

The Daily COVID-19 Literature Surveillance Summary

June 2, 2020



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COVID-19 Daily Literature Surveillance

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LEVEL OF EVIDENCE

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

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

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

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

How to cite the Levels of Evidence Table

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

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

EXECUTIVE SUMMARY

Climate:

- Ethicists, microbiologists, and public health experts discuss strategies for optimizing the pandemic response. Considerations include:
 - [Increased global surveillance measures](#)
 - The [ethical implications](#) of quarantine laws and clinical research
 - Integrating a comprehensive pandemic preparedness strategy for [Latin America](#)

Epidemiology:

- Canadian scientists conducted a [meta-analysis](#) of 22 articles published between January 24 and April 2, 2020 exploring the virulence of SARS-CoV-2 found that:
 - the basic reproduction number of SARS-CoV-2 is 3.15,
 - the average incubation time is 5.08 days,
 - the asymptomatic infection rate is 46%, and
 - the case fatality rate is 3.34% (when asymptomatic cases are accounted for in a sensitivity analysis, case fatality rate is 1.8%).
- [Genetic analysis](#) from 84 COVID-19 patients in New York found “clear evidence of multiple independent SARS-CoV-2 introductions into NYC during the first weeks of March”, with the majority coming from Europe.

Understanding the Pathology:

- Czech researchers studying the [immunologic aspects of COVID-19](#) conclude:
 - Both innate and adaptive immune systems are crucial in mounting a response, but it is unknown whether failure to mobilize the adaptive immune system leads to severe disease
 - IgA response is stronger than the other antibodies generated and more persistent
 - Interleukin(IL)-6 is elevated in greater than 50% of patients
 - "Macrophage Activation Syndrome" may explain the unusual finding of elevated CRP in some COVID-19 patients.
- A review of [mechanisms that predispose obese and diabetic patients](#) to increased risk of severe COVID-19 disease, implicates a chronic inflammatory state, impaired T cell function, and dysfunction of the RAS system.

Transmission and Prevention:

- A [pilot study](#) of a contact tracing strategy in Kentucky reported underwhelming cooperation with contact tracing, finding only 19 of 58 cases provided contact information, with others stating inability or unwillingness to cooperate. This highlights the need for a unique approach to contact tracing in the US.
- A [cross-sectional study](#) from Singapore found SARS-CoV-2 RNA present on 56.7% of surface and air samples from airborne infection isolation rooms (AIIR) of COVID-19 patients. They also found highest contamination rates within the first 2 weeks of illness.

Management:

- A [case-study](#) of 4,500 liver transplant recipients found that only 5 patients (0.1%) contracted COVID-19 post-transplant. All cases were mild and experienced a full recovery. Authors speculate this relatively low incidence rate may result from strong adherence to social isolation and/or a beneficial effect of their immune suppression.
- A [prospective cohort study](#) from Tel Aviv conducted echocardiography on 100 adult COVID-19 patients. They found 32% had a normal echocardiogram, while 20% had clinical deterioration with ventricular deterioration more commonly on the right than left. Authors recommend echocardiography should be limited to patients with clinical decompensation, where it offers most benefit to guide clinical management.

Adjusting Practice:

- The COVID-19 pandemic continues to catalyze the implementation of telemedicine:

- A research letter discusses whole-body skin self-examinations (SSE) via [teledermatology](#) as a potential method to screen for melanoma. Authors cite recent studies showing at-home SSE have a high degree of sensitivity (>75%) and specificity (>87%) at detecting suspicious lesions, suggesting this may be a useful tool in combating transmission and delayed presentation during the pandemic.
- A Penn State physician describes their [new journal club format](#) designed to adapt the huge influx of research during the pandemic.

R&D Diagnosis and Treatment:

- [Clinical microbiologists at NYU](#) found the 5-minute Abbott ID NOW COVID-19 test had a positive predictive value of 94.4% and a negative predictive value of 83.1% (n=101) when compared to the Xpert Xpress SARS-CoV-2 test, suggesting this test may be a useful tool to rule-in disease. However, they caution that a single negative result may not be useful as a rule-out.

Mental Health and Resilience:

- A [US random sample survey](#) from March 10 to March 31, 2020 found that older-aged respondents perceived greater risks of COVID-19 fatality, but overall lower risks of becoming infected or quarantined, losing their job, or running out of money, in addition to less reported depression and anxiety. These findings suggest older-aged adults appeared to have relatively greater optimism and better mental health than their younger counterparts during the early stages of the COVID-19 pandemic in the US.
- [Researchers in India](#) assessed the understanding of quarantine and level of compliance in a cohort of 121 children (ages 9-18) and compared their psychological well-being to a cohort of 131 non-quarantined children. They found that while the majority of the quarantined children (73.55%) understand the reasoning behind quarantine, there was variable compliance to protection measures (only 7.53% correctly following all measures) and that feelings of worry, helplessness, and fear were more commonly reported in the quarantined cohort.

