors of compliance		
Extraversion	$F(5, 256) = 2.21, p < .05$	−0.13
Neuroticism	$R_{adj}^2 = 0.02$	0.02
Agreeableness		0.20**
Conscientiousness		0.02
Openness/Intellect		0.05
Model 2. Dark Triad as predictors of compliance		
Machiavellianism	$F(5, 256) = 2.53, p < .05$	−0.11
Narcissism-Admiration	$R_{adj}^2 = 0.03$	−0.03
Narcissism-Rivalry		−0.08
Psychopathy F1		−0.05
Psychopathy F2		−0.04
Model 3. Characteristics of situation as predictors of compliance		
Duty	$F(5, 256) = 2.21, p < .01$	0.14*
Intellect	$R_{adj}^2 = 0.06$	−0.06
Adversity		−0.11
Mating		−0.22**
pOsitivity		0.04
Negativity		0.23**
Deception		−0.06
Sociality		−0.02

Note. F1 = Factor 1; F2 = Factor 2.
* $p < .05$.
** $p < .01$.

Table 2. Multiple regression models with the Dark Triad traits, the Big Five traits, and perceptions of the situation as predictors of compliance with COVID-19 restrictions.

ENHANCING GLOBAL HEALTH COMMUNICATION DURING A CRISIS: LESSONS FROM THE COVID-19 PANDEMIC

Ratzan SC, Sommariva S, Rauh L.. Public Health Res Pract. 2020 Jun 30;30(2):3022010. doi: 10.17061/phrp3022010.
Level of Evidence: Other - Guidelines and Recommendations

BLUF

A set of guidelines put forth by public health experts in the United States indicate that communication regarding the COVID-19 pandemic must be improved by directly addressing the following:
- Having a clear, singular communicator from the government
- Taking steps to fight the spread of misinformation
- Continuing to maintain peer-reviewed processes for research
- Utilizing social media to address a wider demographic

This article suggests that better communication is required to mitigate the adverse consequences of false information being spread during the COVID-19 pandemic. The full list of recommendations are listed in Figure 1.

ABSTRACT

BACKGROUND/OBJECTIVE: The understanding and practice of public health crisis communication are improved through the study of responses to past crises, but require retooling for present challenges. The 'Addressing Ebola and other outbreaks' checklist contains guiding principles built upon maxims developed from a World Health Organization consultation in response to the mad cow (bovine spongiform encephalopathy) crisis that were later adopted for Ebola. The purpose of this article is to adapt the checklist for the health communication challenges and public health practices that have emerged during the coronavirus disease 2019 (COVID-19) pandemic. The communication challenges of promoting vaccine acceptance are used to illustrate a key area that requires strengthened communication. Type of program or service: Effective communication principles for application during the COVID-19 pandemic.

RESULTS: The COVID-19 pandemic has introduced unique challenges for public health practitioners and health communicators that warrant an expansion of existing health communication principles to take into consideration: the new infodemic (or mis/disinfodemic) challenge - particularly as treatments and vaccines are being developed; communication of risk and uncertainty; health-information behaviours and the instantaneous nature of social media, and the relationship between media literacy and health literacy; the effects of the pandemic on other health issues; and the need for a flexible communication strategy that adapts to the different stages of the pandemic.

LESSONS LEARNT: Principles discussed in this article will help build preparedness capacity and offer communication strategies for moving from the acute phase to the 'next normal' with likely prevention (e.g. herd immunity achieved through vaccination) and societal COVID-19 resilience.

FIGURES

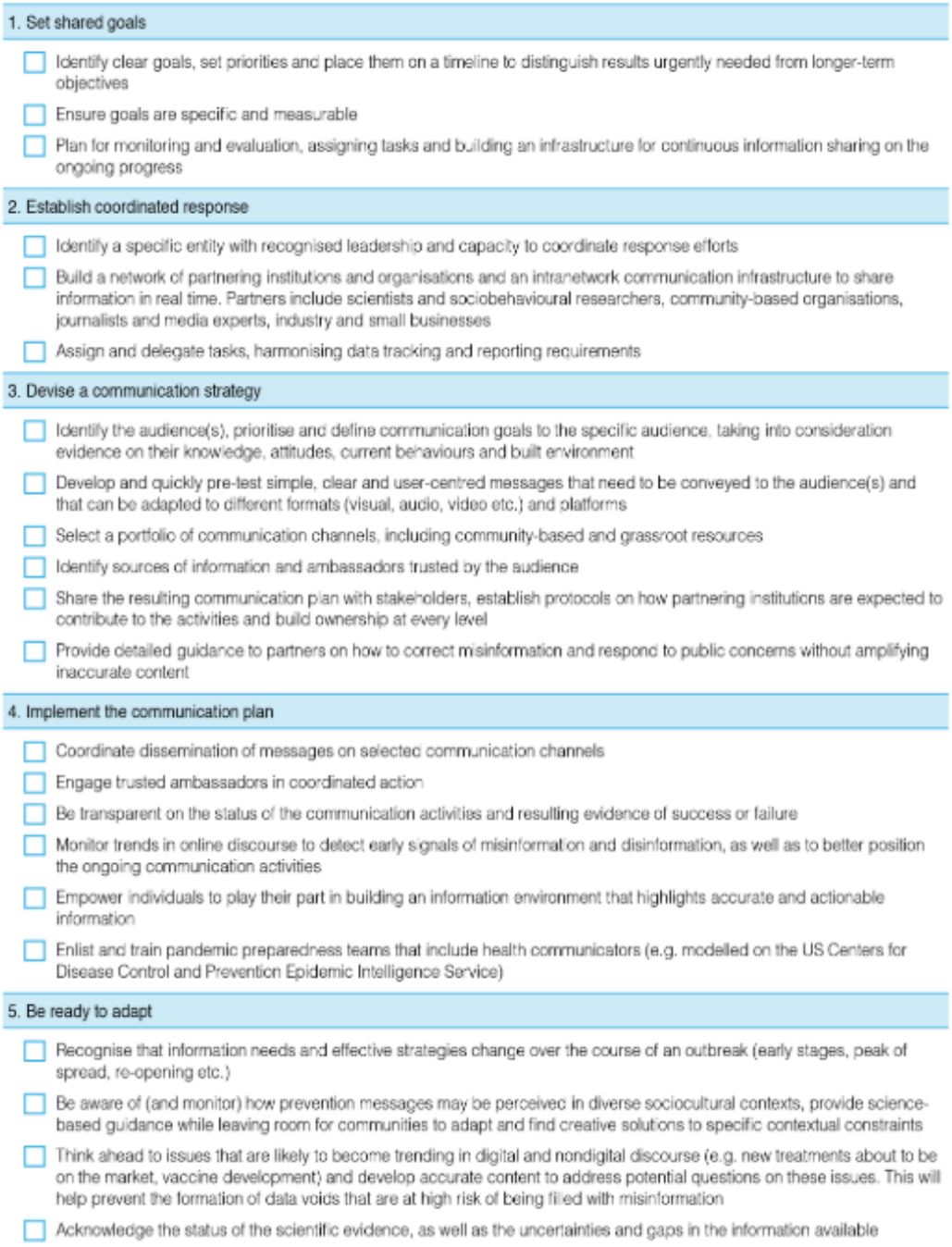


Figure 1. Checklist for effective global health communication practices during COVID-19

AFFECTING THE HEALTHCARE WORKFORCE

THE EXAMINATION OF SLEEP QUALITY FOR FRONTLINE HEALTHCARE WORKERS DURING THE OUTBREAK OF COVID-19

Jahrami H, BaHammam AS, AlGahtani H, Ebrahim A, Faris M, AlEid K, Saif Z, Haji E, Dhahi A, Marzooq H, Hubail S, Hasan Z.. Sleep Breath. 2020 Jun 26. doi: 10.1007/s11325-020-02135-9. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

This cross-sectional study in Bahrain compares sleep quality of frontline healthcare workers (FLHCW; n=138) with that of non-frontline healthcare workers (NFLHCW; n=145) through an online questionnaire using socio-demographics, the Pittsburg Sleep Quality Index (PSQI) and the Perceived Stress Scale (PSS). Female sex (OR 2.0, P = 0.01) and being a non-physician healthcare worker (OR 0.7, P = 0.05) were both independent predictors for poor sleep quality and increased stress, and despite no statistically significant difference, FLHCW scored higher than NFLHCW in the PSQI and PSS (Table 2). This study emphasizes the role of mental health stressors with respect to sleep quality, and the authors urge hospitals to provide preventative measures for their employees.

ABSTRACT

PURPOSE: Few studies have addressed the sleep disturbances of healthcare workers during crisis events of public health. This study aimed to examine the sleep quality of frontline healthcare workers (FLHCW) in Bahrain during the COVID-19 pandemic, and compare it with the sleep quality of non-frontline healthcare workers (NFLHCW).
METHODS: Healthcare workers (n = 280) from multiple facilities belonging to the Ministry of Health, Bahrain, were invited to participate in this cross-sectional study. An online questionnaire, including socio-demographics, the Pittsburgh Sleep Quality Index (PSQI), and the Perceived Stress Scale (PSS), was used to evaluate sleep disturbances and stress levels of healthcare workers. Poor sleep quality was defined as PSQI >= 5 and moderate-severe stress as PSS >= 14. Descriptive statistics were used to compare the scores of FLHCW and NFLHCW. Univariate and multivariate binary logistic regressions were used to identify predictors of poor sleep quality, moderate-severe stress, and the combined problem of poor sleep quality and moderate-severe stress.
RESULTS: A total of 257 participants (129 FLHCW and 128 NFLHCW) provided usable responses. The overall PSQI and PSS scores were 7.0 +- 3.3 and 20.2 +- 7.1, respectively. The FLHCW scored higher in the PSQI and PSS compared with the NFLHCW; however, the differences in the PSQI and PSS scores were not statistically significant. For the FLHCW, 75% were poor sleepers, 85% had moderate-severe stress, and 61% had both poor sleep quality and moderate-severe stress. For the NFLHCW, 76% were poor sleepers, 84% had moderate-severe stress, and 62% had both poor sleep quality and moderate-severe stress. Female sex and professional background were the predictors of poor sleep quality and stress.
CONCLUSIONS: Poor sleep quality and stress are common during the COVID-19 crisis. Approximately, 60% of both FLHCW and NFLHCW have poor sleep quality combined with moderate-severe stress.

FIGURES

Table 2 Findings of the PSQI and PSS scores

Variable	Overall ($N = 257$)	FLHCW ($N = 129$)	NFLHCW ($N = 128$)	P value
PSQI (C1) subjective sleep quality	1.2 ± 0.8	1.3 ± 0.8	1.1 ± 0.7	0.1
PSQI (C2) sleep latency	1.6 ± 1.0	1.4 ± 1.0	1.3 ± 1.0	0.7
PSQI (C3) sleep duration	1.0 ± 1.0	1.0 ± 1.0	1.0 ± 1.1	0.9
PSQI (C4) habitual sleep efficiency	0.7 ± 1.1	0.7 ± 1.0	0.8 ± 1.0	0.5
PSQI (C5) sleep disturbances	1.3 ± 0.6	1.4 ± 0.6	1.2 ± 0.6	0.02*
PSQI (C6) use of sleep-promoting medications	0.4 ± 0.7	0.4 ± 0.7	0.3 ± 0.7	0.4
PSQI (C7) daytime dysfunction	1.1 ± 0.8	1.2 ± 0.8	1.1 ± 0.8	0.3
Global PSQI	*7.0 ± 3.3*	*7.1 ± 3.5*	*6.9 ± 3.1*	*0.4*
Prevalence of poor sleep quality (≥5 points)	191 (75.2%)	94 (74.6%)	97 (75.8%)	0.3
PSS	*20.2 ± 7.1*	*20.7 ± 7.0*	*19.9 ± 7.1*	*0.3*
Prevalence of low stress (0–13 points)	41 (15.9%)	20 (15.5%)	21 (16.4%)	0.1
Prevalence of moderate stress (14–26 points)	172 (66.9%)	81 (62.8%)	91 (71.1%)	
Prevalence of severe stress (27–40 points)	44 (17.1%)	28 (21.7%)	16 (12.5%)	

The italics only to highlight global or overall score

FLHCW, frontline healthcare workers; *NFLHCW*, non-frontline healthcare workers; *PSQI*, Pittsburgh Sleep Quality Index; *PSS*, Perceived Stress Scale

INVESTIGATING THE EFFECTS OF COVID-19 ON GLOBAL MALE SEX WORK POPULATIONS: A LONGITUDINAL STUDY OF DIGITAL DATA

Callander D, Meunier É, DeVeau R, Grov C, Donovan B, Minichiello V, Kim J, Duncan D.. Sex Transm Infect. 2020 Jun 26:sextrans-2020-054550. doi: 10.1136/sextrans-2020-054550. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

American and Australian researchers performed a longitudinal ecological study from November 2019-May 2020 and extracted 19,388 online profiles of male sex workers to examine the effects of COVID-19. They found active and newly created profiles have decreased (59.4%; IRR=0.71, 95% CI 0.69 to 0.74, p less than 0.001)(Figure 1) and users were also more likely to offer web-based services and to mention COVID-19 in the free text section (Table 1). From this, the researchers believe male sex workers are facing economic hardship as a result of COVID-19 and urge governments to include sex workers in financial stimulus packages as well as develop educational risk reduction campaigns to better support sex workers during the pandemic.

