The Daily COVID-19 Literature Surveillance Summary

September 01, 2020

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

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

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

How to cite the Levels of Evidence Table

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

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

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

EXECUTIVE SUMMARY

Epidemiology

- Investigators affiliated with the Laboratorio de Investigacao Medica em Envelhecimento at Universidade de Sao Paulo performed a longitudinal, observational study on 707 COVID-19 patients admitted to a tertiary university hospital in Sao Paulo, Brazil and found that 33% (n=234) of patients had descriptors of delirium (confusional state, disorientation, hallucinations, etc;). Additionally, delirium was independently associated with length of hospital stay, ICU admission, and in-hospital deaths in adults older than the age of 50. Based on these findings, the authors suggest that healthcare workers should assess for delirium among COVID-19 patients, which may help monitor the severity and prognosis of these patients.

Transmission & Prevention

- Authors affiliated with several institutions in China performed a cross-sectional study on the daily COVID-19 cases, air quality, and meteorological factors in 33 locations in China. Among their findings, the authors note an association between relative risk of COVID-19 spread and air quality index (AQI) that was greater between 10 degrees Celsius and 20 degrees Celsius and a possibly stronger AQI impact on confirmed COVID-19 cases between the range of 10% to 20% relative humidity, respectively, suggesting that AQI may play a role in COVID-19 transmission in both low temperatures and low humidity, although further investigation is needed.

- An opinion piece by Lancet Infectious Diseases discusses the changes made to airline travel to mitigate the transmission of SARS-CoV-2 such as closing international borders, mandating masks, reducing passenger numbers, and increasing cleaning efforts. This article suggests that in the future, airlines may permanently increase preventative measures such as utilizing touchless technology, requiring masks and vaccines, improving cleaning, and reducing services to prevent transmission, similar to the increases in airline security seen following the September 11th, 2001 terrorist attacks.

Management

- A literature review was conducted by pharmacists from Yale, Cleveland Clinic, and University of Pittsburgh regarding alternative drugs for managing analgesia, sedation, and paralysis in COVID-19 patients requiring mechanical ventilation in the event of drug shortages, as detailed in the summary section below. These conservative and alternative management strategies for mechanically ventilated ICU patients can ensure sustainability of optimum critical care in the near future as the COVID-19 pandemic wears on.

Adjusting Practice During COVID-19

- A cohort study by oncologists from the Tata Memorial Centre in Mumbai, India including 262 asymptomatic preoperative cancer patients found the following: 21/262 patients (8%) tested positive for COVID-19 during preoperative screening, one patient eventually developed symptoms after testing positive, and of the 16 patients with major post-operative complications, none were attributable to COVID-19. Patients who tested positive were quarantined for 14 days before retesting, and at the time of writing, 13 re-tested as negative and 12 patients followed through with surgery. These findings suggest the utility and importance of screening for COVID-19 in asymptomatic preoperative cancer patients and that this strategy may help in mitigating post-operative COVID-19 complications.

R&D: Diagnosis & Treatments

- A case-control validation study including 50 SARS-CoV-2 positive specimens and 300 SARS-CoV-2 negative specimens combined into various sized pooled samples was conducted in South Korea by physicians and infectious disease researchers, and found that less than or equal to 6 specimens was the ideal specimen number for a pooled testing strategy to avoid decreasing sensitivity. Limitations of the study were as follows: the cutoff cycle threshold (Ct) number in the PCR kit was Ct value <35 within 40 amplification cycles, in addition to cost effectiveness not being analyzed. These findings help inform the upper limit threshold of number of specimens to process for COVID-19 pooled testing strategies to ensure high sensitivity.

TABLE OF CONTENTS

DISCLAIMER **2**
NOW LIVE! 2
LEVEL OF EVIDENCE **3**
EXECUTIVE SUMMARY **4**
TABLE OF CONTENTS **5**
CLIMATE **6**
AFFECTING THE HEALTHCARE WORKFORCE 6
EPIDEMIOLOGY **8**
SYMPTOMS AND CLINICAL PRESENTATION 8
TRANSMISSION & PREVENTION **11**
PREVENTION IN THE COMMUNITY 12
PREVENTION IN THE HOSPITAL 13
MANAGEMENT **14**
ACUTE CARE 15
Critical Care *15*
ADJUSTING PRACTICE DURING COVID-19 ..... **21**
MEDICAL SUBSPECIALTIES 21
Hematology and Oncology *21*
R&D: DIAGNOSIS & TREATMENTS **23**
DEVELOPMENTS IN DIAGNOSTICS 23
DEVELOPMENTS IN TREATMENTS 24
ACKNOWLEDGEMENTS **27**

FACTORS ASSOCIATED WITH RESILIENCE AMONG NON-LOCAL MEDICAL WORKERS SENT TO WUHAN, CHINA DURING THE COVID-19 OUTBREAK

Lin J, Ren YH, Gan HJ, Chen Y, Huang YF, You XM.. BMC Psychiatry. 2020 Aug 24;20(1):417. doi: 10.1186/s12888-020-02821-8.

Level of Evidence: 3 - Local non-random sample

BLUF

A cross sectional online survey study of non-local medical workers (Table 1) at a Wuhan hospital in Feb 2020 conducted by Chinese physicians and nurses found that self-reported resilience correlated positively with active coping styles ($r = .733$, $P < 0.01$), negatively with anxiety ($r = -.498$, $P < 0.01$), and negatively with depression ($r = -.471$, $P < 0.01$) (Table 2). Multivariate linear regression analysis revealed similar relationships (Table 3). Additionally, physicians were found to be more resilient than support staff, which included healthcare assistants, technicians, and nurses. These findings highlight the importance of cultivating resilience, possible through structured interventions/trainings, in medical staff during the COVID-19 pandemic.

ABSTRACT

BACKGROUND: To investigate the resilience of non-local medical workers sent to support local medical workers in treating the outbreak of 2019 novel coronavirus disease (COVID-19). METHODS: In February 2020, non-local medical workers who had been sent to Wuhan as support staff to respond to the COVID-19 outbreak were asked to complete an online survey composed of the Connor Davidson Resilience Scale (CD-RISC), Hospital Anxiety Depression Scale (HADS) and Simplified Coping Style Questionnaire (SCSQ). RESULTS: Survey responses from 114 non-local medical workers were analyzed. CD-RISC scores were high (67.03 +- 13.22). The resilience level was highest for physicians (73.48 +- 11.49), followed by support staff, including health care assistants, technicians (67.78 +- 12.43) and nurses (64.86 +- 13.46). Respondents differed significantly in the levels of education, training/support provided by the respondent's permanent hospital (where he or she normally works), and in their feelings of being adequately prepared and confident to complete tasks ($P < 0.05$). Resilience correlated negatively with anxiety ($r = -.498$, $P < 0.01$) and depression ($r = -.471$, $P < 0.01$) but positively with active coping styles ($r = .733$, $P < 0.01$). Multiple regression analysis showed that active coping (beta = 1.314, $p < 0.05$), depression (beta = -.806, $p < 0.05$), anxiety (beta = - 1.091, $p < 0.05$), and training/support provided by the respondent's permanent hospital (beta = 3.510, $p < 0.05$) were significant associated with resilience. CONCLUSION: Our data show that active coping, depression, anxiety, and training/support provided by the respondent's permanent hospital are associated with resilience. Managers of medical staff should use these data to develop psychosocial interventions aimed at reinforcing the resilience of medical workers during highly stressful and prolonged medical emergencies, as seen during the COVID-19 outbreak.

Table 1 Demographic characteristics and descriptive statistics of resilience in non-local medical workers sent to Wuhan during the COVID-19 outbreak ($n = 114$)

Characteristic	n (%)	Mean (SD)	F/t	P
Sex				
Male	23 (20.2)	69.17 ± 14.09	0.867	0.388
Female	91 (79.8)	66.49 ± 13.02		
Age (years)				
≤ 25	21 (18.4)	69.19 ± 11.50	1.446	0.233
26–30	32 (28.1)	69.31 ± 10.27		
31–40	49 (43.0)	64.08 ± 15.22		
41–50	12 (10.5)	69.25 ± 13.38		
Occupation				
Doctor	21 (18.4)	73.48 ± 11.49	3.640	0.029
Nurse	70 (61.4)	64.86 ± 13.46		
Support staff	23 (20.2)	67.78 ± 12.43		
Marital status				
Single	53 (46.5)	65.70 ± 12.98	−1.006	0.316
Married	61 (53.5)	68.20 ± 13.43		
Education				
Diploma degree	15 (13.2)	57.00 ± 13.78	5.660	0.005
Bachelor's degree	85 (74.6)	68.94 ± 12.62		
Master's degree or above	14 (12.3)	66.21 ± 12.04		
Training/support provided by the respondent's permanent hospital				
Yes	42 (36.8)	71.43 ± 12.71	2.789	0.006
No	72 (63.2)	64.47 ± 12.92		
Adequate preparation				
Yes	81 (71.1)	69.13 ± 12.48	2.715	0.008
No	33 (28.9)	61.91 ± 13.78		
Confidence to complete task			2.557	0.012
Yes	109 (95.6)	67.70 ± 12.48		
No	5(4.4)	52.60 ± 21.56		