ABSTRACT

OBJECTIVES: Recommendations of 'social distancing' and home quarantines to combat the global COVID-19 pandemic have implications for sex and intimacy, including sex work. This study examined the effects of COVID-19 on male sex work globally and investigated how men who sold sex responded to and engaged with the virus in the context of work.
METHODS: This study made use of an existing database of deidentified data extracted from the online profiles maintained by male sex workers on a large, international website. Website engagement metrics were calculated for the periods before (September to December 2019) and during COVID-19 (January to May 2020); Poisson regression analyses were used to assess changes over time before and after, while a content analysis was undertaken to identify modes of engagement with the virus.
RESULTS: Data were collected from 78 399 profiles representing 19 388 individuals. In the 'before' period, the number of active profiles was stable (inter-rate ratio (IRR)=1.01, 95% CI 0.99 to 1.01, p=0.339) but during COVID-19 decreased by 26.3% (IRR=0.90, 95% CI 0.89 to 0.91, p<0.001). Newly created profiles also decreased during COVID-19 (59.4%; IRR=0.71, 95% CI 0.69 to 0.74, p<0.001) after a period of stability. In total, 211 unique profiles explicitly referenced COVID-19; 185 (85.8%) evoked risk reduction strategies, including discontinuation of in-person services (41.2%), pivoting to virtual services (38.9%), COVID-19 status disclosure (20.9%), enhanced sanitary and screening requirements (12.3%) and restricted travel (5.2%). Some profiles, however, seemed to downplay the seriousness of COVID-19 or resist protective measures (14.7%).
CONCLUSIONS: These findings support the contention that COVID-19 has dramatically impacted the sex industry; globally, male sex workers may be facing considerable economic strain. Targeted education and outreach are needed to support male sex workers grappling with COVID-19, including around the most effective risk reduction strategies. Those involved with the sex industry must have access to state-sponsored COVID-19 financial and other aid programmes to support individual and public health.

FIGURES

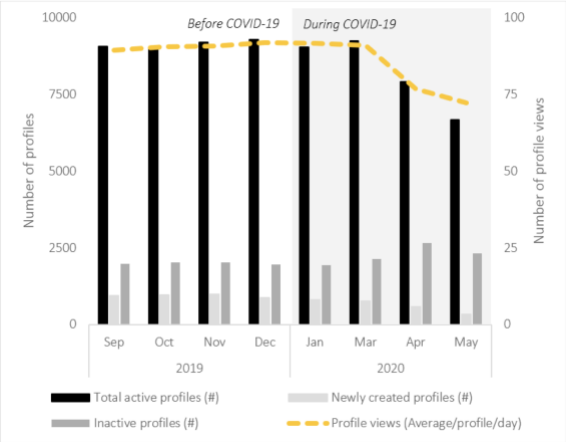


Figure 1. Number of active, inactive and newly created male sex work profiles and average daily views per profile before (September 2019 to January 2020) and during (January to May 2020) the COVID-19 pandemic, by month.

Table 1 Content analysis results of online male sex workers' reactions to and engagement with COVID-19*

Theme	Subtheme	Example	n (%)
Risk reduction			181 (85.8)
	In-person service discontinuation	'Due to COVID-19 I will not be doing any in person modeling, massaging, etc.'	87 (41.2)
	Virtual sex work services offered†	'Webcam sessions only provided during COVID-19.'	82 (38.9)
	COVID-19 status disclosure	'Tested for Covid 19 antibody 04/28/20 negative.'	44 (20.9)
	Enhanced client requirements	'Social distancing is priority so screening clients to be safe.'	26 (12.3)
	Restricted sex work travel	'Travels are subject to change if further government restrictions put in place.'	11 (5.2)
Social reactions			51 (24.2)
	Expressions of solidarity	'We can meet after! For your safety and mine. For now let's help each other stay safe.'	20 (9.5)
	Dismiss or downplay pandemic	'Grounded and ready to play #Covid mode'; 'Don't let COVID ruin all our fun!'	31 (14.7)

*Analysis conducted using 211 unique profiles that referenced COVID-19.
†Virtual services in this context include only those with specific reference to COVID-19.

Table 1. Content analysis results of online male sex workers' reactions to and engagement with COVID-19

RACIAL DISPARITY OF CORONAVIRUS DISEASE 2019 (COVID-19) IN AFRICAN AMERICAN COMMUNITIES

Kullar R, Marcelin JR, Swartz TH, Piggott DA, Macias Gil R, Mathew TA, Tan T.. J Infect Dis. 2020 Jun 30:jiaa372. doi: 10.1093/infdis/jiaa372. Online ahead of print.
Level of Evidence: Other - Guidelines and Recommendations

BLUF

This review cites research illustrating that African Americans are disproportionately infected and hospitalized due to COVID-19 infection (Figure 1) and constitute over 1/3 of the reported COVID-19 related deaths in the United States (Figure 2), with these totals far exceeding those of other races. These disparities faced by African Americans, among many others, are a result of structural racism that has existed in the United States since it was founded, and the authors provide several recommendations (as detailed in the summary below) to reduce disadvantageous health inequality moving forward.

SUMMARY

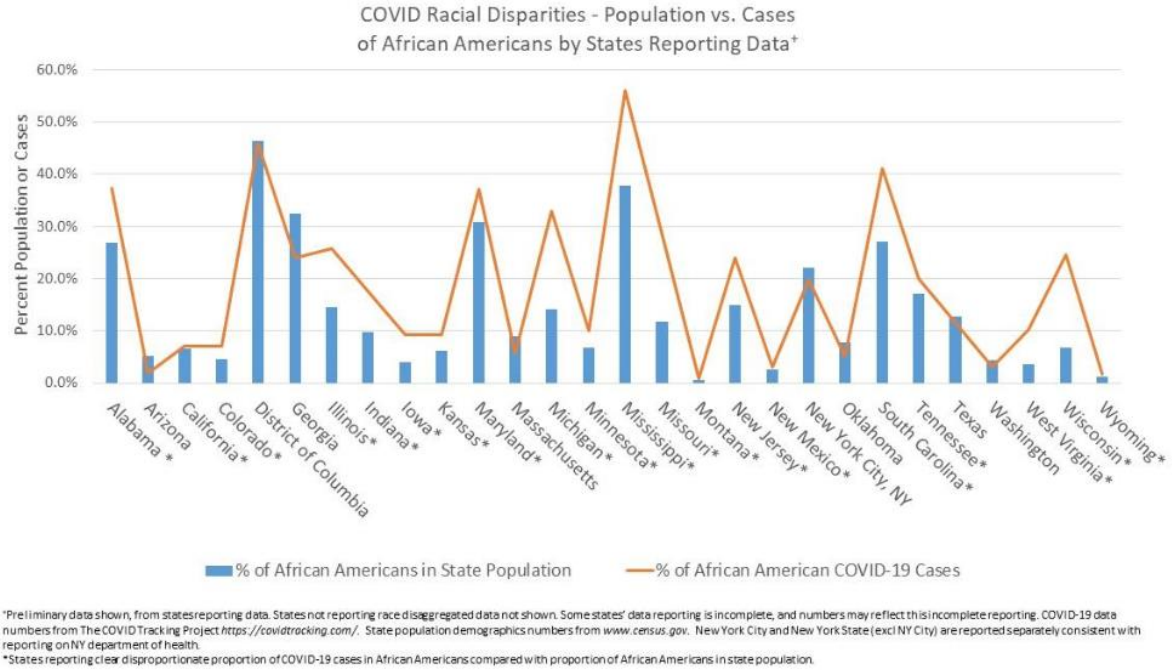
Recommendations to reduce racial disparity in African American communities:

- Require states to provide all data on race vs. health outcomes for COVID-19 patients, in addition to testing availability and access
- Encourage respected members of the community to distribute accurate and evidence-based information regarding infection transmission and prevention
- Utilize technology to coordinate prevention messages and safe patient care between healthcare providers
- Ensure that information is widely available in multiple languages, including on social media, and is culturally appropriate
- Promote Medicaid expansion across all 50 states
- Decrease food, work, childcare, and financial insecurities by implementing programs that directly address them
- Increase access to primary care
- Promote evidence-based understanding by encouraging African Americans to participate in research, as both researchers and subjects

ABSTRACT

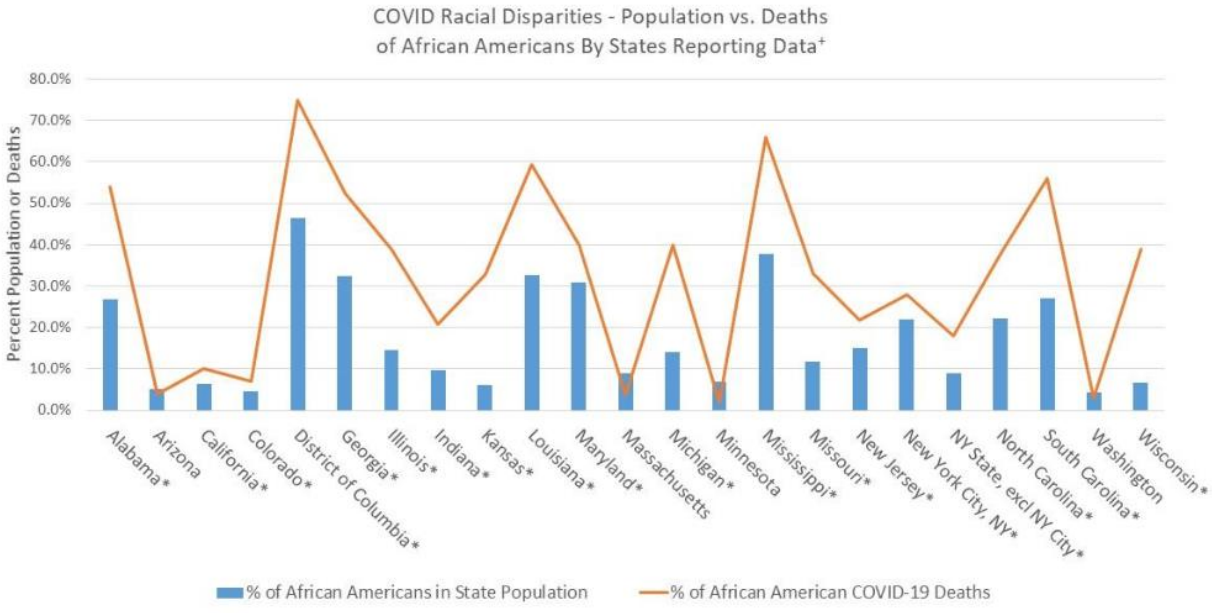
The COVID-19 pandemic has unveiled unsettling disparities in the outcome of the disease among African Americans. These disparities are not new, but are rooted in structural inequities that must be addressed to adequately care for communities of color. We describe the historical context of these structural inequities, their impact on the progression of COVID-19 in the African American (Black) community, and suggest a multifaceted approach to addressing these healthcare disparities. Of note, terminology from survey data cited for this article varied from Blacks, African Americans or both; for consistency, we use African Americans throughout.

FIGURES



+Preliminary data shown, from states reporting data. States not reporting race disaggregated data not shown. Some states' data reporting is incomplete, and numbers may reflect this incomplete reporting. COVID-19 data numbers from The COVID Tracking Project *https://covidtracking.com/*. State population demographics numbers from *www.census.gov*. New York City and New York State (excl NY City) are reported separately consistent with reporting on NY department of health.
*States reporting clear disproportionate proportion of COVID-19 cases in African Americans compared with proportion of African Americans in state population.

Figure 1



+Preliminary data shown, from states reporting data. States not reporting race disaggregated data not shown. Some states' data reporting is incomplete, and numbers may reflect this incomplete reporting. COVID-19 data numbers from The COVID Tracking Project *https://covidtracking.com/*. State population demographics numbers from *www.census.gov*. New York City and New York State (excl NY City) are reported separately consistent with reporting on NY department of health.
*States reporting clear disproportionate proportion of COVID-19 cases in African Americans compared with proportion of African Americans in state population.

Figure 2

OCULAR SURFACE EXPRESSION OF SARS-COV-2 RECEPTORS

Leonardi A, Rosani U, Brun P.. Ocul Immunol Inflamm. 2020 Jun 26:1-4. doi: 10.1080/09273948.2020.1772314. Online ahead of print.