Table 2 Correlations among resilience, anxiety, depression and coping style in non-local medical workers ($n = 114$)

	Resilience	Active coping	Passive coping	Anxiety	Depression
Resilience	1				
Active coping	0.733**	1			
Passive coping	0.012	0.109	1		
Anxiety	−0.498**	−0.423**	−0.041	1	
Depression	−0.471**	−0.366**	0.270**	0.380**	1

** $P<0.05$

Table 3 Multiple linear regression analyses to identify factors that influence resilience

Model	Nonstandardized Coefficients		Standardized Coefficient	t	Sig.
	B	Std. Error	Beta		
Constant	50.189	7.091		7.007	0.000
Active coping	1.314	0.159	0.562	8.276	0.000
Depression	−0.806	0.274	0.193	−2.940	0.004
Anxiety	−1.091	0.412	−0.178	−2.647	0.009
Received training/support provided by the respondent's permanent hospital	3.510	1.633	0.129	2.1493	0.034

$R = 0.790$; $R^2 = 0.624$; Adjusted $R^2 = 0.610$
Dependent Variable: resilience

DELIRIUM AND ADVERSE OUTCOMES IN HOSPITALIZED PATIENTS WITH COVID-19

Garcez FB, Aliberti MJR, Poco PCE, Hiratsuka M, de Fatima Takahashi S, Coelho VA, Salotto DB, Moreira MLV, Jacob Filho W, Avelino Silva TJ.. J Am Geriatr Soc. 2020 Aug 24. doi: 10.1111/jgs.16803. Online ahead of print.
Level of Evidence: 3 - Cohort study or control arm of randomized trial

BLUF

Investigators affiliated with the Laboratorio de Investigacao Medica em Envelhecimento at Universidade de Sao Paulo performed a longitudinal, observational study on 707 COVID-19 patients admitted to a tertiary university hospital in Sao Paulo, Brazil between March and May 2020 and found that 33% (n=234) of patients had descriptors of delirium (confusional state, disorientation, hallucinations, etc; Table 1). Additionally, delirium was independently associated with length of hospital stay, ICU admission, and in-hospital deaths in adults older than the age of 50 (Table 2, 3). Based on these findings, the authors suggest that healthcare workers should assess for delirium among COVID-19 patients, which may help monitor the severity and prognosis of these patients.

ABSTRACT

BACKGROUND: Little is known about the association between acute mental changes and adverse outcomes in hospitalized adults with COVID-19. OBJECTIVES: To investigate the occurrence of delirium in hospitalized patients with COVID-19 and explore its association with adverse outcomes. DESIGN: Longitudinal observational study. SETTING: Tertiary university hospital dedicated to the care of severe cases of COVID-19 in Sao Paulo, Brazil. PARTICIPANTS: 707 patients aged >=50 years consecutively admitted to the hospital between March and May 2020. MEASUREMENTS: We completed detailed reviews of electronic medical records to collect our data. We identified delirium occurrence using the Chart-based Delirium Identification Instrument (CHART-DEL). Trained physicians with a background in geriatric medicine completed all CHART-DEL assessments. We complemented our baseline clinical information using telephone interviews with participants or their proxy. Our outcomes of interest were in-hospital death, length of stay, admission to intensive care, and ventilator utilization. We adjusted all multivariable analyses for age, sex, clinical history, vital signs, and relevant laboratory biomarkers (lymphocyte count, C-reactive protein, glomerular filtration rate, D-dimer, albumin). RESULTS: Overall, we identified delirium in 234 participants (33%). On admission, 86 (12%) were delirious. We observed 263 deaths (37%) in our sample, and in-hospital mortality reached 55% in patients who experienced delirium. Delirium was associated with in-hospital death, with an adjusted odds ratio [aOR] of 1.75 (95% confidence interval [95%CI]= 1.15-2.66); the association held both in middle-aged and older adults. Delirium was also associated with increased length of stay, admission to intensive care, and ventilator utilization. CONCLUSION: Delirium was independently associated with in-hospital death in adults aged >=50 years with COVID-19. Despite the difficulties for patient care during the pandemic, clinicians should routinely monitor delirium when assessing severity and prognosis of COVID-19 patients. This article is protected by copyright. All rights reserved.

	Total N=707	No delirium N=473	Delirium N=234	P-value
Age (years)				<0.001
50-64	339 (48)	258 (55)	81 (35)	
65-79	274 (39)	176 (37)	98 (42)	
≥80	94 (13)	39 (8)	55 (24)	
Age (years)	66 (±11)	64 (±10)	70 (±11)	<0.001
Female	303 (43)	212 (45)	91 (39)	0.13
Dementia	30 (4)	8 (2)	22 (9)	<0.001
Diabetes	299 (42)	201 (42)	98 (42)	0.88
Cerebrovascular disease	52 (7)	23 (5)	29 (12)	<0.001
Coronary disease	98 (14)	69 (15)	29 (12)	0.43
Hypertension	483 (68)	322 (68)	161 (69)	0.67
Obesity	182 (26)	137 (29)	45 (19)	0.005
Cancer	104 (15)	52 (11)	52 (22)	<0.001
Chronic pulmonary disease	70 (10)	50 (11)	20 (9)	0.40
Charlson score	1 (0, 4)	1 (0, 3)	2 (1, 5)	<0.001
Polypharmacy (≥5 meds)	238 (34)	157 (33)	81 (35)	0.18
Previously independent	517 (73)	378 (80)	139 (59)	<0.001
Number of typical symptoms	3 (2, 4)	3 (3, 5)	3 (2, 4)	<0.001
Supplemental oxygen	513 (73)	333 (70)	180 (77)	0.067
MAP <70 mmHg	39 (6)	19 (4)	20 (9)	0.012
Lymphocytes (cels/mm3)	900 (610, 1330)	977 (650, 1374)	835 (600, 1200)	0.004
C-reactive protein	132 (72, 226)	127 (68, 218)	149 (82, 239)	0.067
GFR (mL/min)	70 (32, 98)	75 (38, 104)	56 (27, 90)	<0.001
D-dimer (ng/mL)	1748 (838, 7244)	1485 (719, 5633)	3143 (1142, 13728)	<0.001
Albumin (g/dL)	3.1 (2.8, 3.4)	3.2 (2.9, 3.4)	2.9 (2.6, 3.2)	<0.001
Total days in ICU	2 (0, 10)	0 (0, 8)	5 (0, 12)	<0.001
Ventilator utilization	289 (41)	167 (35)	122 (53)	0.038
Length of stay (days)	11 (6, 16)	10 (6, 15)	13 (8, 20)	<0.001
In-hospital death	273 (39)	144 (30)	129 (55)	<0.001

Data are presented as mean (±SD) or median (IQR) for continuous measures, and N (%) for categorical measures.; MAP: mean arterial pressure; GFR: glomerular filtration rate; ICU: intensive care unit.

Table 1. Baseline characteristics of hospitalized middle-aged and older adults with COVID-19, according to delirium occurrence.

	Occurrence	Unadjusted estimates (95%CI)	Adjusted estimates[a] (95%CI)	Adjusted P-value
In-hospital death	129 (55)	2.81 (2.03-3.88)	1.75 (1.15-2.66)	0.009
Length of stay	13 (8, 20)	1.34 (1.22-1.47)	1.36 (1.24-1.50)	<0.001
Ventilator utilization	122 (53)	1.99 (1.45-2.74)	1.99 (1.30-3.05)	0.001
Admission to intensive care	165 (71)	2.78 (1.99-3.89)	3.32 (2.11-5.23)	<0.001

Occurrence results are presented as N (%) for categorical outcomes and median (IQR) for continuous outcomes.
CI: confidence interval.
[a]Estimates are presented as odds ratios for dichotomous outcomes, and incidence rate ratios for length of stay. All multivariable analyses were adjusted for age, sex, literacy, previous diagnoses, Charlson comorbidity index, polypharmacy, days of symptoms, oxygen support, temperature, mean arterial pressure, lymphocyte count, C-reactive protein, glomerular filtration rate, D-dimer, and albumin.

Table 2. Association between delirium and adverse outcomes in hospitalized middle-aged and older adults with COVID-19 (N=707).

Outcome	Occurrence	Unadjusted estimates (95%CI)	Adjusted estimates[a] (95%CI)	P-value
In-hospital death				
50-64yrs | No delirium	54 (21)	Ref.	Ref.	
50-64yrs | Delirium	40 (49)	3.69 (2.17-6.73)	1.93 (1.01-3.68)	0.046
≥65yrs | No delirium	90 (41)	2.72 (1.82-4.07)	1.40 (0.82-2.39)	0.22
≥65yrs | Delirium	89 (58)	5.25 (3.38-8.15)	2.33 (1.29-4.21)	<0.001
Length of stay				
50-64yrs | No delirium	10 (6, 15)	Ref.	Ref.	
50-64yrs | Delirium	15 (10, 24)	1.60 (1.38-1.86)	1.47 (1.27-1.71)	<0.001
≥65yrs | No delirium	10 (6, 15)	1.03 (0.92-1.15)	1.04 (0.92-1.16)	0.53
≥65yrs | Delirium	12 (7, 19)	1.22 (1.08-1.38)	1.31 (1.15-1.50)	<0.001
Ventilator utilization				
50-64yrs | No delirium	75 (29)	Ref.	Ref.	
50-64yrs | Delirium	51 (63)	4.15 (2.45-7.01)	2.80 (1.45-5.38)	0.002
≥65yrs | No delirium	92 (43)	1.71 (1.18-2.46)	1.05 (0.63-1.74)	0.84
≥65yrs | Delirium	71 (46)	2.11 (1.39-3.20)	1.51 (0.84-2.70)	0.16
Admission to intensive care				
50-64yrs | No delirium	105 (41)	Ref.	Ref.	
50-64yrs | Delirium	67 (83)	2.23 (3.72-13.1)	6.19 (2.89-13.2)	<0.001
≥65yrs | No delirium	116 (54)	1.71 (1.18-2.46)	1.01 (0.63-1.62)	0.95
≥65yrs | Delirium	99 (65)	2.67 (1.76-4.04)	2.17 (1.24-3.82)	0.007

Occurrence results are presented as N (%) for categorical outcomes and median (IQR) for continuous outcomes.
CI: confidence interval.
[a]Estimates are presented as odds ratios for dichotomous outcomes, and incidence rate ratios for length of stay. All multivariable analyses were adjusted for age, sex, literacy, previous diagnoses, Charlson comorbidity index, polypharmacy, days of symptoms, oxygen support, temperature, mean arterial pressure, lymphocyte count, C-reactive protein, glomerular filtration rate, D-dimer, and albumin.

Table 3. Association between delirium occurrence and adverse outcomes, according to age group, in hospitalized patients with COVID-19 (N=707).

TRANSMISSION & PREVENTION

POSSIBLE ENVIRONMENTAL EFFECTS ON THE SPREAD OF COVID-19 IN CHINA

Xu H, Yan C, Fu Q, Xiao K, Yu Y, Han D, Wang W, Cheng J.. Sci Total Environ. 2020 Aug 20;731:139211. doi: 10.1016/j.scitotenv.2020.139211. Epub 2020 May 7.
Level of Evidence: Other - Mechanism-based reasoning

BLUF

Authors affiliated with several institutions in China (including Shanghai Jiao Tong University and Wuhan Environmental Protection Science Academy) performed a cross-sectional study between January 29 to February 15, 2020 on the daily COVID-19 cases, air quality, and meteorological factors in 33 locations (Figure 2) of China. Among their findings, the authors note an association between relative risk of COVID-19 spread and air quality index (AQI) that was greater between 10 degrees Celsius and 20 degrees Celsius and a possibly stronger AQI impact on confirmed COVID-19 cases between the range of 10% to 20% relative humidity, respectively (Table 2, 3). These finding suggests that AQI may play a role in COVID-19 transmission in both low temperatures and low humidity, although further investigation is needed.

SUMMARY

Additional findings show a statistically significant lag effect of AQI on COVID-19-verified cases for lag days 1-3, with relative risk (RR) values as follows:
- lag day 1 (RR=1.0009, CI: 1.0004-1.0013)
- lag day 2 (RR=1.0007, CI: 1.0003-1.0012)
- lag day 3 (RR = 1.0008, CI: 1.0003-1.0012)

ABSTRACT

At the end of 2019, a novel coronavirus, designated as SARS-CoV-2, emerged in Wuhan, China and was identified as the causal pathogen of COVID-19. The epidemic scale of COVID-19 has increased dramatically, with confirmed cases increasing across China and globally. Understanding the potential affecting factors involved in COVID-19 transmission will be of great significance in containing the spread of the epidemic. Environmental and meteorological factors might impact the occurrence of COVID-19, as these have been linked to various diseases, including severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS), whose causative pathogens belong to the same virus family as SARS-CoV-2. We collected daily data of COVID-19 confirmed cases, air quality and meteorological variables of 33 locations in China for the outbreak period of 29 January 2020 to 15 February 2020. The association between air quality index (AQI) and confirmed cases was estimated through a Poisson regression model, and the effects of temperature and humidity on the AQI-confirmed cases association were analyzed. The results show that the effect of AQI on confirmed cases associated with an increase in each unit of AQI was statistically significant in several cities. The lag effect of AQI on the confirmed cases was statistically significant on lag day 1 (relative risk (RR) = 1.0009, 95% confidence interval (CI): 1.0004, 1.0013), day 2 (RR = 1.0007, 95% CI: 1.0003, 1.0012) and day 3 (RR = 1.0008, 95% CI: 1.0003, 1.0012). The AQI effect on the confirmed cases might be stronger in the temperature range of 10 C <= T < 20 C than in other temperature ranges, while the RR of COVID-19 transmission associated with AQI was higher in the relative humidity (RH) range of 10% <= RH < 20%. Results may suggest an enhanced impact of AQI on the COVID-19 spread under low RH.

FIGURES

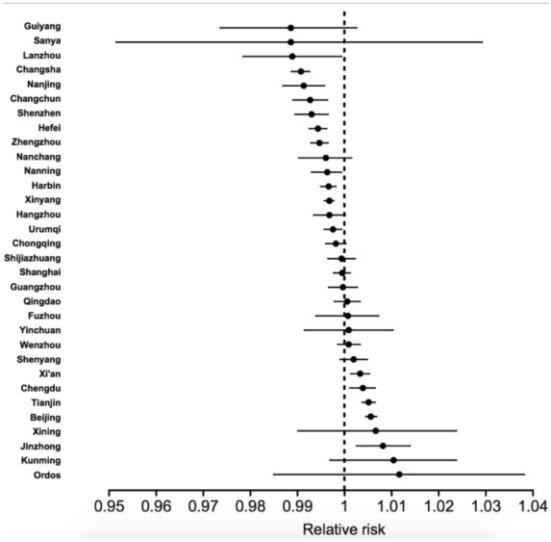

Fig. 2. Association of COVID-19 confirmed cases and increase of each AQI unit for different cities.

Table 3. Effect of different humidity ranges on AQI – COVID 19 confirmed cases association.

Humidity range	Relative risk, 95% CI
10% ≤ RH < 20%	1 (1, 1) (reference group)
20% ≤ RH < 40%	0.99327799 (0.86661034, 1.15354)
40% ≤ RH < 60%	0.99077184 (0.86443011, 1.15062239)
60% ≤ RH < 80%	0.98974706 (0.86353798, 1.14943006)
80% ≤ RH ≤ 100%	0.98975936 (0.86354868, 1.14944439)

Table 2. Effect of different temperature ranges on AQI – COVID 19 confirmed cases association.

Temperature range	Relative risk, 95% CI
$T < -20$ °C (– 22.8 ≤ °C $T < -20$ °C)	1 (1, 1) (reference group)
–20 °C ≤ $T < -10$ °C	1.0039684 (1.00114264, 1.00704327)
–10 °C ≤ $T < 0$ °C	1.00711894 (1.0044128, 1.01009672)
0 °C ≤ $T < 10$ °C	1.00635137 (1.00372986, 1.00925885)
10 °C ≤ $T < 20$ °C	1.00886322 (1.00613776, 1.01185857)
$T \geq 20$ °C (20 °C ≤ $T < 24.9$ °C)	1.00646535 (1.00396607, 1.00897226)

PREVENTION IN THE COMMUNITY

AIR TRAVEL IN THE TIME OF COVID-19

The Lancet Infectious Diseases.. Lancet Infect Dis. 2020 Sep;20(9):993. doi: 10.1016/S1473-3099(20)30647-2.
Level of Evidence: Other - Expert Opinion

BLUF

An opinion piece by Lancet Infectious Diseases discusses the changes made to airline travel to mitigate the transmission of SARS-CoV-2 such as closing international borders, mandating masks, reducing passenger numbers, and increasing cleaning efforts. This article suggests that in the future, airlines may permanently increase preventative measures such as utilizing touchless technology, requiring masks and vaccines, improving cleaning, and reducing services to prevent transmission, similar to the increases in airline security seen following the September 11th, 2001 terrorist attacks.

ATYPICAL COVID-19: PREVENTING TRANSMISSION FROM UNEXPECTED CASES

Chow A, Htun HL, Mar Kyaw W, Hou A, Tan G, Tan HN, Koh LW, Thong BY, Ang B.. Infect Control Hosp Epidemiol. 2020 Aug 13:1-9. doi: 10.1017/ice.2020.419. Online ahead of print.
Level of Evidence: 4 - Case-series, case-control, or historically controlled studies

BLUF

Physicians and epidemiologists from Singapore report that there was no COVID-19 transmission to the 247 individuals who came into contact with five atypical COVID-19 patients presenting without acute respiratory symptoms at Tan Tock Seng Hospital in Singapore (Table 1) between January 23rd, 2020 and July 25th, 2020. The authors highlight the importance of clear PPE policies and a strong hospital surveillance system incorporating rapid contact tracing and monitoring staff sicknesses in order to prevent nosocomial transmission of atypical COVID-19.

SUMMARY

The authors highlight that Tan Tock Seng Hospital implemented strict personal protective equipment (PPE) policies for both the designated COVID-19 areas (fever-zones) as well as other areas of the hospital (non-fever-zones). In fever-zones, every staff member was instructed to wear N95 respirators, gowns, gloves, and eye protection, while patients and visitors were required to wear surgical masks. At non-fever-zones, COVID-19 contact tracing measures were implemented and all individuals were instructed to wear surgical masks and follow standard precautions.