Level of Evidence: Other - Mechanism-based reasoning

BLUF

Authors from Italy and Germany examined the transcriptome of 18 conjunctiva epithelial cell samples and 6 ex-vivo cornea samples and found that the conjunctiva and cornea both express ACE2 at a low level and basigin/CD147/EMMPRIN (BSG) and transmembrane serine protease 2 (TMPRSS2) at moderate levels (Figure 1). Since these proteins are known to interact with the spike proteins of SARS-CoV-2, these findings support the possibility that SARS-CoV-2 can transmit through the eyes, warranting further study on this mode of transmission and the need for eye protection for healthcare workers.

ABSTRACT

PURPOSE: The spike proteins of SARS-CoV-2 interact with ACE2 or basigin/CD147 receptors, regulating human-to-human transmissions of COVID-19 together with serine protease TMPRSS2. The expression of these receptors on the ocular surface is unknown.
MATERIAL AND METHODS: Gene expression of SARS-CoV-2 receptors was investigated in conjunctival epithelial cell samples and in ex-vivo cornea samples using microarray or transcriptome sequencing.
RESULTS: ACE2 is expressed in conjunctival samples at a low level, while BSG and TMPRSS2 are expressed at intermediate levels in both conjunctiva and cornea. Other receptors such as ANPEP, AGTR2 are expressed at low level in the conjunctiva. Two RNA editing enzymes involved in antiviral responses, APOBEC3A, and ADAR-1 were also highly expressed.
CONCLUSIONS: The ocular surface may represent an entry point for the SARS-CoV-2 in the human body. The conjunctiva and the cornea can adopt antiviral countermeasures which may explain the low prevalence of eye involvement.

FIGURES

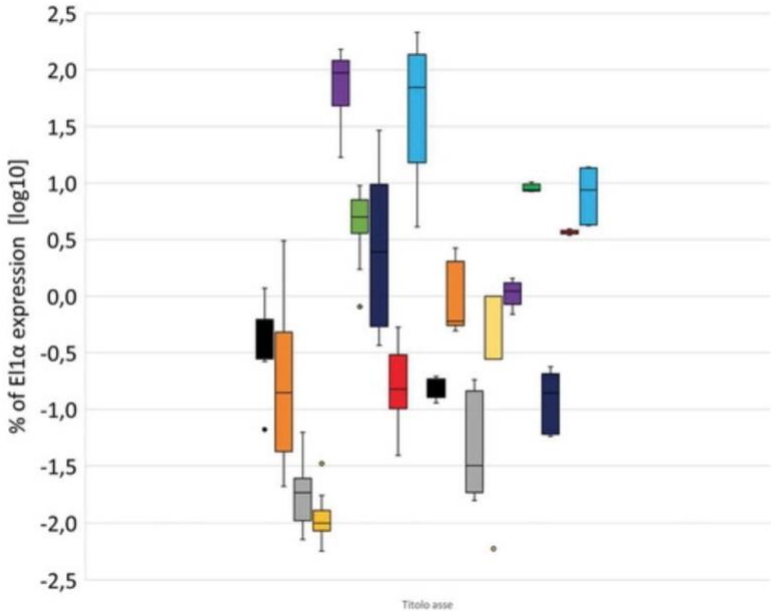


Figure 1. Box and whiskers plot of the expression values of angiotensin converting enzyme 2 (ACE2), aminopeptidase N (ANPEP), dipeptidyl peptidase 4 (DPP4), angiotensin II receptor type 2 (ATGR2), polymeric immunoglobulin receptor (PIGR), basigin (BSG/CD147), transmembrane serine protease 2 (TMPRSS2), apolipoprotein B mRNA editing enzyme catalytic polypeptide-like 3A (APOBEC3A) and double-stranded RNA-specific adenosine deaminase (ADAR-1) in 18 conjuntival and 6 cornea normal samples. Expression values are reported in percentages as log-transformed differences between the expression of the given gene and the expression of El1α.

THE CYTOKINE STORM AND COVID-19

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

BLUF

A literature review conducted at the Medical College of Jinan University in China explores the association between cytokine storm and COVID-19 severity. The authors suggest that early control of these cytokine storms with immunomodulators such as corticosteroids and cytokine antagonists such as tocilizumab is a promising route of improved survival in COVID-19 patients.

ABSTRACT

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

COVID-19 SEVERITY CORRELATES WITH AIRWAY EPITHELIUM-IMMUNE CELL INTERACTIONS IDENTIFIED BY SINGLE-CELL ANALYSIS

Chua RL, Lukassen S, Trump S, Hennig BP, Wendisch D, Pott F, Debnath O, Thürmann L, Kurth F, Völker MT, Kazmierski J, Timmermann B, Twardziok S, Schneider S, Machleidt F, Müller-Redetzky H, Maier M, Krannich A, Schmidt S, Balzer F, Liebig J, Loske J, Suttorp N, Eils J, Ishaque N, Liebert UG, von Kalle C, Hocke A, Witzenrath M, Goffinet C, Drosten C, Laudi S, Lehmann I, Conrad C, Sander LE, Eils R.. Nat Biotechnol. 2020 Jun 26. doi: 10.1038/s41587-020-0602-4. Online ahead of print.
Level of Evidence: Other - Mechanism-based reasoning

BLUF

Investigators from Germany performed single cell RNA sequencing on nasopharyngeal and bronchial samples from 24 patients and found an average 3-fold increase of ACE2 receptor expression in patients with COVID-19 (n=19) compared with the healthy control group (n=5; Figure 2). Further, patients with critical COVID-19 (n=11) had greater interactions between various immune cells, including macrophage populations capable of producing a wide spectrum of inflammatory markers, compared to moderate COVID-19 cases (n=8, Figure 4). Their findings suggest that the inhibition of chemokine receptors CCR1 and CCR5, which were found to be highly expressed in critical COVID-19 cases, may decrease immune hyperactivation and thus may serve as potential therapeutic targets.

ABSTRACT

To investigate the immune response and mechanisms associated with severe coronavirus disease 2019 (COVID-19), we performed single-cell RNA sequencing on nasopharyngeal and bronchial samples from 19 clinically well-characterized patients with moderate or critical disease and from five healthy controls. We identified airway epithelial cell types and states vulnerable to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. In patients with COVID-19, epithelial cells showed an average three-fold increase in expression of the SARS-CoV-2 entry receptor ACE2, which correlated with interferon signals by immune cells. Compared to moderate cases, critical cases exhibited stronger interactions between epithelial and immune cells, as indicated by ligand-receptor expression profiles, and activated immune cells, including inflammatory macrophages expressing CCL2, CCL3, CCL20, CXCL1, CXCL3, CXCL10, IL8, IL1B and TNF. The transcriptional differences in critical cases compared to moderate cases likely contribute to clinical observations of heightened inflammatory tissue damage, lung injury and respiratory failure. Our data suggest that pharmacologic inhibition of the CCR1 and/or CCR5 pathways might suppress immune hyperactivation in critical COVID-19.

Fig. 4: Immune–epithelial cell interaction in COVID-19.

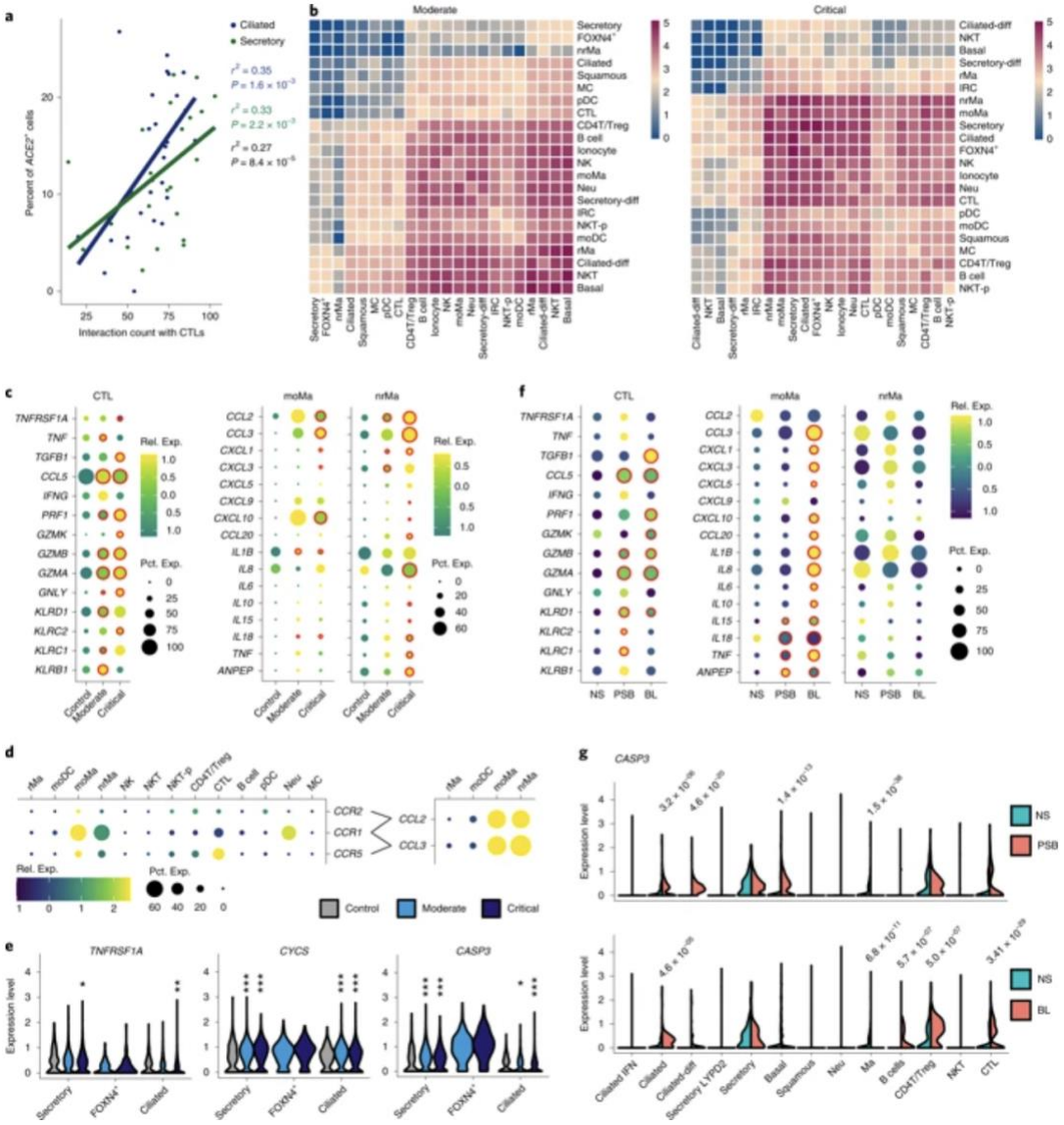


Figure 4. a, Schematic representation of the experimental workflow. Depicted are the sampling sites (left) and the 3′ scRNA-seq library preparation using 10X Genomics (middle) followed by data analysis revealing cell type identity (right). b, Overview of the patient cohort. Given are age, sex and COVID-19 severity as well as onset of symptoms, hospitalization duration and sampling time points in days after onset of symptoms, with all patients being temporally aligned to the day of positive SARS-CoV-2 test. Admission to the ICU is also depicted if applicable. One patient required ECMO. We obtained NSs from all patients and, in addition, PSBs and BLs from patients BIH-CoV-01 and BIH-CoV-04 (marked with *). The sampling day relative to the onset of symptoms is given as a number in a square or triangle.

Fig. 2: Identification, distribution and classification of cells from the upper respiratory tract.

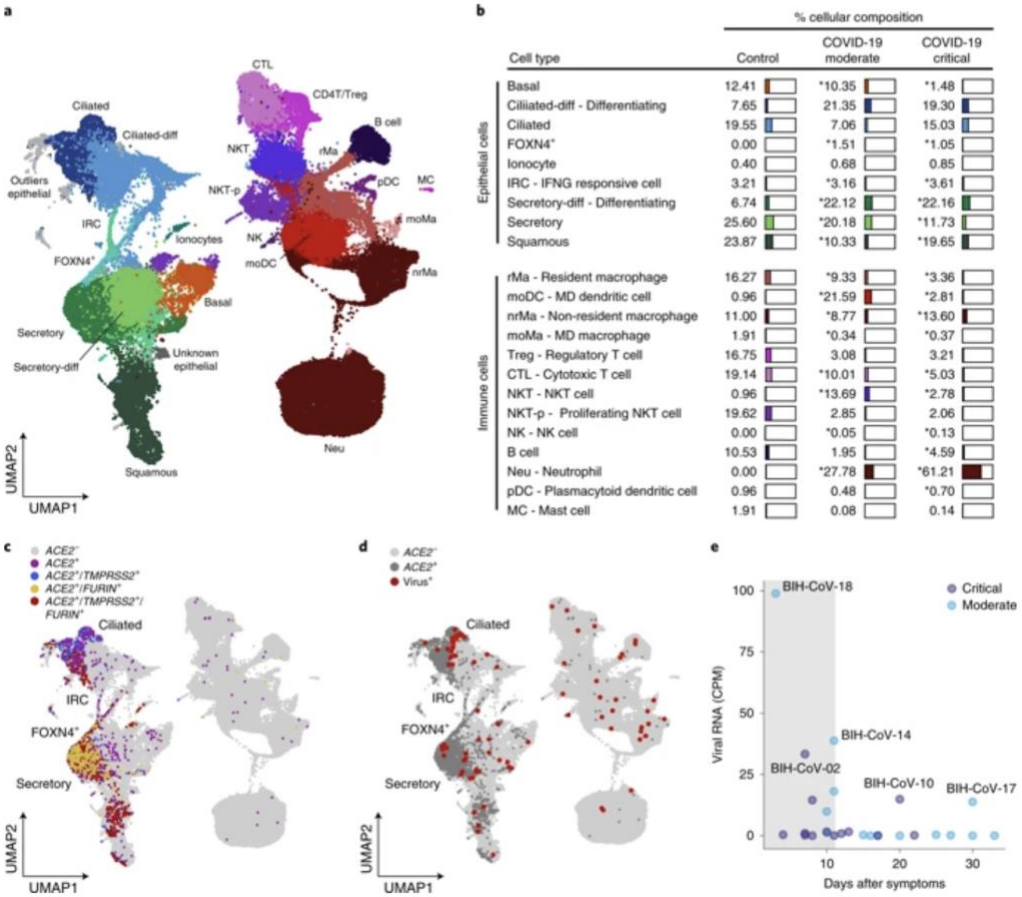


Figure 2. a, UMAP displaying all identified cell types and states. b, Table displaying the total contribution of each cell type aggregated for the controls. COVID-19 moderate and critical cases in percentage of total epithelial and immune cell types, respectively. Significant differences compared to control samples as calculated by logistic regression followed by Tukey's post hoc test and Benjamini–Hochberg correction ($P < 0.05$; see Supplementary Table 2 for exact values) are indicated by *. c, Distribution of ACE2+, ACE2+/TMPRSS2+, ACE2+/FURIN+ and ACE2+/TMPRSS2+/FURIN+ cells across all cell types within the UMAP. d, UMAP depicting ACE2+ cells (dark gray) and virus RNA+ cells (red circles). e, Viral RNA reads within aggregated pseudo-bulks for each patient sample in CPM against days after symptoms. Typically, only very low numbers of viral RNA reads were detected 11 d after first symptoms and later. NS samples were used in this analysis: n = 5 controls, n = 8 patients with moderate COVID-19 and n = 11 patients with critical COVID-19.

Fig. 3: Inferred differentiation pathways for epithelial cells from the upper respiratory tract.

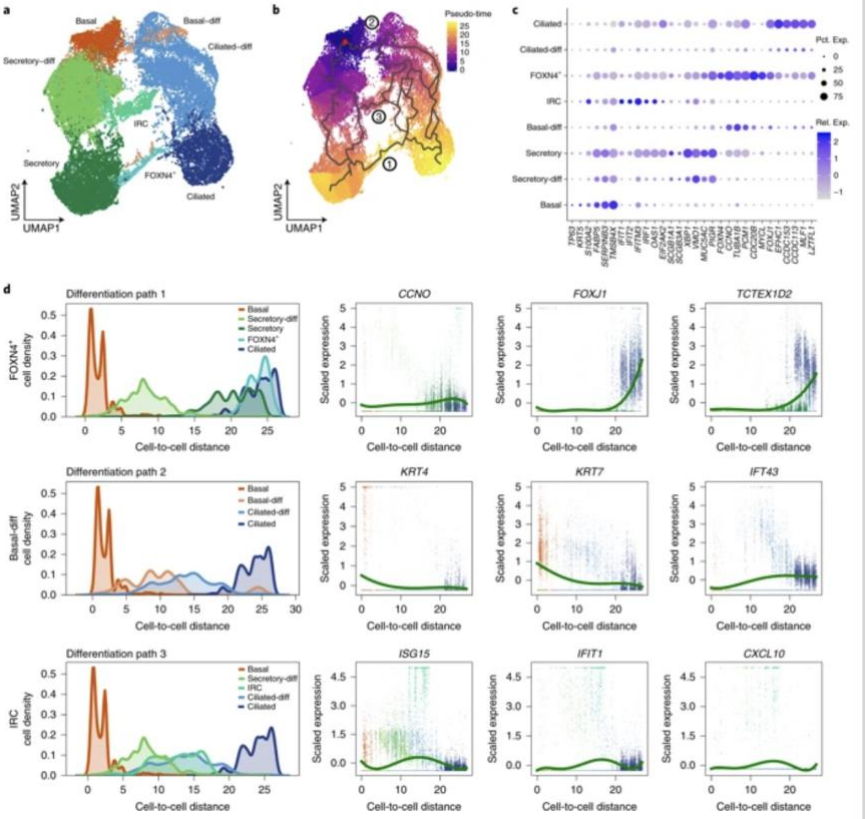


Figure 2. a, UMAP displaying all identified cell types and states. b, Table displaying the total contribution of each cell type aggregated for the controls. COVID-19 moderate and critical cases in percentage of total epithelial and immune cell types, respectively. Significant differences compared to control samples as calculated by logistic regression followed by Tukey's post hoc test and Benjamini–Hochberg correction ($P < 0.05$; see Supplementary Table 2 for exact values) are indicated by *. c, Distribution of ACE2+, ACE2+/TMPRSS2+, ACE2+/FURIN+ and ACE2+/TMPRSS2+/FURIN+ cells across all cell types within the UMAP. d, UMAP depicting ACE2+ cells (dark gray) and virus RNA+ cells (red circles). e, Viral RNA reads within aggregated pseudo-bulks for each patient sample in CPM against days after symptoms. Typically, only very low numbers of viral RNA reads were detected 11 d after first symptoms and later. NS samples were used in this analysis: n = 5 controls, n = 8 patients with moderate COVID-19 and n = 11 patients with critical COVID-19.

NEW INSIGHTS INTO THE NEUROLOGICAL EFFECTS OF COVID-19

Wood H.. Nat Rev Neurol. 2020 Jun 26. doi: 10.1038/s41582-020-0386-7. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

This article summarizes neurological findings in 84 COVID-19 patients from three studies in the United States, Belgium, and Sweden, respectively, specifically noting evidence of
1. hypoxic injury upon post-mortem neuropathological analysis of brain tissue,
2. abnormalities of parenchymal brain tissue on MRI, and
3. axonal injury indicated by increased neurofilament (NfL) light chain levels in patients' plasma.

These findings suggest injury to the central nervous system (CNS) occurs in patients with COVID-19 and indicates a need for further research into whether SARS-CoV-2 is directly involved in the CNS damage observed.

ENVIRONMENTAL CONCERN REGARDING THE EFFECT OF HUMIDITY AND TEMPERATURE ON 2019-NCOV SURVIVAL: FACT OR FICTION

Harmooshi NN, Shirbandi K, Rahim F.. Environ Sci Pollut Res Int. 2020 Jun 26. doi: 10.1007/s11356-020-09733-w. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

A literature review article by authors from Iran explores the effects of temperature, humidity, climate, skin, cloth barriers, and disinfects on the survivability and transmissibility of COVID-19 and found that COVID-19 can survive for up to 9 days at 25 °C, and that lifespan will be shortened if the temperature rises to 30 °C. They also found that the virus has a longer lifespan in 50% humidity compared to 30% humidity. These findings suggest that higher temperature and lower humidity may reduce the stability of COVID-19, but alcohol based disinfectants, masks, and social distancing are still the most effective ways to reduce disease burden.

ABSTRACT

The new coronavirus, called 2019-nCoV, is a new type of virus that was first identified in Wuhan, China, in December 2019. Environmental conditions necessary for survival and spread of 2019-nCoV are somewhat transparent but unlike animal coronaviruses. We are poorly aware of their survival in environment and precise factors of their transmission. Countries located in east and west of globe did not have a significant impact on prevalence of disease among communities, and on the other hand, north and south have provided a model for relative prediction of disease outbreaks. The 2019-nCoV can survive for up to 9 days at 25 C, and if this temperature rises to 30 C, its lifespan will be shorter. The 2019-nCoV is sensitive to humidity, and lifespan of viruses in 50% humidity is longer than that of 30%. Also, temperature and humidity are important factors influencing the COVID-19 mortality rate and may facilitate 2019-nCoV transmission. Thus, considering the available and recent evidence, it seems that low temperatures, as well as dry and unventilated air, may affect stability and transmissibility of 2019-nCoV.

DIAGNOSTIC RADIOLOGY

QUANTITATIVE CHEST CT ANALYSIS IN COVID-19 TO PREDICT THE NEED FOR OXYGENATION SUPPORT AND INTUBATION

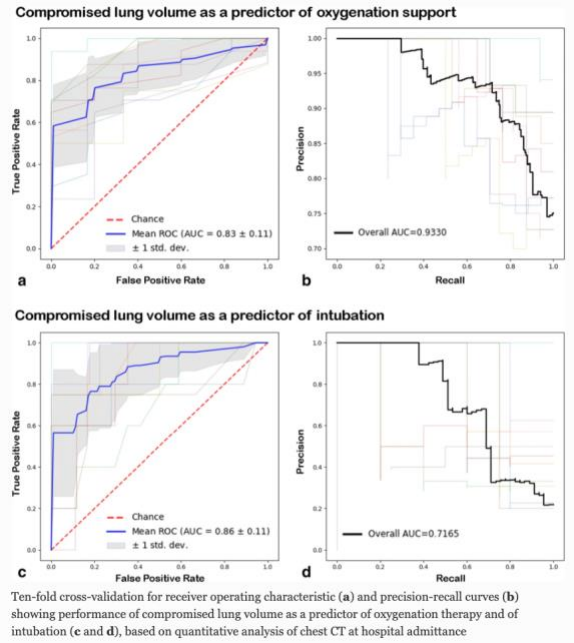
Lanza E, Muglia R, Bolengo I, Santonocito OG, Lisi C, Angelotti G, Morandini P, Savevski V, Politi LS, Balzarini L.. Eur Radiol. 2020 Jun 26. doi: 10.1007/s00330-020-07013-2. Online ahead of print.
Level of Evidence: 4 - Case-series or casecontrol studies, or poor quality prognostic cohort study

BLUF

A single-center, retrospective cohort study conducted at University Hospital in Milan, Italy from January 25 to April 28, 2020 found that the percent of compromised lung volume, as determined by a quantitative computer tomography (QCT) analysis, was an effective predictor of intubation and mortality risk among 222 hospitalized patients with COVID-19 (logistic regression, p less than 0.001) with values in the 6-23% range associated with risk for oxygenation therapy and values above 23% associated with high intubation risk (Figure 2, Table 3). This study adds to the existing literature that compromised lung volume and QCT can be used to triage COVID-19 patients upon arrival at a hospital.

ABSTRACT

OBJECTIVE: Lombardy (Italy) was the epicentre of the COVID-19 pandemic in March 2020. The healthcare system suffered from a shortage of ICU beds and oxygenation support devices. In our Institution, most patients received chest CT at admission, only interpreted visually. Given the proven value of quantitative CT analysis (QCT) in the setting of ARDS, we tested QCT as an outcome predictor for COVID-19.
METHODS: We performed a single-centre retrospective study on COVID-19 patients hospitalised from January 25, 2020, to April 28, 2020, who received CT at admission prompted by respiratory symptoms such as dyspnea or desaturation. QCT was performed using a semi-automated method (3D Slicer). Lungs were divided by Hounsfield unit intervals. Compromised lung (%CL) volume was the sum of poorly and non-aerated volumes (- 500, 100 HU). We collected patient's clinical data including oxygenation support throughout hospitalisation.
RESULTS: Two hundred twenty-two patients (163 males, median age 66, IQR 54-6) were included; 75% received oxygenation support (20% intubation rate). Compromised lung volume was the most accurate outcome predictor (logistic regression, $p < 0.001$). %CL values in the 6-23% range increased risk of oxygenation support; values above 23% were at risk for intubation. %CL showed a negative correlation with PaO2/FiO2 ratio ($p < 0.001$) and was a risk factor for in-hospital mortality ($p < 0.001$).
CONCLUSIONS: QCT provides new metrics of COVID-19. The compromised lung volume is accurate in predicting the need for oxygenation support and intubation and is a significant risk factor for in-hospital death. QCT may serve as a tool for the triaging process of COVID-19. KEY POINTS: Quantitative computer-aided analysis of chest CT (QCT) provides new metrics of COVID-19. The compromised lung volume measured in the - 500, 100 HU interval predicts oxygenation support and intubation and is a risk factor for in-hospital death. Compromised lung values in the 6-23% range prompt oxygenation therapy; values above 23% increase the need for intubation.