ABSTRACT

Little is known about the transmissibility of COVID-19 from patients with atypical presentations. Five COVID-19 patients presenting without acute respiratory symptoms exposed 247 contacts during their hospital stay. After 14 days of close surveillance, 19 contacts developed respiratory symptoms and were screened for SARS-CoV-2. None were infected with COVID-19.

FIGURES

Characteristics	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Age (years)	68	80	55	90	42
Gender	Female	Male	Male	Female	Male
Race	Chinese	Chinese	Chinese	Chinese	Chinese
Pre-existing conditions	Nasal tip basal cell carcinoma	Eosinophilic granulomatosis with polyangiitis, gastric adenocarcinoma, chronic renal impairment, active hepatitis B infection	Nil	Alzheimer's disease, hypertension, hyperlipidemia, diabetes mellitus, paroxysmal atrial fibrillation	Hyperlipidaemia, gastroesophageal reflux,
Presenting symptoms	Nausea and abdominal pain	Persistent middle finger tenderness and upper limb swelling	Fever, muscle pain, rash and nausea	Vomiting, lethargy, and foul-smelling urine	Chest pain and palpitations
Admitting diagnosis	Nausea likely secondary to gallbladder stones	Infective tenosynovitis	Pulmonary tuberculosis, Dengue Fever	Pneumonia, Functional decline	Atypical chest pain
Radiologic evidence of pneumonia	Yes	Yes	Yes	Yes	No
Managed at the outset at COVID-19 designated areas in the ED/clinic	No	No	No	No	Yes
Time to isolation at COVID-19 designated areas in ED/clinic (hours)	NA	NA	3	3	NA
Admitted from ED/clinic directly to a single room	No	No	Yes	Yes	Yes, but subsequently de-isolated
Time in an open ward (hours)	48	44	NA	NA	147
Length of hospitalisation (days)	8	13	11	6	9
Total no. of exposed contacts	92	33	35	20	67
No. of contacts with unprotected exposure					
Patients	34	4	0	0	9
Visitors	6	0	0	0	0
Caregivers	2	0	0	0	0
Staff	1	0	0	0	0
No. of contacts with protected[a,b] exposure					
Patients	0	0	0	1[a]	0
Visitors	0	0	0	0	10[b]
Caregivers	0	0	0	0	0
Staff	49 (42[a] and 7[b])	29 (28[a] and 1[b])	35 (15[a] and 20[b])	19 (13[a] and 6[b])	48[a]
No. of symptomatic contacts screened for SARS-CoV-2	11	3	5	0	0
No. of asymptomatic contacts screened for SARS-CoV-2	0	0	0	0	48
No. of contacts confirmed with COVID-19	0	0	0	0	0

[a]Surgical Mask; [b]N95 respirator, gown, gloves, eye protection

Table 1. Characteristics of patients and the exposed contacts.

MANAGEMENT

MANAGING COVID-19 WITH A CLINICAL DECISION SUPPORT TOOL IN A COMMUNITY HEALTH NETWORK: ALGORITHM DEVELOPMENT AND VALIDATION

McRae MP, Dapkins IP, Sharif I, Anderman J, Fenyo D, Sinokrot O, Kang SK, Christodoulides NJ, Vurmaz D, Simmons GW, Alcorn TM, Daoura MJ, Gisburne S, Zar D, McDevitt JT.. J Med Internet Res. 2020 Aug 24;22(8):e22033. doi: 10.2196/22033.
Level of Evidence: Other - Modeling

BLUF

Investigators affiliated with multiple medical institutions (including New York University School of Medicine and New York University College of Dentistry) assessed the 2-tiered model on clinical decision support system (CDSS) and mobile app (Figure 1) among data from 701 COVID-19-positive patients within the Family Health Centers network at New York University Langone Health. The authors found that both the internal validation and external validation of the Tier 1 model (the Outpatient Model) had areas under the curve (AUCs) of 0.79 (internal validation: CI 0.74-0.84; external validation: Cl 0.70-0.88; Table 2,3). The internal validation and external validation of the Tier 2 model (The Biomarker Model) had AUCs of 0.95 (CI 0.92-0.98) and 0.97 (CI 0.95-0.99), respectively (Table 2, 3). Based on these findings, the authors believe that the CDSS and mobile app can help healthcare workers with decision-making regarding COVID-19 management and, thus, improve patient quality of care and outcomes.

SUMMARY

The first tier – Outpatient Model -Tier 1 utilized non-laboratory data such as gender, age, systolic blood pressure, BMI, symptoms and co-morbidities. The purpose of Tier 1 was to ascertain the necessity of hospitalization and/or subsequent Tier 2 testing. The second tier – Biomarker model, utilized biomarker measurements such as cardiac troponin, C-reactive protein, procalcitonin and D-dimer and was used to indicate possible disease severity. Data was collected between January 10 and February 18, 2020 from Zhongnan Hospital of Wuhan University to verify Tier 1 and Tier 2 models. Data from 160 COVID-19 hospitalized patients validated Tier 1 and data from 375 hospitalized COVID-19 patients validated Tier 2.

ABSTRACT

BACKGROUND: The COVID-19 pandemic has resulted in significant morbidity and mortality, with large numbers of patients requiring intensive care threatening to overwhelm healthcare systems globally. There is an urgent need for a COVID-19 disease severity assessment that can assist in patient triage and resource allocation for patients at risk for severe disease. OBJECTIVE: The goal of this study was to develop, validate, and scale a clinical decision support system and mobile app to assist in COVID-19 severity assessment, management, and care. METHODS: Model training data from 701 patients with COVID-19 were collected across practices within the Family Health Centers network at New York University Langone Health. A two-tiered model was developed. Tier 1 uses easily available, non-laboratory data to help determine whether biomarker-based testing and/or hospitalization is necessary. Tier 2 predicts probability of mortality using biomarker measurements (CRP, PCT, D-dimer) and age. Both Tier 1 and Tier 2 models were validated using two external datasets from hospitals in Wuhan, China comprising 160 and 375 patients, respectively. RESULTS: All biomarkers were measured at significantly higher levels in patients that died vs. those that were not hospitalized or discharged (P < .001). The Tier 1 and Tier 2 internal validation had AUC (95% confidence interval) of 0.79 (0.74-0.84) and 0.95 (0.92-0.98), respectively. The Tier 1 and Tier 2 external validation had AUCs of 0.79 (0.74-0.84) and 0.97 (0.95-0.99), respectively. CONCLUSIONS: Our results demonstrate validity of the clinical decision support system and mobile app, which are now ready to assist healthcare providers in making evidence-based decisions in managing COVID-19 patient care. The deployment of these new capabilities has potential for immediate impact in community clinics, sites whereby application of such tools could lead to improvements in patient outcomes and cost containment. CLINICALTRIAL:

FIGURES

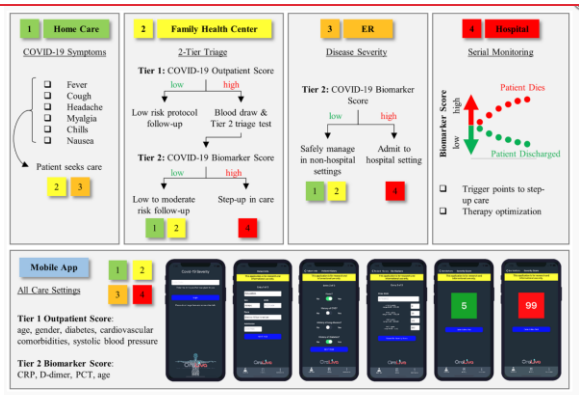

Figure 1. Clinical decision support system and mobile app for managing COVID-19 care. COVID-19: coronavirus disease; CRP: C-reactive protein; PCT: procalcitonin.

	Tier 1 Outpatient Model	Tier 2 Biomarker Model
AUC[a]	0.79 (0.74-0.84)	0.95 (0.92-0.98)
Sensitivity	0.73 (0.69-0.76)	0.89 (0.86-0.92)
Specificity	0.73 (0.69-0.76)	0.89 (0.86-0.92)
PPV[b]	0.34 (0.30-0.38)	0.70 (0.65-0.74)
NPV[c]	0.93 (0.91-0.95)	0.97 (0.94-0.98)

[a]AUC: area under the curve.

[b]PPV: positive predictive value.

[c]NPV: negative predictive value.

Table 2. Internal validation performance in terms of AUC, sensitivity, specificity, PPV, and NPV (95% CI) from 5-fold cross-validation. The Tier 1 and 2 models were trained and tested using data from Family Health Centers at New York University.

	Tier 1 Outpatient Model	Tier 2 Biomarker Model
AUC[a]	0.79 (0.70-0.88)	0.97 (0.95-0.99)
Sensitivity	0.76 (0.68-0.82)	0.89 (0.84-0.93)
Specificity	0.73 (0.65-0.80)	0.93 (0.89-0.96)
PPV[b]	0.50 (0.42-0.58)	0.94 (0.90-0.96)
NPV[c]	0.89 (0.83-0.94)	0.88 (0.83-0.92)

[a]AUC: area under the curve.