Ten-fold cross-validation for receiver operating characteristic (**a**) and precision-recall curves (**b**) showing performance of compromised lung volume as a predictor of oxygenation therapy and of intubation (**c** and **d**), based on quantitative analysis of chest CT at hospital admittance

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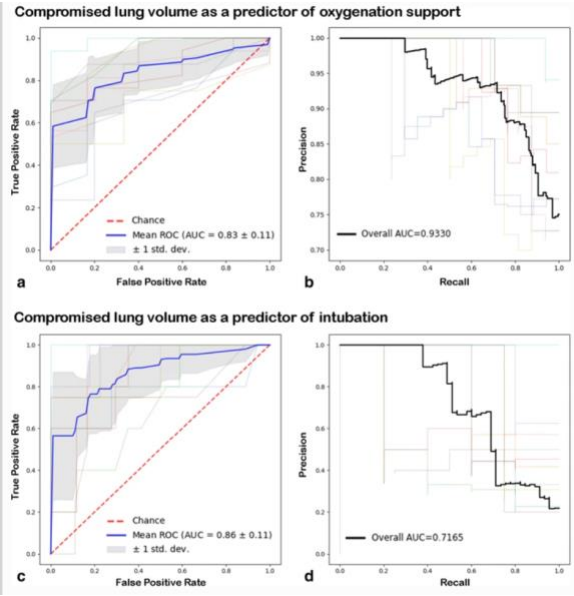


Figure 2: Ten-fold cross-validation for receiver operating characteristic (a) and precision-recall curves (b) showing performance of compromised lung volume as a predictor of oxygenation therapy and of intubation (c and d), based on quantitative analysis of chest CT at hospital admittance

Table 3 Details of oxygenation support and results of quantitative lung CT analysis

Oxygen therapy					
	No oxygenation support	**Low-flow O_2**	**High-flow O_2**	**Intubated**	**Overall**
Patients	56 (25%)	63 (29%)	58 (26%)	45 (20%)	222
PaO_2/FIO_2	..	244.4 (207.4–320)	171.43 (122.22–229.63)	128.6 (95.4–211.1)	192.0 (122.22–251.5)
Death rate	2 (1%)	15 (7%)	26 (12%)	21 (9%)	64 (29%)
Healing rate	54 (24%)	46 (21%)	30 (13%)	20 (9%)	150 (68%)
Lung segmentation median lung volume % (IQR)					
	No oxygenation support	**Low-flow O_2**	**High-flow O_2**	**Intubated**	**Overall**
Hyperinflated	15 (4.5–22)	8 (2–18)	8 (3–12)	3 (1–7)	6 (2–16)
Normal	78.5 (71–84)	77 (72–83)	77 (70–83)	61 (45–72)	76 (67–83)
Poorly aerated	5 (4–6)	8 (5–13)	11 (6–15)	22 (13–33)	9 (5–15)
Non-aerated	1 (1–2)	2 (1–4)	2 (1–3)	6 (3–16)	2 (1–4)
Compromised	6 (5–9)	11 (7–16)	13.5 (7–17)	32 (15–50)	12 (7–20)
Total (cm^3)	4726.3 (3835.8–5590.9)	4115.22 (3246.3–4915.2)	3946.51 (2826.1–4663.7)	3332.7 (2458.1–4222.6)	4057.4 (3132.3–4916.1)
Predictive value					
% Lung volume		**Any O_2**	**Low-flow O_2**	**High-flow O_2**	**Intubation**
Poorly aerated [median (IQR)]		9 (6–13)	8 (5–13)	11 (7–15)	22 (13–33)
p value			<0.001	0.08	0.4	< 0.001
Sensitivity, specificity			90.0%, 51.1%	..	..	52.8%, 97.1%
Accuracy			80.0%	..	..	88%
Compromised lung [median (IQR)]			14.5 (9–25)	11 (7–16)	14.5 (10–19)	32 (15–50)
p value			<0.001	0.13	0.14	< 0.001
Sensitivity, specificity			90.0%, 51.1%	..	..	55.6%, 97.8%
Accuracy			80.0%	..	..	89.1%

Figure 2: Ten-fold cross-validation for receiver operating characteristic (a) and precision-recall curves (b) showing performance of compromised lung volume as a predictor of oxygenation therapy and of intubation (c and d), based on quantitative analysis of chest CT at hospital admittance

CRITICAL CARE

CRITICALLY ILL PATIENTS WITH COVID-19 WITH ECMO AND ARTIFICIAL LIVER PLASMA EXCHANGE: A RETROSPECTIVE STUDY

Liu J, Dong YQ, Yin J, He G, Wu X, Li J, Qiu Y, He X.. Medicine (Baltimore). 2020 Jun 26;99(26):e21012. doi: 10.1097/MD.0000000000021012.
Level of Evidence: 3 - Non-randomized controlled cohort/follow-up study

BLUF

A single-center retrospective study in China between January 22-March 20, 2020, reviewed 23 critically-ill COVID-19 patients and found six patients required extracorporeal membrane oxygenation (ECMO) while nine required artificial liver plasma exchange. All patients received similar treatment (see below). Patients on ECMO had increased CRP, bilirubin, and pH within the first 72-hours, while patients receiving artificial liver plasma exchange showed decreased levels of cytokines post-intervention (suggesting benefit for more critically ill patients) (Table 5). Both therapies improved PaO2/FiO2 ratios (Tables 6 and 7). Overall mortality in all patients was zero on day 28 (lower than cited rates in similar populations). The author suggests these interventions, mechanical ventilation, and other supportive therapies may improve survival however additional studies are needed.

SUMMARY

Treatment:
"Lopinavir/ritonavir (2 tablets every 12 hours) combined with Arbidol (200 mg 3 times a day) were used as for the basic treatment scheme. Chloroquine phosphate was used if the basic scheme did not work. Glucocorticoids (40 mg every 12 hours) combined with intravenous immunoglobulin (0.4 g/kg of body weight) were administered once daily for at least 3 consecutive days for those who needed high-level ventilator support. Microecologics such as prebiotics or probiotics were given to patients who showed intestinal microbial dysbiosis. Human serum albumin was used for those suffering hypoproteinemia. Traditional Chinese Medicine was used as supportive therapy."

ABSTRACT

COVID-19 is an emerging infectious disease capable of causing severe pneumonia. We aimed to characterize a group of critically ill patients in a single-center study.This was a retrospective case series of 23 patients with confirmed COVID-19-related critical illness in the intensive care unit (ICU) of a hospital in Hangzhou Zhejiang Province between January 22 and March 20, 2020.Of the 23 critically ill patients, the median age was 66 years (interquartile range [IQR] 59-80 years). The median time from disease onset to ICU admission was 10 days (IQR 6-11 days), to mechanical ventilation (MV) was 11 days (IQR 7.75-13 days), to artificial liver plasma exchange was 12 days (IQR 9.75-14.75 days), and to extracorporeal membrane oxygenation (ECMO) was 22 days (IQR 17.5-30 days). Nine patients required high flow oxygen. Fourteen patients received MV. Six required ECMO. Nine received artificial liver plasma exchange. Mortality was 0 at day 28.Mortality was 0 at day 28 in our single-center study. Extracorporeal membrane oxygenation reduced the requirements for ventilator support. Artificial liver plasma exchange significantly reduced inflammatory cytokine levels. These supportive therapies helped to extend the patients' survival times and increase the chance of follow-up treatments.

FIGURES

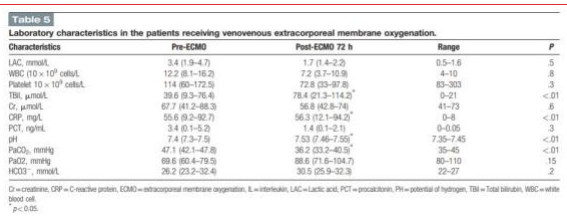


Table 5
Laboratory characteristics in the patients receiving venovenous extracorporeal membrane oxygenation.

Characteristics	Pre-ECMO	Post-ECMO 72 h	Range	P
LAC, mmol/L	3.4 (1.9–4.7)	1.7 (1.4–2.2)	0.5–1.6	.5
WBC (10×10^9 cells/L	12.2 (8.1–16.2)	7.2 (3.7–10.9)	4–10	.8
Platelet 10×10^9 cells/L	114 (60–172.5)	72.8 (33–97.8)	83–303	.3
TBIL, μmol/L	39.6 (9.3–76.4)	78.4 (21.3–114.2)*	0–21	<.01
Cr, μmol/L	67.7 (41.2–88.3)	56.8 (42.8–74)	41–73	.6
CRP, mg/L	55.6 (9.2–92.7)	56.3 (12.1–94.2)*	0–8	<.01
PCT, ng/mL	3.4 (0.1–5.2)	1.4 (0.1–2.1)	0–0.05	.3
pH	7.4 (7.3–7.5)	7.53 (7.46–7.55)*	7.35–7.45	<.01
$PaCO_2$, mmHg	47.1 (42.1–47.8)	36.2 (33.2–40.5)*	35–45	<.01
PaO2, mmHg	69.6 (60.4–79.5)	88.6 (71.6–104.7)	80–110	.15
$HCO3^-$, mmol/L	26.2 (23.2–32.4)	30.5 (25.9–32.3)	22–27	.2

Cr = creatinine, CRP = C-reactive protein, ECMO = extracorporeal membrane oxygenation, IL = interleukin, LAC = Lactic acid, PCT = procalcitonin, PH = potential of hydrogen, TBil = Total bilirubin, WBC = white blood cell.
*$p < 0.05$.

Table 5. Laboratory characteristics in the patients receiving venovenous extracorporeal membrane oxygenation.

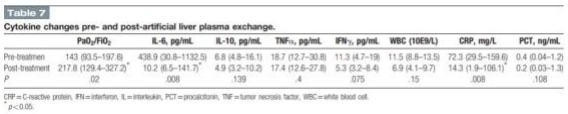


Table 7

Cytokine changes pre- and post-artificial liver plasma exchange.

	PaO_2/FiO_2	IL-6, pg/mL	IL-10, pg/mL	TNF_α, pg/mL	IFN_γ, pg/mL	WBC (10E9/L)	CRP, mg/L	PCT, ng/mL
Pre-treatmen	143 (93.5–197.6)	438.9 (30.8–1132.5)	6.8 (4.8–16.1)	18.7 (12.7–30.8)	11.3 (4.7–19)	11.5 (8.8–13.5)	72.3 (29.5–159.6)	0.4 (0.04–1.2)
Post-treatment	217.8 (129.4–327.2)*	10.2 (6.5–141.7)*	4.9 (3.2–10.2)	17.4 (12.6–27.8)	5.3 (3.2–8.4)	6.9 (4.1–9.7)	14.3 (1.9–106.1)*	0.2 (0.03–1.3)
P	.02	.008	.139	.4	.075	.15	.008	.108

CRP = C-reactive protein, IFN = interferon, IL = interleukin, PCT = procalcitonin, TNF = tumor necrosis factor, WBC = white blood cell.
* $p < 0.05$.

Table 7. Cytokine changes pre- and post-artificial liver plasma exchange.

Ventilator parameters	Pre-ECMO MV setting	Post-ECMO MV setting	P
PaO_2/FiO_2	96 (55.4–103.8)	329.4 (269.8–398.4)*	<.01
PEEP, cmH_2O	11.5 (9.2–12)	5.2 (4.6–5.8)*	<.01
Minute volume, L/min	6.8 (5.6–8.9)	9.3 (8–11.1)*	<.05
Tidal volume, mL	525 (287.5–625)	650 (500–800)*	<.05
Peak inspiratory pressure, cmH_2O	28.5 (25–30.5)	20 (18.8–21)*	<.05
Respiratory rate, breaths/min	18 (14.3–25.5)	15 (13.5–22.8)	.4

ECMO = extracorporeal membrane oxygenation, MV = mechanical ventilation.
* $p < 0.05$.

Table 7. Cytokine changes pre- and post-artificial liver plasma exchange.

GERIATRICS

THE ANOTHER SIDE OF COVID-19 IN ALZHEIMER'S DISEASE PATIENTS: DRUG-DRUG INTERACTIONS

Balli N, Kara E, Demirkan K.. Int J Clin Pract. 2020 Jun 27:e13596. doi: 10.1111/ijcp.13596. Online ahead of print.
Level of Evidence: 5 - Mechanism-based reasoning

BLUF

This article by clinical pharmacy faculty in Turkey investigates the drug-drug interactions of drugs used to treat COVID-19 and Alzheimer's disease (AD) in the elderly population. The CYP450 system is involved in the metabolism of acetylcholinesterase inhibitors as well as Lopinavir, Chloroquine and Hydoxychloroquine, which may lead to an increased, potentially toxic level of medication in a patient's system with concomitant administration. Monitoring for drug-drug interactions and choosing safer options for COVID-19 treatment in patients with AD is critically important.

ABSTRACT

Coronavirus Disease 2019 (COVID-19) outbreak caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has become a major public health problem. The elderly people are the most affected population by the COVID-19 outbreak in terms of mortality and morbidity. Delirium caused by hypoxia, a prominent clinical feature of COVID-19, may increase the need for treatment of Alzheimer's disease (AD) patients (1). Therefore, drug-drug interactions should be considered in AD patients while receiving COVID-19 treatment.

ADJUSTING PRACTICE DURING COVID-19

ACUTE CARE

AEROMEDICAL EVACUATIONS DURING THE COVID-19 PANDEMIC: PRACTICAL CONSIDERATIONS FOR PATIENT TRANSPORT

Lemay F, Vanderschuren A, Alain J.. CJEM. 2020 Jun 24:1-5. doi: 10.1017/cem.2020.434. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

Physicians from Quebec Aeromedical Evacuation Services who have organized transfers for 50 COVID-19 patients since March 11, 2020 discuss strategies to maximize patient and crew safety, enhance intubation protocols between facilities, establish protocols for early transfers, improve in-flight communications, and managing cross-contamination within aircraft (see below for details).

SUMMARY

The authors make five primary suggestions:

1. Partnering facilities and aeromedical organizations should develop shared protocols regarding their approach to mechanical ventilation and early intubation prior to transfer.
2. Early transfer of patients with ARDS to avoid placing the patient in a prone position that will increase risks of accidental dislodgement of equipment (ET tubes and IV access).
3. Improve in-flight communication by having patient information communicated to the aeromedical team before arrival and dedicated personnel in the uncontaminated zone to communicate in-flight changes to the receiving facility.
4. Fly at a lower altitude to prevent potential emergencies associated with high-altitude flights (cabin decompression leading to oxygen mask requirements)
5. All on-board crew members should wear N95 respirators once the patient boards and patient isolation areas should be established in larger aircraft (Figure 1).

FIGURES

Figure 1: An example of zones on a transfer aircraft, with the red cargo door designated for patients and medical staff as a "contaminated zone" and the front yellow door designated for uncontaminated flight personnel.

MEDICAL SUBSPECIALTIES

DERMATOLOGY

ULTRAVIOLET AND COVID-19 PANDEMIC

Türsen Ü, Türsen B, Lotti T.. J Cosmet Dermatol. 2020 Jun 23. doi: 10.1111/jocd.13559. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

Turkish dermatologic researchers discuss how in-office dermatologic treatments such as cabin-type or local devices have been halted in order to minimize the risks of COVID-19 contact or droplet transmission and examine the literature on alternative treatments and implications. They recommend at-home phototherapy treatment alternatives (see below). Additionally, they suggest ultraviolet-C rays (UV-C rays) could be used to inactivate the virus and warn that vitamin D levels should be monitored to reduce the risk of infection (see summary for further details).

SUMMARY

As of March 2020, ultraviolet treatments have been halted due to the risk of viruses living on surfaces and transmitting through the psoralen and UV-A (PUVA) treatment cabins. The authors suggest other at-home phototherapy treatment options such as:
- PUVA-Sol (use of oral or topical psoralen followed by sun exposure useful especially for psoriasis)
- Turban PUVAsol (localized immunomodulatory therapy using topical methoxsalen in a turban fashion with sun exposure for alopecia areata treatment)
- Dead Sea climatotherapy (useful for short therapy of moderate to severe psoriasis)
- Other FDA approved topical treatments (effective for vitiligo or psoriasis)

The researchers report UV-C rays have been recommended to help sterilize equipment and surfaces during the pandemic and believe germicidal UVC may efficiently inactivate bacteria and viruses, however therapy for local infections remains unknown.

While researchers acknowledge the limited reports of COVID-19 patients' vitamin D levels, they recommend screening for vitamin D deficiency as previous literature revealed insufficient levels can increase the risk of viral infection. Deficiencies should be treated with supplements or sunlight.

ABSTRACT

Coronaviruses cause COVID-19 and it is a extremely infectious viral infection. In this article, we will discuss the potential phototherapy problems and also alternative options for dermatologists, ultraviolet treatment against covid-19 virus, vitamin D-associated problems in these coronavirus days.

ENDOCRINOLOGY

SEDENTARINESS AND PHYSICAL ACTIVITY IN TYPE 2 DIABETES MELLITUS DURING THE COVID-19 PANDEMIC

Balducci S, Coccia EM.. Diabetes Metab Res Rev. 2020 Jun 27:e3378. doi: 10.1002/dmrr.3378. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

Italian authors reviewed the effects of physical activity in patients with type 2 diabetes mellitus (T2DM) during the COVID-19 pandemic. The authors cite previous studies that link physical activity with reduced incidence and duration of upper respiratory tract infections and improved mobilization of immune cells to suggest that physical activity may be associated with better outcomes if infected with COVID-19. They acknowledge this evidence is limited but recommend T2DM patients continue their recommended level of physical activity to enhance metabolic health and immunity (Figure 1).

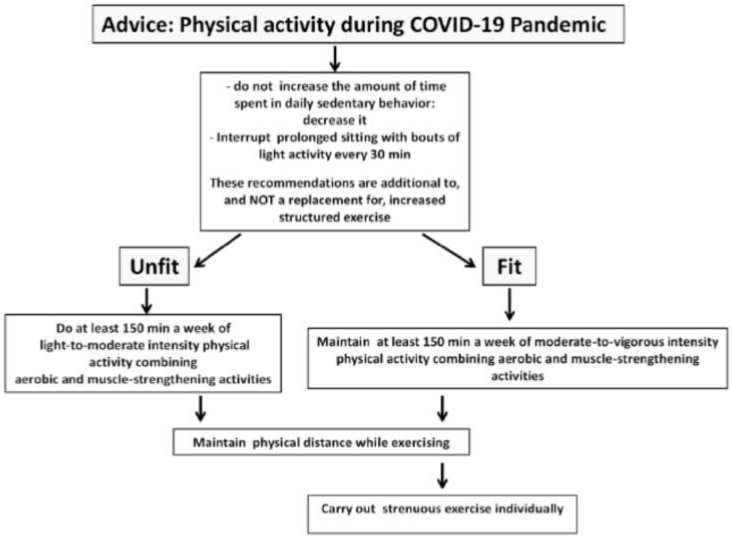


Figure 1. Lifestyle (Sedentary Time and Physical Activity) suggestions for T2DM patients during COVID-19 Pandemic

Figure 1. Lifestyle (Sedentary Time and Physical Activity) suggestions for T2DM patients during COVID-19 Pandemic

EVALUATION OF NOVEL CORONAVIRUS DISEASE (COVID-19) USING QUANTITATIVE LUNG CT AND CLINICAL DATA: PREDICTION OF SHORT-TERM OUTCOME

Matos J, Paparo F, Mussetto I, Bacigalupo L, Veneziano A, Perugin Bernardi S, Biscaldi E, Melani E, Antonucci G, Cremonesi P, Lattuada M, Pilotto A, Pontali E, Rollandi GA.. Eur Radiol Exp. 2020 Jun 26;4(1):39. doi: 10.1186/s41747-020-00167-0.
Level of Evidence: 4 - Case-control studies, or "poor or non-independent reference standard

BLUF

A single-center study conducted March 1-22, 2020 enrolled 106 patients (median age 63.5 years, 38.7% women) with pneumonia symptoms, SARS-CoV-2 positive by RT-PCR. Data was input into models and the authors determined C-reactive protein ($p<0.001$) and lymphocyte % ($p=0.008$) correlated with volume of disease (VoD) from CT scan. The author concluded VoD predicted from CRP and lymphocyte % allows good estimation of COVID-19 burden while Support Vector Machine model (AUC=0.92) best predicts the short term outcome of COVID-19 (Figure 5).

ABSTRACT

BACKGROUND: Computed tomography (CT) enables quantification of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, helping in outcome prediction.
METHODS: From 1 to 22 March 2020, patients with pneumonia symptoms, positive lung CT scan, and confirmed SARS-CoV-2 on reverse transcription-polymerase chain reaction (RT-PCR) were consecutively enrolled. Clinical data was collected. Outcome was defined as favourable or adverse (i.e., need for mechanical ventilation or death) and registered over a period of 10 days following CT. Volume of disease (VoD) on CT was calculated semi-automatically. Multiple linear regression was used to predict VoD by clinical/laboratory data. To predict outcome, important features were selected using a priori analysis and subsequently used to train 4 different models.
RESULTS: A total of 106 consecutive patients were enrolled (median age 63.5 years, range 26-95 years; 41/106 women, 38.7%). Median duration of symptoms and C-reactive protein (CRP) was 5 days (range 1-30) and 4.94 mg/L (range 0.1-28.3), respectively. Median VoD was 249.5 cm3 (range 9.9-1505) and was predicted by lymphocyte percentage ($p = 0.008$) and CRP ($p < 0.001$). Important variables for outcome prediction included CRP (area under the curve [AUC] 0.77), VoD (AUC 0.75), age (AUC 0.72), lymphocyte percentage (AUC 0.70), coronary calcification (AUC 0.68), and presence of comorbidities (AUC 0.66). Support vector machine had the best performance in outcome prediction, yielding an AUC of 0.92. CONCLUSIONS: Measuring the VoD using a simple CT post-processing tool estimates SARS-CoV-2 burden. CT and clinical data together enable accurate prediction of short-term clinical outcome.

Volume of disease (cm^3; median, range)	249.5 (9.9–1505)
Uni/bilateral	
Unilateral	7/106 (6.6%)
Bilateral	99/106 (93.4%)
Affected lobes	
Only lower lobe(s)	5/106 (4.7%)
Lower lobe(s) + at least one other lobe	97/106 (91.5%)
No lower lobe involvement	4/106 (3.8%)
Gradient	
Apicobasal gradient	49/106 (46.2%)
No apicobasal gradient	57/106 (53.8%)
Distribution	
Peripheral	39/106 (36.8%)
Central	2/106 (1.9%)
Mixed	65/106 (61.3%)
CT pattern	
Pure GGO	11/106 (10.4%)
GGO + septal thickening	46/106 (43.4%)
GGO + consolidation	49/106 (46.2%)
Predominant type	
GGO	79/106 (74.5%)
Consolidation	27/106 (25.5%)
CT sign	
Reverse halo	7/106 (6.6%)
Linear opacities	66/106 (62.3%)
Nodules	28/106 (26.4%)
Secondary findings	
Emphysema	13/106 (12.3%)
Fibrosis	8/106 (7.5%)
Enlarged lymph nodes (≥ 10 mm short axis)	33/106 (31.1%)
Pleural effusion	10/106 (9.4%)
Pleural thickening	15/106 (14.15%)
Aortic Calcification	45/106 (42.5%)
Coronary calcification	53/106 (50.0%)
Other	
Pneumomediastinum	1/106 (0.9%)
Iatrogenic pneumothorax and subcutaneous emphysema	1/106 (0.9%)

GGO Ground-glass opacities

Table 2. Quantitative and qualitative computed tomography (CT) findings related to COVID-19, and secondary CT findings.

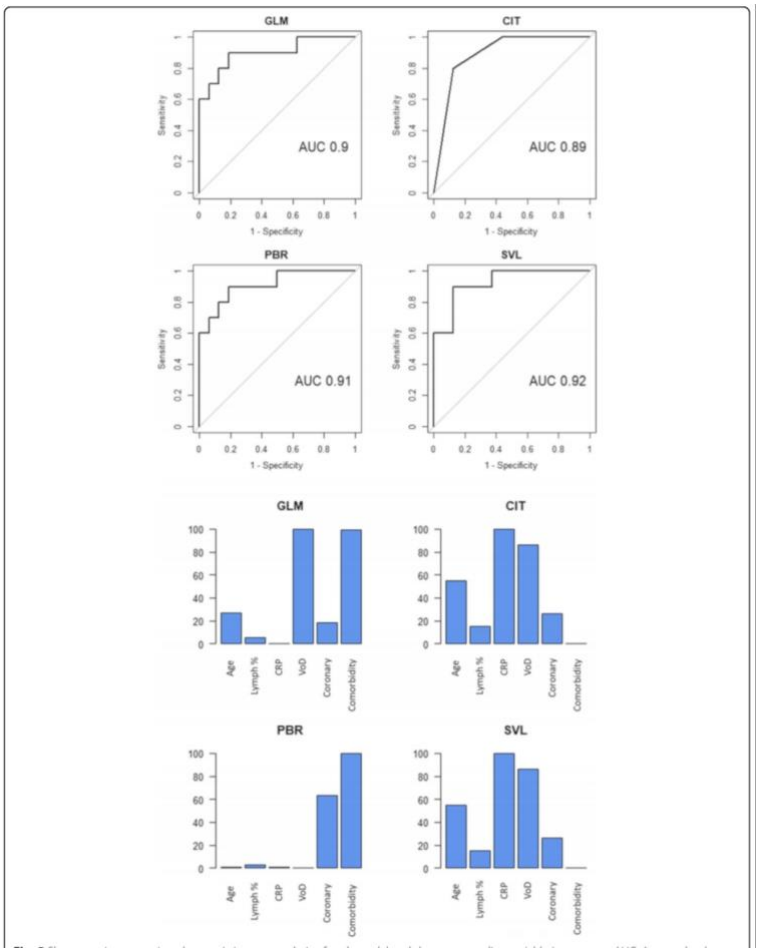


Figure 5. Shows receiver operating characteristic curve analysis of each model and the corresponding variable importance. CIT - Conditional inference trees, GLM - Generalised linear model, PBR - Penalised binomial regression, SVL - Support vector machine with the linear kernel. VoD, Volume of disease.