[b]PPV: positive predictive value.

[c]NPV: negative predictive value.

Table 3. External validation performance in terms of AUC, sensitivity, specificity, PPV, and NPV (95% CI). The Tier 1 Outpatient Model was evaluated on the Zhongnan Hospital dataset [26]. The Tier 2 model was evaluated on the Tongji Hospital dataset [21].

ACUTE CARE

CRITICAL CARE

COMPARISON OF THE CLINICAL COURSE OF COVID-19 PNEUMONIA AND ACUTE RESPIRATORY DISTRESS SYNDROME IN 2 PASSENGERS FROM THE CRUISE SHIP DIAMOND PRINCESS IN FEBRUARY 2020

Matsumura K, Toyoda Y, Matsumoto S, Kawai Y, Mori T, Omasa K, Fukada T, Yamada M, Kazamaki T, Furugori S, Hiroe N, Senoo S, Shimizu M, Funabiki T, Yamazaki M.. Am J Case Rep. 2020 Aug 19;21:e926835. doi: 10.12659/AJCR.926835.
Level of Evidence: 4 - Case-series

BLUF

A case series conducted by Japanese researchers compared the clinical course of acute respiratory distress syndrome (ARDS) due to COVID-19 in two passengers from the Diamond Princess Cruise Ship in February 2020, the details of which are summarized below. Due to the differences in exacerbation and progression of illness seen on CT scans of the two patients, the authors recommend tailoring treatment options to each individual case depending on CT scan findings.

SUMMARY

Case 1: 72-year-old male passenger of Diamond Princess was admitted with respiratory distress and fever, with initial CT showing "a mosaic-like pattern comprising multiple ground-glass opacities (GGOs) in both lungs" (Figure 1A). On day 5 of admission, the patient required mechanical ventilation followed by veno-venous extracorporeal membrane oxygenation (VV ECMO). His subsequent CT scan showed "large diffuse areas with a crazy-paving pattern mixed with consolidation on the peripheral side in both lungs" (Figure 1B). After antiviral treatment on day 18, his CT showed "exacerbation of consolidation on both dorsal sides due to atelectasis and unchanged GGOs on the ventral side" (Figure 1C). Patient was eventually weaned off VV ECMO and follow up CT showed that "consolidation and GGOs were mostly resolved" (Figure 1D).

Case 2: 70-year old male passenger admitted on February 12th with cough, malaise, nausea, vomiting, and fever, with his initial CT scan showing "bilateral subpleural GGOs" (Figure 2A). On day 4 of admission, he required intubation and mechanical ventilation, and his post-intubation CT showed diffuse GGOs with improvement of the initial subpleural GGOs (Figure 2B). His respiratory condition improved after steroid treatment, and he was eventually extubated and discharged. Before discharge on day 25, CT scan showed disappearance of GGOs (Figure 2C).

ABSTRACT

BACKGROUND Patients with coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 can rapidly progress to acute respiratory distress syndrome (ARDS). Because clinical diagnosis of ARDS includes several diseases, understanding the characteristics of COVID-19-related ARDS is necessary for precise treatment. We report 2 patients with ARDS due to COVID-19-associated pneumonia. CASE REPORT Case 1 involved a 72-year-old Japanese man who presented with respiratory distress and fever. Computed tomography (CT) revealed subpleural ground-glass opacities (GGOs) and consolidation. Six days after symptom onset, reverse transcription-polymerase chain reaction (RT-PCR) testing confirmed the diagnosis of COVID-19-associated pneumonia. He was intubated and received veno-venous extracorporeal membrane oxygenation (ECMO) 8 days after symptom onset. Follow-up CT revealed large diffuse areas with a crazy-paving pattern and consolidation, which indicated progression of COVID-19-associated pneumonia. Following treatment with antiviral medications and supportive measures, the patient was weaned off ECMO after 20 days. Case 2 involved a 70-year-old Asian man residing in Canada who presented with cough, malaise, nausea, vomiting, and fever. COVID-19-associated pneumonia was diagnosed based on a positive result from RT-PCR testing. The patient was then transferred to the intensive care unit and intubated 8 days after symptom onset. Follow-up CT showed that while the initial subpleural GGOs had improved, diffuse GGOs appeared, similar to those observed upon diffuse alveolar damage. He was administered systemic steroid therapy for ARDS and extubated after 6 days. CONCLUSIONS Because the pattern of symptom exacerbation in COVID-19-associated pneumonia cases seems inconsistent, individual treatment management, especially the CT-based treatment strategy, is crucial.

FIGURES

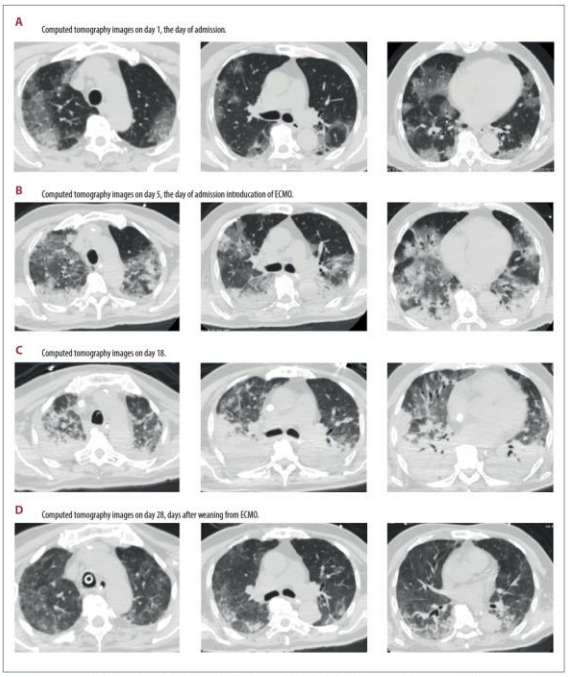

Figure 1. Chest computed tomographic images of a 72-year-old patient with severe acute respiratory distress syndrome due to COVID-19-associated pneumonia. (A) Images obtained on the day of admission exhibit multiple ground-glass opacities with a mosaic-like pattern in bilateral lungs. (B) Images taken on the fifth day, after intubation and introduction of veno-venous extracorporeal membrane oxygenation (VV ECMO), show diffuse large regions with a crazy-paving pattern in both lungs mixed with consolidation on the peripheral side. (C) Images taken on the 18th day show exacerbation of consolidation of both dorsal sides due to atelectasis and unchanged ground-glass opacities. (D) Images taken on the 28th day, 3 days after weaning off VV ECMO, reveal almost resolved consolidation in both lungs.

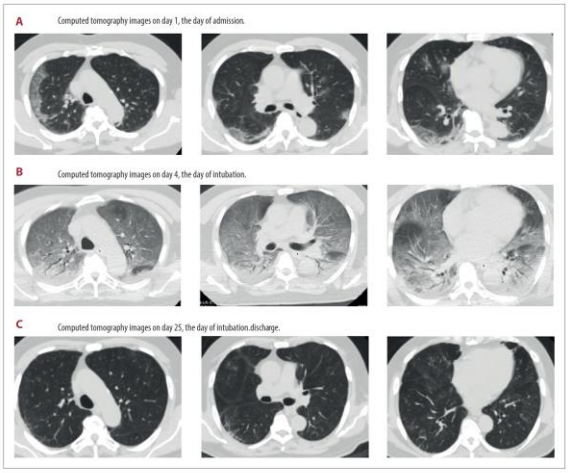

Figure 2. Chest computed tomographic images of a 70-year-old patient with moderate acute respiratory distress syndrome due to COVID-19-associated pneumonia. (A) Chest computed tomographic images obtained on the day of admission revealed bilateral subpleural ground-glass opacities. (B) Images taken on the fourth day after intubation show initial shrinking of ground-glass opacity shadows and their subsequent spreading. The shadows resemble those in diffuse alveolar damage. (C) Images taken on the 25th day before discharge reveal the absence of ground-glass opacities.

SEDATION, ANALGESIA, AND PARALYSIS IN COVID-19 PATIENTS IN THE SETTING OF DRUG SHORTAGES

Ammar MA, Sacha GL, Welch SC, Bass SN, Kane-Gill SL, Duggal A, Ammar AA.. J Intensive Care Med. 2020 Aug 26:885066620951426. doi: 10.1177/0885066620951426. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

A literature review was conducted by pharmacists from Yale, Cleveland Clinic, and University of Pittsburgh regarding alternative drugs for managing analgesia, sedation, and paralysis in COVID-19 patients requiring mechanical ventilation in the event of drug shortages, as detailed in the summary section below. These conservative and alternative management strategies for mechanically ventilated ICU patients can ensure sustainability of optimum critical care in the near future as the COVID-19 pandemic wears on.

SUMMARY

Pharmacists affiliated with Cleveland Clinic, University of Pittsburgh, and Yale-New Haven Health System present a narrative literature review on alternative treatments for sedation, analgesia, and paralysis in mechanically ventilated COVID-19 patients to handle drug shortages and patient surges.

Analgesia (Table 1):
- Since COVID-19 patients experience pain due to mechanical ventilation, IV fentanyl and IV morphine are conventionally used analgesics.
- Remifentanil, a selective mu-opioid receptor agonist, is an alternative in contingency care and due to its rapid offset, the patient experiences longer pain duration during extubation and post-treatment ($p<0.05$).
- Sufentanil and alfentanil (5-10 times more potent than fentanyl) are used in crisis care. Sufentanil is available in the sublingual form with 53% bioavailability.
- Conservation strategies include enteral oxycodone/morphine in patients with normal gastrointestinal motility and multimodal analgesic approach.

Sedation (Table 2):
- Dexmedetomidine is suggested for light sedation and propofol is conventionally suggested for deep sedation.
- Propofol can cause hypertriglyceridemia. Since COVID-19 patients may present with hemophagocytic lymphohistiocytosis (HLH) with hypertriglyceridemia, alternatives to propofol should be considered if triglycerides exceed 800mg/dl.
- Ketamine is considered for both light and deep sedation in contingency care, and due to its analgesic effect, it conserves the opioid drug shortages.
- Non-benzodiazepines are preferred over benzodiazepines and the latter is recommended only in contingency care. Daily awakening trials assessing patients' sedative needs play a vital role in severe drug shortages.

Paralysis (Table 4):
- Neuromuscular blocking agents (NMBA) are preferred in mechanically ventilated COVID-19 patients with moderate-severe ARDS due to their ability to increase chest wall compliance and facilitating lung recruitment.
- Atracurium, rocuronium, vecuronium can be used as alternatives to existing cisatracurium in contingency care and pancuronium in crisis care.

ABSTRACT

The rapid spread of the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has led to a global pandemic. The 2019 coronavirus disease (COVID-19) presents with a spectrum of symptoms ranging from mild to critical illness requiring intensive care unit (ICU) admission. Acute respiratory distress syndrome is a major complication in patients with severe COVID-19 disease. Currently, there are no recognized pharmacological therapies for COVID-19. However, a large number of COVID-19 patients require respiratory support, with a high percentage requiring invasive ventilation. The rapid spread of the infection has led to a surge in the rate of hospitalizations and ICU admissions, which created a challenge to public health, research, and medical communities. The high demand for several therapies, including sedatives, analgesics, and paralytics, that are often utilized in the care of COVID-19 patients requiring mechanical ventilation, has created pressure on the supply chain resulting in shortages in these critical medications. This has led clinicians to develop conservation strategies and explore alternative therapies for sedation, analgesia, and paralysis in COVID-19 patients. Several of these alternative approaches have demonstrated acceptable levels of sedation, analgesia, and paralysis in different settings but they are not commonly used in the ICU. Additionally, they have unique pharmaceutical properties, limitations, and adverse effects. This narrative review summarizes the literature on alternative drug therapies for the management of sedation, analgesia, and paralysis in COVID-19

patients. Also, this document serves as a resource for clinicians in current and future respiratory illness pandemics in the setting of drug shortages.

FIGURES

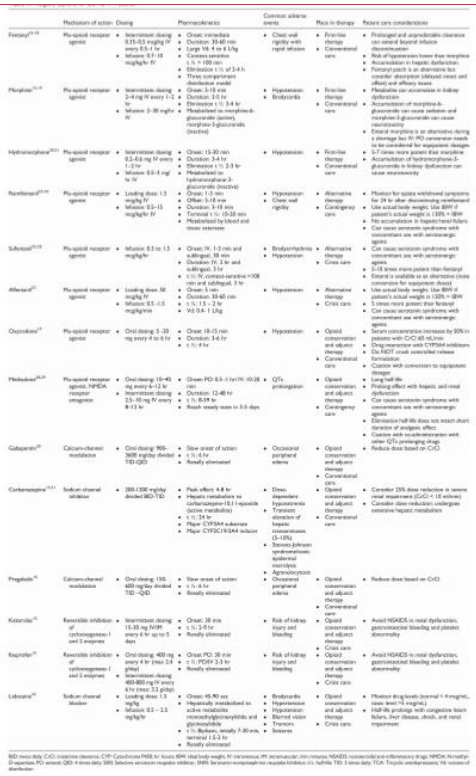

Table 1: "Analgesic Options for COVID-19 Patients".

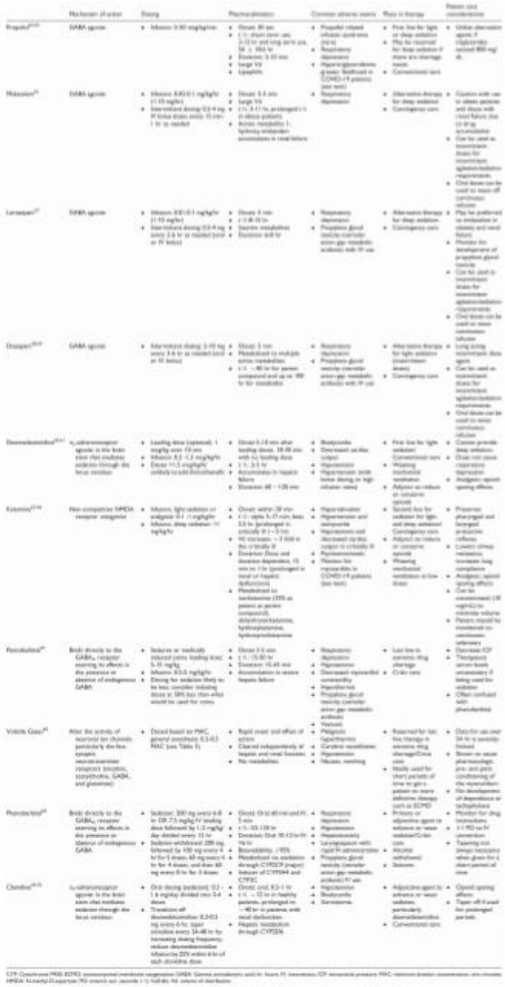

Table 2: " Sedative Options for COVID-19 Patients".

	Mechanism of action	Dosing	Pharmacokinetics	Common adverse events	Place in therapy	Patient care considerations
Atracurium	Nondepolarizing NMBA Intermediate-acting	• Intermittent dosing: Bolus 0.4-0.5 mg/kg • Infusion: 5-20 mcg/kg/min	• Onset: 3-5 min • t ½: initial, 2 min and terminal, 20 min • Duration: 20-35 min • Hoffman elimination	• Histamine release (hypotension) • Laudanosine metabolite (flushing, seizure)	• Alternative first-line continuous infusion • Contingency care	• Hypotension with rapid administration • Not effected by renal and hepatic dysfunction
Cisatracurium	Nondepolarizing NMBA Intermediate-acting	• Intermittent dosing: Bolus 0.1-0.2 mg/kg • Infusion: 1-4 mcg/kg/min • Fixed dose infusion: 37.5 mg/hr	• Onset: 2-3 min • t ½: 22-29 min • Duration: 30-60 min • Hoffman elimination	• Bronchospasm (rare) • Bradycardia (rare)	• First line continuous infusion • Conventional care	• Most commonly studied NMBA in ARDS • Not effected by renal and hepatic dysfunction
Pancuronium	Nondepolarizing NMBA Long-acting	• Intermittent dosing: Bolus 0.05-0.1 mg/kg • Infusion: 0.8 -1.7 mcg/kg/min	• Onset: 2-3 min • t ½: 89-161 min • Duration: 60-100 min • 45-70% renal, 15% hepatic • Active metabolite	• Vagal blockade, sympathetic stimulation (hypotension, tachycardia)	• Alternative intermittent bolus • Crisis care	• Monitoring pupillary reflex unreliable due to antimuscarinic effects
Rocuronium	Nondepolarizing NMBA Intermediate-acting	• Intermittent dosing: Bolus 0.6 - 1.2 mg/kg • Infusion: 8-12 mcg/kg/min	• Onset: 1-2 min • Alpha t ½, 1-2 min and beta t ½, 1-2 hr • Duration: 20-35 min • 33% renal, < 75% hepatic	• Vagal blockade at higher doses	• Intermittent bolus/ Conventional care • Second-line continuous infusion/ Contingency care	• Preferred in renal dysfunction over vecuronium
Vecuronium	Nondepolarizing NMBA Intermediate-acting	• Intermittent dosing: Bolus 0.1 mg/kg • Infusion: 0.8 -1.7 mcg/kg/min	• Onset: 3-4 min • t ½: 4 min • Duration: 20-45 min • 10-50% renal, 35-50% hepatic • Active metabolite: 3-desacetyl vecuronium (renally eliminated)	• Vagal blockade at higher doses	• Intermittent bolus/ Conventional care • Second-line continuous infusion/ Contingency care	• Preferred in hepatic dysfunction over rocuronium

ARDS: Acute respiratory distress syndrome; hr: hours; min: minutes; NMBA: neuromuscular blocking agent

Table 4: "Paralytic Options for COVID-19 Patients".

HEMATOLOGY AND ONCOLOGY

MANDATORY PREOPERATIVE COVID-19 TESTING FOR CANCER PATIENTS-IS IT JUSTIFIED?