DEVELOPMENTS IN TREATMENTS

IN-SILICO INVESTIGATION OF PHYTOCHEMICALS FROM ASPARAGUS RACEMOSUS AS PLAUSIBLE ANTIVIRAL AGENT IN COVID-19

Chikhale RV, Sinha SK, Patil RB, Prasad SK, Shakya A, Gurav N, Prasad R, Dhaswadikar SR, Wanjari M, Gurav SS.. J Biomol Struct Dyn. 2020 Jun 24:1-15. doi: 10.1080/07391102.2020.1784289. Online ahead of print.
Level of Evidence: 5 - Mechanism-based reasoning

BLUF

An in-silico study analyzing the effectiveness of phytochemicals present in Asparagus racemosus against two SARS-CoV-2 proteins - spike receptor-binding domain (RBD) (S protein) and Nsp15 Endoribonuclease (N protein) through docking and molecular dynamics studies (MDS) followed by MM-GBSA (Molecular mechanics - Generalised Born Solvent Accessibility). Remdesivir was the reference drug used and the study results suggest some of the phytochemicals tested may have improved docking and binding in comparison (results summarized below)

SUMMARY

- The docking analysis (Schrodinger Glide module) and affinity studies showed Asparocide-C has the highest docking score against S and N proteins (-7.542, -7.165 respectively), followed by other phytochemicals and Remdesivir with the lowest score (Table 2, 3).
- Molecular Dynamics (100ns) study depicted Asparocide-C and Asparocide-F stabilized spike protein complex and Nsp15

Endoribonuclease respectively with low RMSD than other phytochemicals.
- These were followed by MM-GBSA binding free energy, suggesting Asparocide D and C bound to spike RBD (-66.49, -62.61 Kcal/mol respectively) and Asparocide D and F with N protein (-72.46, -55.19 Kcal/mol respectively).
- Remdesevir exhibited a low binding affinity to both S and N protein than other phytochemicals (evident from Table 1).

ABSTRACT

COVID-19 has ravaged the world and is the greatest of pandemics in human history, in the absence of treatment or vaccine the mortality and morbidity rates are very high. The present investigation was undertaken to screen and identify the potent leads from the Indian Ayurvedic herb, Asparagus racemosus (Willd.) against SARS-CoV-2 using molecular docking and dynamics studies. The docking analysis was performed on the Glide module of Schrodinger suite on two different proteins from SARS-CoV-2 viz. NSP15 Endoribonuclease and spike receptor-binding domain. Asparoside-C, Asparoside-D and Asparoside -F were found to be most effective against both the proteins as confirmed through their docking score and affinity. Further, the 100 ns molecular dynamics study also confirmed the potential of these compounds from reasonably lower root mean square deviations and better stabilization of Asparoside-C and Asparoside-F in spike receptor-binding domain and NSP15 Endoribonuclease respectively. MM-GBSA based binding free energy calculations also suggest the most favourable binding affinities of Asparoside-C and Asparoside-F with binding energies of -62.61 and -55.19 Kcal/mol respectively with spike receptor-binding domain and NSP15 Endoribonuclease. HighlightsAsparagus racemosus have antiviral potentialPhytochemicals of Shatavari showed promising in-silico docking and MD resultsAsparaoside-C and Asparoside-F has good binding with target proteinsAsparagus racemosus holds promise as SARS-COV-2 (S) and (N) proteins inhibitor Communicated by Ramaswamy H. Sarma.

FIGURES

Table 4. Binding free energy components for the protein ligand complexes calculated by MM-GBSA analysis.

	MM-GBSA*						
Compounds	ΔE_{VDW}	ΔE_{ELE}	ΔG_{GB}	ΔG_{Surf}	ΔG_{gas}	ΔG_{Sol}	ΔG_{bind}
6M0J							
AsparosideC	−35.36 (11.09)	−26.07 (9.44)	54.24 (9.48)	−5.84 (1.60)	−111.00 (15.62)	48.39 (8.42)	−62.61 (8.95)
AsparosideD	−27.58 (7.17)	−41.21 (16.73)	54.61 (13.72)	−5.12 (1.10)	−115.98 (21.37)	49.48 (12.89)	−66.49 (10.28)
ShatawarinI	−35.45 (4.28)	−24.34 (13.49)	47.34 (10.97)	−5.34 (0.70)	−97.19 (15.55)	41.99 (10.49)	−55.19 (6.81)
Remdesivir	−29.02 (3.59)	−48.96 (7.82)	58.92 (6.14)	−4.98 (0.36)	−72.39 (9.14)	53.94 (5.88)	−18.45 (4.64)
6W01							
AsparosideC	−29.19 (3.63)	−65.14 (16.10)	72.17 (10.64)	−6.96 (0.53)	−124.62 (10.09)	65.20 (11.20)	−51.42 (6.11)
AsparosideD	−36.70 (4.59)	−50.19 (24.12)	67.51 (20.59)	−6.13 (0.75)	−133.84 (24.98)	61.37 (20.02)	−72.46 (7.02)
AsparosideF	−30.51 (5.46)	−62.78 (20.97)	82.24 (16.76)	−5.53 (0.69)	−132.02 (21.22)	76.71 (16.30)	−55.30 (6.06)
Remdesivir	−17.18 (7.29)	−16.34 (11.16)	28.14 (11.97)	−2.71 (0.94)	−25.55 (16.69)	25.43 (11.26)	−0.12 (6.89)

*All energies are in Kcal/mol with standard deviation in parenthesis.
ΔE_{VDW} = van der Waals contribution from MM; ΔE_{ELE} = electrostatic energy as calculated by the MM force field; ΔG_{GB} = the electrostatic contribution to the solvation free energy calculated by GB; ΔG_{Surf} = solvent-accessible surface area; ΔG_{Sol} = solvation free energy; ΔG_{gas} = gas phase interaction energy; ΔG_{bind} =Binding free energy.

Table 4: Binding free energy components of ligand complexes calculated by MM-GBSA [Molecular mechanics - Generalised Born Solvent Accessibility].

[This table shows that the binding energies against S protein - Asparocide-D (-66.49 Kcal/mol), Asparocide-C (-62.61 Kcal/mol), and Remdesevir (-18.45 Kcal/mol).
Binding energies against N protein - Asparocide-D (-72.46Kcal/mol), Asparocide-F (-55.19 Kcal/mol), and Remdesevir (-0.12 Kcal/mol).]

Table 1. List of bio-actives with docking scores with the PDB: **6W01** and PDB: **6M0J** of SARS-CoV-2.

			Docking Score	
Sr. No.	Pubchem CID	Name	6W01	6M0J
1	158598	Asparoside-C	−7.542	−7.165
2	158597	Asparoside-D	−7.069	−6.445
3	101406647	Shatavarin-I (Asparaoside-B)	−6.524	−5.524
4	101847691	Shatavarin-X	−6.431	−5.621
5	102253062	Racemoside-A	−6.238	−5.993
6	101422489	Asparoside-A	−6.03	−5.396
7	101847687	Shatavarin-VI	−5.747	−3.961
8	102253063	Racemoside-B	−5.713	−5.409
9	129626614	Asparagoside-F	−5.609	−6.615
10	5280343	Quercetin	−5.605	−4.519
11	158595	Asparanin-D	−5.551	−5.001
12	44203607	Shatavaroside-B	−5.477	−5.348
13	5280863	Kaempferol	−5.357	−4.569
14	273773749	Curillin-H	−5.254	−5.952
15	121304016	Remdesivir	−5.28	−5.94

Table 1: List of bioactive ligands with docking scores against Spike protein receptor binding domain and Nsp15 Endoribonuclease. [It is inferred from the above table that Docking scores of Asparocide-C is the highest for both S and N proteins (-7.452, -7.165 respectively) than other ligands. Remdesevir exhibits docking scores of -5.28 and -5.94 adaonst S and N proteins respectively.]

Table 2. Binding interaction of different bioactive herbal ligands with the active site of SARS-CoV-2 spike RBD (PDB ID: **6M0J**).

S. No.	Ligand	Interaction (PDB-6M0J) H-Bonding	No. of H-Bond HBD	HBA
1	Asparoside-C	Gly 496, Gln 414, Ser 494, Thr 415, Tyr 453	6	2
2	Asparoside-D	Gly 502, Ser 494, Lys 417, Asp 420 Tyr 449, Gln 498	4	3
3	Shatavarin-I	Gly 447, Lys 444, Glu 406, Arg 403, Gly 496	4	3
4	Shatavarin-X	Gly 496, Lys 417, Glu 406,Gln 409,Tyr 453, Arg 403	2	5
5	Racemoside-A	Glu 484, Gly 496, Ser 494	4	1
6	Remdesivir	Arg 403, Glu 406, Tyr 453	1	2

H-Bond: Hydrogen Bonding, HBD: Hydrogen bond donor, HBA: Hydrogen bond acceptor in respect to ligand.

Table 3. Binding interaction of different bioactive herbal ligands with the active site of SARS-CoV-2 NSP15 endoribonuclease (PDB ID: **6W01**).

S. No.	Ligand	Interaction (PDB-6M0J) H-Bonding	No. of H-Bond HBD	HBA
1	Asparoside-C	Glu 234, Gly 230, Val 292, Hip 235, Asp 240	5	3
2	Asparoside-F	Glu 234, Gly 230, Ala 232, Hip 235, Asp 240, Glu 340, Val 339	5	3
3	Asparoside-D	Glu 340, His 243, Gln 245, Asp 240, Asn 278, Leu 346	6	1
4	Rutin	Asp 240, Gln 245, Hip 235, Hip 250, Glu 340	4	3
5	Racemoside-A	Thr 341, Hip 235, Glu 340, Hip 250	3	3
6	Remdesivir	Val 292, Hip 235, Thr 341	1	2

H-Bond: Hydrogen Bonding, HBD: Hydrogen bond donor, HBA: Hydrogen bond acceptor in respect to ligand.

Table 1: List of bioactive ligands with docking scores against Spike protein receptor binding domain and Nsp15 Endoribonuclease.[It is inferred from the above table that Docking scores of Asparocide-C is the highest for both S and N proteins (-7.452, -7.165 respectively) than other ligands.
Remdesevir exhibits docking scores of -5.28 and -5.94 adaonst S and N proteins respectively.]

IDENTIFICATION OF A POTENTIAL PEPTIDE INHIBITOR OF SARS-COV-2 TARGETING ITS ENTRY INTO THE HOST CELLS

Baig MS, Alagumuthu M, Rajpoot S, Saqib U.. Drugs R D. 2020 Jun 26. doi: 10.1007/s40268-020-00312-5. Online ahead of print.
Level of Evidence: Other - Modeling

BLUF

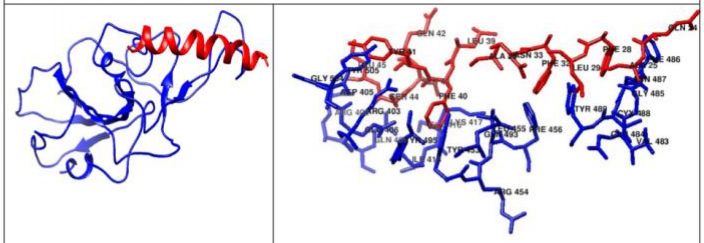
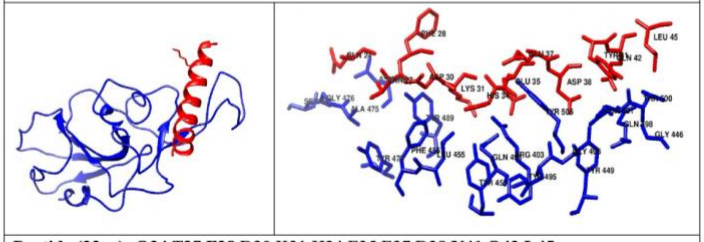
An in-silico study conducted by researchers at the Indian Institute of Technology Indore (IITI) utilized docking and molecular dynamics simulations and found that their inhibitory peptide of 18-amino acids (truncated down from initially 25 amino acids) has the capacity to interfere with the interaction of SARS-CoV-2 S-glycoprotein with the ACE2 receptor, preventing viral entry into the cell (Table 2, Figure 4). Based on their findings, the authors suggest that inhibitory peptides may be developed as SARS-CoV-2 treatment and are continuing their investigation in this area with cell-based assays.