Nekkanti SS, Vasudevan Nair S, Parmar V, Saklani A, Shrikhande S, Sudhakar Shetty N, Joshi A, Murthy V, Patkar N, Khattry N, Gupta S.. J Surg Oncol. 2020 Aug 25. doi: 10.1002/jso.26187. Online ahead of print.
Level of Evidence: 3 - Non -randomized controlled cohort/follow-up study

BLUF

A cohort study by oncologists from the Tata Memorial Centre in Mumbai, India from April 18 - June 20, 2020 including 262 asymptomatic preoperative cancer patients (Table 1) found the following: 21/262 patients (8%; Table 2) tested positive for COVID-19 during preoperative screening, one patient eventually developed symptoms after testing positive, and of the 16 patients with major post-operative complications, none were attributable to COVID-19 (Table 3). Patients who tested positive were quarantined for 14 days before retesting, and at the time of writing, 13 re-tested as negative and 12 patients followed through with surgery. These findings suggest the utility and importance of screening for COVID-19 in asymptomatic preoperative cancer patients and that this strategy may help in mitigating post-operative COVID-19 complications.

ABSTRACT

BACKGROUND: Severe acute respiratory syndrome coronavirus 2 has caused substantial disruptions in routine clinical care. Emerging data show that surgery in coronavirus disease (COVID)-positive cases can be associated with worsening of clinical outcomes and increased postoperative mortality. Hence, preoperative COVID-19 testing for all patients before elective surgery was implemented in our institution. MATERIALS AND METHODS: Two hundred and sixty-two asymptomatic cancer patients were preoperatively tested for COVID-19 using reverse-transcription polymerase chain reaction technique with nasopharyngeal and oropharyngeal swabbing. All negative patients were operated within 72 hours, and positive patients were quarantined for a minimum 14 days before re-swabbing. RESULTS: In our cohort, 21 of 262 (8.0%) asymptomatic preoperative patients, who were otherwise fit for surgery, tested positive. After adequate quarantine and a negative follow-up test report, 12 of 21 (57%) had an operation. No major postoperative morbidity due to COVID-19 was noted during the immediate postoperative period before discharge from the hospital. CONCLUSION: Routine preoperative COVID-19 testing was successful in identifying asymptomatic viral carriers. There was no incidence of symptomatic COVID-19 disease in the postoperative period, and there was no incidence of morbidity attributable to COVID-19. These data suggested a beneficial role for mandatory preoperative COVID-19 testing.

TABLE 1 Distribution of various clinical factors

	Number (%), total = 262
Age	
Mean	48.5
Median	50.0
Gender	
Female	175 (66.7)
Male	87 (33.2)
Cancer sites	
Head and neck	35 (13.4)
Breast	142 (54.2)
Gastrointestinal	85 (32.1)
Cancer stage	
I/II	65 (24.8)
III	146 (55.7)
IV	43 (16.4)
Non-cancerous[a]	8 (3.1)

[a]Procedures like stoma closure, revision mastectomy, and neck node biopsies.

TABLE 2 Preoperative COVID-19 status

	Number (%)
Initial COVID-19 report	
Negative	230 (87.9)
Positive	18 (6.8)
Inconclusive	14 (5.3)
Total	262
Final report after re-swabbing for inconclusive cases	
Negative	241 (92.0)
Positive	21 (8.0)
Total	262

Gender versus preoperative COVID-19 status

	COVID-19 report		
Gender	Negative (%)	Positive (%) (95% CI)	Total
Female	161	14 (8.0) (4.4-13.0)	175
Male	80	7 (8.1) (3.3-15.0)	262
Total	241	21 (8.0) (5.0-11.0)	262

Abbreviations: CI, confidence interval; COVID-19, coronavirus disease 2019.

TABLE 3 Postoperative complications

Postoperative complications	n = 249 (%)
None	198 (79.5)
Minor	34 (13.7)
Major	16 (6.4)
Death	1 (0.4)

Note: Grading using Clavien-Dindo classification (grade I/II: minor; grade III/IV: major; grade V: death).[15]

POOLING UPPER RESPIRATORY SPECIMENS FOR RAPID MASS SCREENING OF COVID-19 BY REAL-TIME RT-PCR

Kim SY, Lee J, Sung H, Lee H, Han MG, Yoo CK, Lee SW, Hong KH.. Emerg Infect Dis. 2020 Aug 26;26(10). doi: 10.3201/eid2610.201955. Online ahead of print.
Level of Evidence: 4 - Case-series, case-control, or historically controlled studies

BLUF

A case-control validation study including 50 SARS-CoV-2 positive specimens and 300 SARS-CoV-2 negative specimens combined into various sized pooled samples was conducted in South Korea by physicians and infectious disease researchers, and found that less than or equal to 6 specimens was the ideal specimen number for a pooled testing strategy to avoid decreasing sensitivity. Limitations of the study were as follows: the cutoff cycle threshold (Ct) number in the PCR kit was Ct value <35 within 40 amplification cycles (Figures 1, 2), in addition to cost effectiveness not being analyzed. These findings help inform the upper limit threshold of number of specimens to process for COVID-19 pooled testing strategies to ensure high sensitivity.

ABSTRACT

To validate the specimen-pooling strategy for real-time reverse transcription PCR detection of severe acute respiratory syndrome coronavirus 2, we generated different pools including positive specimens, reflecting the distribution of cycle threshold values at initial diagnosis. Cumulative sensitivities of tested pool sizes suggest pooling of <6 specimens for surveillance by this method.

FIGURES

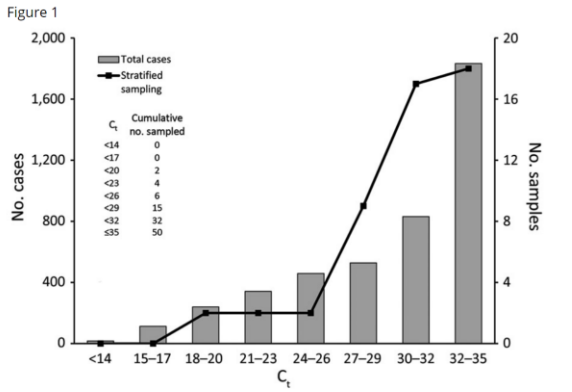

Figure 1. Distribution of RdRp gene threshold cycle (Ct) values for specimens from 4,364 confirmed patients in South Korea at their initial diagnosis of coronavirus disease (COVID-19) and the specimens selected by stratified sampling. This figure shows the first RdRp gene Ct values of patients receiving a COVID-19 diagnosis (bars). We selected positive samples with the stratified sampling method based on that distribution (line). Cumulative numbers of selected specimens per stratum are shown. Ct, cycle threshold.

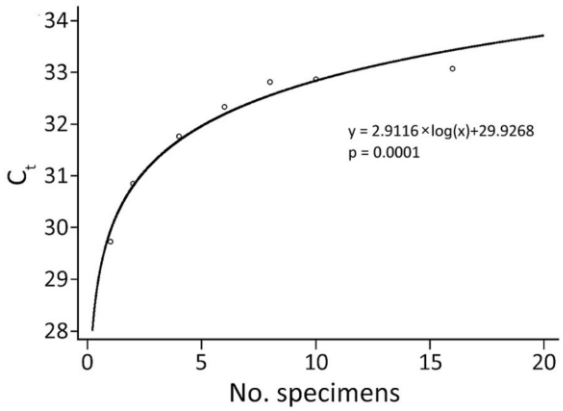

Figure 2. Mean Ct values of RdRp genes of 50 specimens from coronavirus disease patients in South Korea by pool size. The trend line shows logarithmic regression. Ct, cycle threshold.

DEVELOPMENTS IN TREATMENTS

RECENT ADVANCES IN THERAPEUTIC MODALITIES AND VACCINES TO COUNTER COVID-19/SARS-COV-2

Bilal M, Iqbal HMN.. Hum Vaccin Immunother. 2020 Aug 26:1-9. doi: 10.1080/21645515.2020.1794685. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

A scoping review by researchers from China and Mexico discussed potential COVID-19 treatment and vaccine options such as anti-viral drugs, protease-inhibitors and spike (S) protein-angiotensin converting enzyme 2 (ACE2) blockers due to their effectiveness in treating SARS-CoV and MERS-CoV patients as well as activity against SARS-CoV-2 in vitro; while live-attenuated, viral vector, DNA-based, RNA-based, and protein based vaccines are being explored (Table 1). Authors suggest current knowledge of coronaviruses similar to SARS-CoV-2 could offer insight for advancements in novel COVID-19 treatment and vaccine development.

SUMMARY

Summary of potential therapeutics as follows:
- anti-virals: opinavir-ritonavir, arbidol, and remdesivir
- protease-inhibitors: cinanserin and diarylheptanoids
- S protein-ACE2 blockers: monoclonal antibodies, chloroquine, emodin, and promazine

ABSTRACT

The novel coronavirus disease (COVID-19) caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) has rapidly spread across the world. This resulted an alarming number of fatalities with millions of confirmed infected cases, pretending severe public health, economic, and social threats. There is no specific therapeutic drugs or licensed vaccines or treatments to fight against lethal COVID-19 infections. Given the significant threats of COVID-19, the global organizations are racing to identify epidemiological and pathogenic mechanisms of COVID-19 to find treatment regimens and effective therapeutic modalities for future prevention. Herein, we reviewed the therapeutic interventions and vaccines for COVID-19 based on the existing knowledge and understanding of similar coronaviruses, including MERS-CoV and SARS-CoV. The information constitutes a paramount intellectual basis to sustenance ongoing research for the discovery of vaccines and therapeutic agents. This review signifies the most available frontiers in the viral vaccine development approaches to counter the COVID-19/SARS-CoV-2.

FIGURES

Vaccine platform	Vaccine candidate	Target antigen	Animal model	PMID	PMCID	References
Parainfluenza virus 5 (PIV5)-based vaccine	PIV5/MERS-S	S protein	Yes – Specific-pathogen-free 6-week-old C57BL/6 and BALB/c mice	32265331	PMC7157776	Li et al.[47]
Vector vaccine	Modified vaccinia virus Ankara (MVA)-based vaccine	S protein	No	32320037	PMC7172913	Koch et al.[48]
Recombinant	VSVΔG-MERS	S protein	Yes – eight 2-year-old male rhesus monkeys	29246504	PMC7113862	Liu et al.[49]
DNA vaccine, Recombinant	pcDNA3.1-S	S protein	Six-to eight-week-old specific pathogen-free female BALB/c mice	28314581	PMC5481280	Chi et al.[50]
DNA vaccine, Recombinant	pcDNA3.1-SΔCD	S protein	Six-to eight-week-old specific pathogen-free female BALB/c mice	28314581	PMC5481280	Chi et al.[50]
DNA vaccine, Recombinant	pcDNA3.1-S1	S protein	Six-to eight-week-old specific pathogen-free female BALB/c mice	28314581	PMC5481280	Chi et al.[50]
DNA vaccine	pcDNA-N	N protein	Yes – Eight-week-old female BALB/c mice	19186202	PMC7115532	Hu et al.[51]
Live-attenuated S. typhimurium						
DNA vaccine	pcDNA-S	S protein	Yes – Six- to 8-week-old female BALB/c mice	17496640	PMC1951058	Hu et al.[52]
DNA vaccine	pcDNA-IL-2	S protein	Yes – Six- to 8-week-old female BALB/c mice	17496640	PMC1951058	Hu et al.[52]
DNA vaccine	pcDNA-S + pcDNA-IL-2	S protein	Yes – Six- to 8-week-old female BALB/c mice	17496640	PMC1951058	Hu et al.[52]
DNA vaccine	pcDNA3.1	S protein	Yes – Six- to 8-week-old female BALB/c mice	17496640	PMC1951058	Hu et al.[52]
DNA vaccine	PBS	S protein	Yes – Six- to 8-week-old female BALB/c mice	17496640	PMC1951058	Hu et al.[52]
DNA vaccine	CSI022	S protein	Yes – Six- to 8-week-old female BALB/c mice	17496640	PMC1951058	Hu et al.[52]
DNA vaccine	N protein DNA vaccine	N protein	Yes – Female Balb/c mice	16423399	PMC7112551	Shi et al.[53]
DNA vaccine	M protein DNA vaccine	M protein	Yes – Female Balb/c mice	16423399	PMC7112551	Shi et al.[53]
DNA vaccine	N + M protein DNA vaccine	N, M proteins	Yes – Female Balb/c mice	16423399	PMC7112551	Shi et al.[53]
DNA vaccine	CTLA4-S DNA vaccine	S protein	Yes – Male Balb/c (H-2^d) mice	15993989	PMC7115571	Woo et al.[54]
DNA vaccine	Salmonella-CTLA4-S DNA vaccine	S protein	Yes – Male Balb/c (H-2^d) mice	15993989	PMC7115571	Woo et al.[54]
DNA vaccine	Salmonella-tPA-S DNA vaccine	S protein	Yes – Male Balb/c (H-2^d) mice	15993989	PMC7115571	Woo et al.[54]
Recombinant	Recombinant spike polypeptide vaccine	S protein	Yes – Male Balb/c (H-2^d) mice	15993989	PMC7115571	Woo et al.[54]
DNA vaccine	tPA-S DNA vaccine	S protein	Yes – Male Balb/c (H-2^d) mice	15993989	PMC7115571	Woo et al.[54]
DNA vaccine	N protein DNA vaccine	N protein	Yes – Six-week-old female BALB/c mice	15582659	PMC7111813	Zhao et al.[55]

Table 1. Overview of vaccine production platforms and vaccine candidates for various Coronaviruses.

MECHANISM AND INHIBITION OF THE PAPAIN-LIKE PROTEASE, PLPRO, OF SARS-COV-2

Klemm T, Ebert G, Calleja DJ, Allison CC, Richardson LW, Bernardini JP, Lu BG, Kuchel NW, Grohmann C, Shibata Y, Gan ZY, Cooney JP, Doerflinger M, Au AE, Blackmore TR, van der Heden van Noort GJ, Geurink PP, Ovaa H, Newman J, Riboldi-Tunnicliffe A, Czabotar PE, Mitchell JP, Feltham R, Lechtenberg BC, Lowes KN, Dewson G, Pellegrini M, Lessene G, Komander D.. EMBO J. 2020 Aug 26:e106275. doi: 10.15252/embj.2020106275. Online ahead of print.
Level of Evidence: Other - Mechanism-based reasoning

BLUF

Biomedical researchers from Australia, Canada, and The Netherlands explored SARS-CoV-2 proteases (specifically ubiquitin and ubiquitin-like binding sites) as possible pharmacologic targets for COVID-19 treatment and found non-covalent substrates including viral polyprotein, degradative Lys-48-polyubiquitin and antiviral interferon-stimulated gene 15 (ISG15) signals all interacted with SARS-CoV-2 papain-like protease (PLpro; Figures 1A,2A), suggesting they may be promising candidates for development of COVID-19 therapies.

ABSTRACT

The SARS-CoV-2 coronavirus encodes an essential papain-like protease domain as part of its non-structural protein (nsp)-3, namely SARS2 PLpro, that cleaves the viral polyprotein, but also removes ubiquitin-like ISG15 protein modifications as well as, with lower activity, Lys48-linked polyubiquitin. Structures of PLpro bound to ubiquitin and ISG15 reveal that the S1 ubiquitin-binding site is responsible for high ISG15 activity, while the S2 binding site provides Lys48 chain specificity and cleavage efficiency. To identify PLpro inhibitors in a repurposing approach, screening of 3,727 unique approved drugs and clinical compounds against SARS2 PLpro identified no compounds that inhibited PLpro consistently or that could be validated in counterscreens. More promisingly, non-covalent small molecule SARS PLpro inhibitors also target SARS2 PLpro, prevent self-processing of nsp3 in cells and display high potency and excellent antiviral activity in a SARS-CoV-2 infection model.

FIGURES

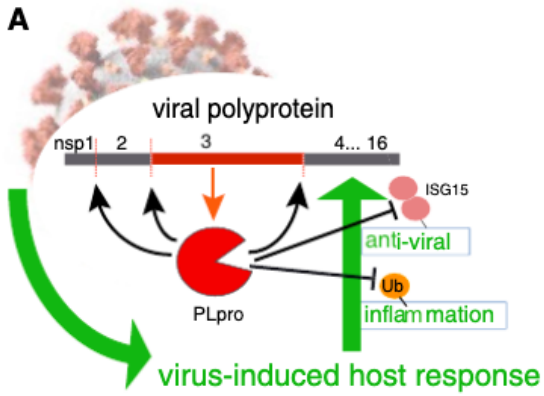

Figure 1A. Cartoon of coronavirus PLpro activities. PLpro is encoded as one of various domains of the 1,900 amino acid non-structural protein nsp3 and is thought to have three functions: (i) cleaving the viral polyprotein to generate mature nsp1, nsp2 and nsp3; (ii) hydrolysing ubiquitin chains important for inflammatory responses and(iii) removing interferon-stimulated gene 15 (ISG15) modifications from proteins, reversing antiviral responses.

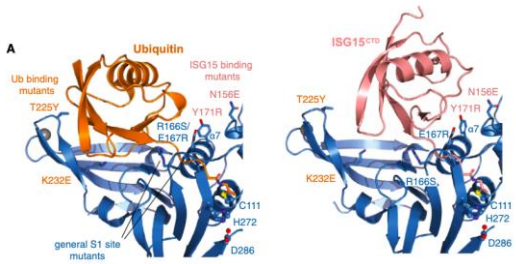

Figure 2A. Detail of the S1 ubiquitin-binding site of SARS2 PLpro, bound to ubiquitin (left) and ISG15 (right), highlighting differential interactions of ubiquitin with the Fingers subdomain, and of ISG15 with the Thumb subdomain of PLpro.

ACKNOWLEDGEMENTS

CONTRIBUTORS

Alisa Malyavko
Diep Nguyen
Julia Ghering
Krithika Kumarasan
Maryam Naushab
Sameer Kandula
Sara Rutz
Shayan Ebrahimian
Veronica Graham

EDITORS

Alvin Rafou
Maggie Donovan
Michelle Arnold

SENIOR EDITORS

Allison Hansen
Avery Forrow
Cameron Richards

EXECUTIVE SENIOR EDITOR

Thamanna Nishath

CHIEF EDITOR

Brennan Enright

ADVISOR

Will Smith