ABSTRACT

BACKGROUND AND OBJECTIVE: Coronavirus disease (COVID-19) is an ongoing pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Due to the incessant spread of the disease with substantial morbidity and mortality rates, there is an urgent demand for effective therapeutics and vaccines to control and diminish this pandemic. A critical step in the crosstalk between the virus and the host cell is the binding of SARS-CoV-2 spike protein to the angiotensin-converting enzyme 2 (ACE2) receptor present on the surface of the host cells. Hence, inhibition of this interaction could be a promising strategy to combat the SARS-CoV-2 infection.
METHODS: Docking and Molecular Dynamics (MD) simulation studies revealed that designed peptide maintains their secondary structure and provide a highly specific and stable binding (blocking) to SARS-CoV-2. RESULTS: We have designed a novel peptide that could inhibit SARS-CoV-2 spike protein interaction with ACE2, thereby blocking the cellular entry of the virus.
CONCLUSION: Our findings suggest that computationally developed inhibitory peptide may be developed as an anti-SARS-CoV-2 agent for the treatment of SARS-CoV-2 infection. We further plan to pursue the peptide in cell-based assays and eventually for clinical trials.

FIGURES

Table 2 Interacting residues (1) at the interface of SARS-CoV-2 and the docked 18 aa peptide; and (2) at the interface of SARS-CoV-2 and the docked 23 aa peptide

1) At the interface of SARS-CoV-2 (blue) and the docked 18 aa peptide (red).

Peptide (18 aa): Q24 A25 **F28** L29 F32 E33 A36 L39 F40 **Y41 Q42** S43 S44 **L45**
SARS-CoV-2: R403 D405 E406 R408 Q409 G416 K417 I418 **Y453** R454 **L455**
F456 V483 E484 G485 F486 **N487** C488 **Y489 Q493 Y495** G504 **Y505**
2.) At the interface of SARS-CoV-2 (blue) and the docked 23 aa peptide (red).

Peptide (23aa): Q24 T27 **F28** D30 K31 H34 E35 E37 D38 **Y41 Q42 L45**
SARS-CoV-2: R403 G446 Y449 **Y453 L455 F456** Y473 A475 G476 S477 **N487 Y489 Q493 Y495** G496 Q498 T500 N501 **Y505**

The underlined and bold residues are making strong interactions between the peptides and SARS-CoV-2 spike protein

SARS-CoV-2 severe acute respiratory syndrome coronavirus 2, *ACE2* angiotensin-converting enzyme 2, *PD* peptidase domain

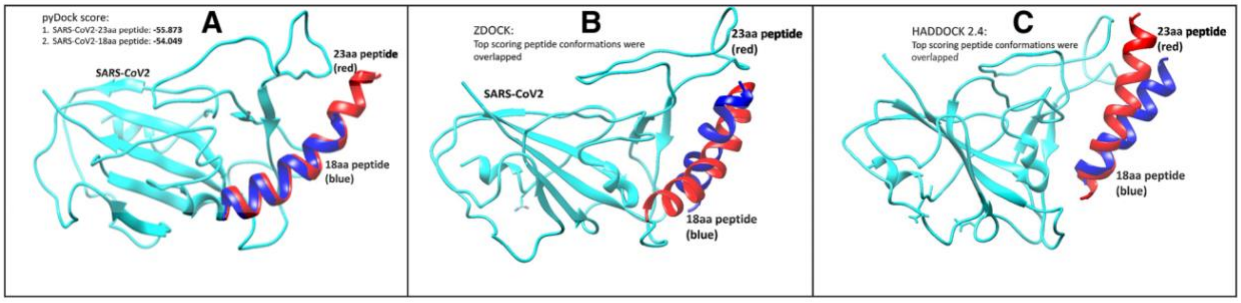


Fig. 4 SARS-CoV-2 (Cyan) interaction with the 18aa-derived peptide (blue) along with the original peptide of 23-amino acid (red). Dockings were performed using different software packages: **a** pyDock; **b** ZDOCK; and **c** HADDOCK 2.4. *SARS-CoV-2* severe acute respiratory syndrome coronavirus 2

HYDROXYCHLOROQUINE, COVID-19 AND DIABETES. WHY IT IS A DIFFERENT STORY

Stoian AP, Catrinoiu D, Rizzo M, Ceriello A.. Diabetes Metab Res Rev. 2020 Jun 27. doi: 10.1002/dmrr.3379. Online ahead of print.

Level of Evidence: Other - Expert Opinion

BLUF

In this expert opinion, a group of international researchers discuss the role of hydroxychloroquine in the management of COVID-19. Though previous studies have demonstrated that the medication is not an effective treatment for the virus, the

researchers have hypothesized that hydroxychloroquine may be beneficial in managing COVID-19 symptoms in diabetics due to its anti-hyperglycemic effects. Further research is necessary to explore these potential therapeutic effects.

PHARMACOINFORMATICS AND MOLECULAR DYNAMICS SIMULATION STUDIES REVEAL POTENTIAL COVALENT AND FDA-APPROVED INHIBITORS OF SARS-COV-2 MAIN PROTEASE 3CL(PRO)

Alamri MA, Tahir Ul Qamar M, Mirza MU, Bhadane R, Alqahtani SM, Muneer I, Froeyen M, Salo-Ahen OMH.. J Biomol Struct Dyn. 2020 Jun 24:1-13. doi: 10.1080/07391102.2020.1782768. Online ahead of print.
Level of Evidence: Other - Mechanism-based reasoning

BLUF

Researchers in Saudia Arabia and China conducted an in-silico study using pharmacoinformatics, molecular dynamic, and molecular docking simulations to determine that two current protease inhibitors (paritaprevir and simeprevir) could potentially act against the SARS-CoV-2 virus, specifically by inhibiting the SARS-CoV-2 3-chymotrypsin-like protease (3CLpro) which plays a key role in virus transcription and replication (Figure 5). This research suggests that these drugs may be good candidates for clinical trials to determine their efficacy in COVID-19 patients.

SUMMARY

Summarizing excerpt:
"The binding affinity, mechanism, and stability of binding of these compounds to SARS-CoV-2 3CLpro were investigated by molecular docking and MD simulations. The potential warheads identified in this study could serve as a guideline to design covalent inhibitors targeting the catalytic Cys145. Moreover, the FDA approved anti-HCV drugs, paritaprevir and simeprevir may also play a key role in expediting the drug discovery process and could be tested in clinical trials as a treatment for COVID-19."

ABSTRACT

The SARS-CoV-2 was confirmed to cause the global pandemic of coronavirus disease 2019 (COVID-19). The 3-chymotrypsin-like protease (3CLpro), an essential enzyme for viral replication, is a valid target to combat SARS-CoV and MERS-CoV. In this work, we present a structure-based study to identify potential covalent inhibitors containing a variety of chemical warheads. The targeted Asinex Focused Covalent (AFCL) library was screened based on different reaction types and potential covalent inhibitors were identified. In addition, we screened FDA-approved protease inhibitors to find candidates to be repurposed against SARS-CoV-2 3CLpro. A number of compounds with significant covalent docking scores were identified. These compounds were able to establish a covalent bond (C-S) with the reactive thiol group of Cys145 and to form favorable interactions with residues lining the substrate-binding site. Moreover, paritaprevir and simeprevir from FDA-approved protease inhibitors were identified as potential inhibitors of SARS-CoV-2 3CLpro. The mechanism and dynamic stability of binding between the identified compounds and SARS-CoV-2 3CLpro were characterized by molecular dynamics (MD) simulations. The identified compounds are potential inhibitors worthy of further development as COVID-19 drugs. Importantly, the identified FDA-approved anti-hepatitis-C virus (HCV) drugs paritaprevir and simeprevir could be ready for clinical trials to treat infected patients and help curb COVID-19. Communicated by Ramaswamy H. Sarma.

FIGURES

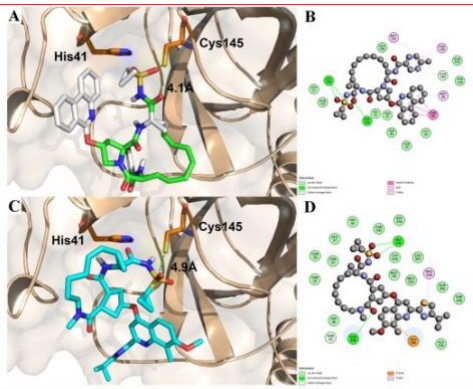


Figure 5. 3D binding mode and 2D molecular interactions of identified candidate compounds within the active site of SARS-CoV-2 3CL^{pro} (PDB ID 6LU7); (**A–B**) paritaprevir; (**C–D**) simeprevir. The catalytic dyad His41, Cys145 within the active site is shown in orange sticks.

Figure 5. 3D binding mode and 2D molecular interactions of identified candidate compounds within the active site of SARS-CoV-2 3CLpro (PDB ID 6LU7); (A–B) paritaprevir; (C–D) simeprevir. The catalytic dyad His41, Cys145 within the active site is shown in orange sticks

THE EXAMINATION OF SLEEP QUALITY FOR FRONTLINE HEALTHCARE WORKERS DURING THE OUTBREAK OF COVID-19

Jahrami H, BaHammam AS, AlGahtani H, Ebrahim A, Faris M, AlEid K, Saif Z, Haji E, Dhahi A, Marzooq H, Hubail S, Hasan Z.. Sleep Breath. 2020 Jun 26. doi: 10.1007/s11325-020-02135-9. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

A cross-sectional study was conducted in Bahrain during April 2020 on 129 front line healthcare workers (FLHCW) and 128 non-front line healthcare workers (NFLHCW) to assess and compare sleep quality during the COVID-19 pandemic. Although not statistically significant, using the Pittsburgh Sleep Quality Index (PSQI) to measure sleep quality and the Perceived Stress Scale (PSS) to measure stress, it was found that FLHCW had poorer sleep quality and higher perceived stress. Individual measures of sleep disturbance and stress are demonstrated in Table 2. This study may suggest that in light of the COVID-19 pandemic, intervention should be put in place to improve healthcare worker stress levels and sleep quality.

ABSTRACT

PURPOSE: Few studies have addressed the sleep disturbances of healthcare workers during crisis events of public health. This study aimed to examine the sleep quality of frontline healthcare workers (FLHCW) in Bahrain during the COVID-19 pandemic, and compare it with the sleep quality of non-frontline healthcare workers (NFLHCW).
METHODS: Healthcare workers (n = 280) from multiple facilities belonging to the Ministry of Health, Bahrain, were invited to participate in this cross-sectional study. An online questionnaire, including socio-demographics, the Pittsburgh Sleep Quality Index (PSQI), and the Perceived Stress Scale (PSS), was used to evaluate sleep disturbances and stress levels of healthcare workers. Poor sleep quality was defined as PSQI >= 5 and moderate-severe stress as PSS >= 14. Descriptive statistics were used to compare the scores of FLHCW and NFLHCW. Univariate and multivariate binary logistic regressions were used to identify predictors of poor sleep quality, moderate-severe stress, and the combined problem of poor sleep quality and moderate-severe stress.
RESULTS: A total of 257 participants (129 FLHCW and 128 NFLHCW) provided usable responses. The overall PSQI and PSS scores were 7.0 +- 3.3 and 20.2 +- 7.1, respectively. The FLHCW scored higher in the PSQI and PSS compared with the NFLHCW; however, the differences in the PSQI and PSS scores were not statistically significant. For the FLHCW, 75% were poor sleepers, 85% had moderate-severe stress, and 61% had both poor sleep quality and moderate-severe stress. For the NFLHCW, 76% were poor sleepers, 84% had moderate-severe stress, and 62% had both poor sleep quality and moderate-severe stress. Female sex and professional background were the predictors of poor sleep quality and stress.
CONCLUSIONS: Poor sleep quality and stress are common during the COVID-19 crisis. Approximately, 60% of both FLHCW and NFLHCW have poor sleep quality combined with moderate-severe stress.

FIGURES

Table 1 Socio-demographic characteristics of the study participants

Variable	Overall $N = 257$	FLHCW $N = 129$	NFLHCW $N = 128$	P Value
Sex				
Male	77 (30.0%)	40 (31.0%)	37 (28.9%)	0.7
Female	180 (70.0%)	89 (69.0%)	91 (71.1%)	
Marital status				
Single	28 (10.9%)	16 (12.4%)	12 (9.4%	0.5
Married	229 (89.1%)	113 (87.6%)	116 (90.6%)	
Professional background				
Medical doctor	80 (31.1%)	43 (33.3%)	25 (19.5%)	0.2
Registered nurse	119 (46.3%)	53 (41.1%)	66 (51.6%)	
Allied healthcare professionals	58 (22.6%)	33 (25.6%)	37 (28.9%)	
Age (year)	40.2 ± 9.7	39.7 ± 9.9	40.5 ± 9.5	0.7

FLHCW, frontline healthcare workers; *NFLHCW*, non-frontline healthcare workers

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CONTRIBUTORS

Akshara Malla
Alisa Malyavko
Alvin Rafou
Ben Showalter
Carter Butuk
Eva Shelton
Jesse Abelson
Julia Ghering
Krithika Kumarasan
Maresa Woodfield
Maya Patel
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