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WHAT WE NEED TO CONSIDER DURING AND AFTER THE SARS-COV-2 PANDEMIC

Valdivia-Granda WA, Richt JA.. Vector Borne Zoonotic Dis. 2020 May 29. doi: 10.1089/vbz.2020.2652. Online ahead of print.

Level of Evidence: Other

BLUF

A biotech CEO and microbiologist together comment on the global and financial burden levied by the pandemic, urging for an increase in integrated global biosurveillance to prevent future pandemics, especially from coronaviruses (Figure 1). They also discuss potential animal vectors for human transmission and review the highlights and risks of vaccine development before suggesting increased outbreak modeling, molecular diagnostics, and communication measures in order to coordinate global responses.

ABSTRACT

Even though extreme containment and mitigation strategies were implemented by numerous governments around the world to slow down the spread of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), the number of critically ill patients and fatalities keeps rising. This crisis has highlighted the socioeconomic disparities of health care systems within and among countries. As new CoVID policies and responses are implemented to lessen the impact of the virus, it is imperative (1) to consider additional mitigation strategies critical for the development of effective countermeasures, (2) to promote long-term policies and strict regulations of the trade of wildlife and live animal markets, and (3) to advocate for necessary funding and investments in global health, specifically for the prevention of and response to natural and manmade pandemics. This document considers some of these challenges.

FIGURES

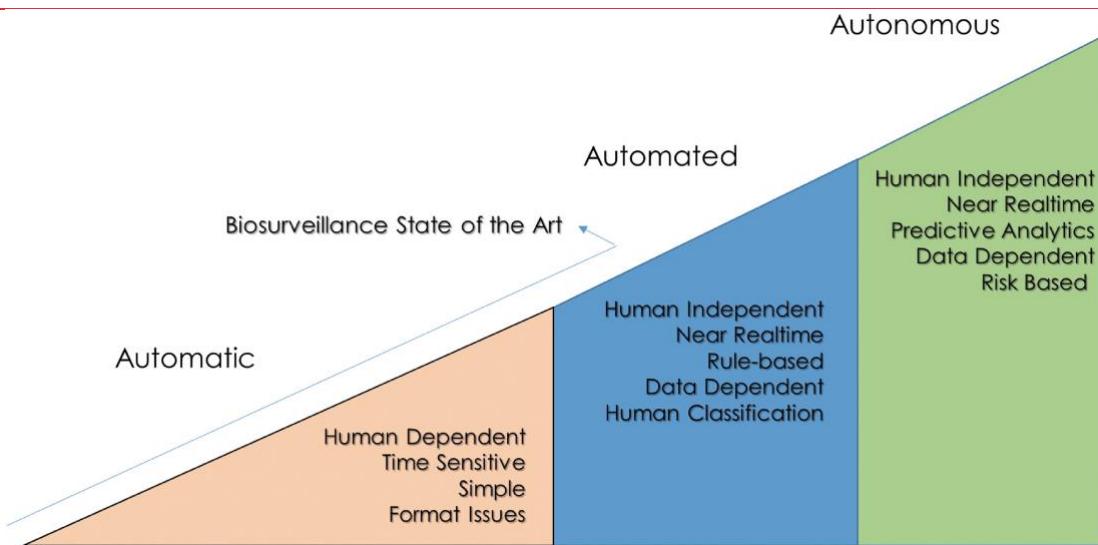


Figure 1: Current state of biosurveillance systems.

DISPARITIES

PREPARING FOR THE COMING TRANSNATIONAL CANCER CRISIS AMID THE COVID-19 PANDEMIC

Ip EC, Lee SF.. Cancer Causes Control. 2020 May 29. doi: 10.1007/s10552-020-01310-3. Online ahead of print.

Level of Evidence: Other

BLUF

An oncologist and an ethics/law professor in Hong Kong reflect upon lockdown measures instated in China during March and April of the COVID-19 pandemic. They note that many people with chronic and life-threatening diseases experienced notable barriers to health care during lockdown, resulting in delays in diagnosis and treatment. They propose countries shift more medical resources back to patients with cancer and other life-threatening diseases and prepare for a resurgence of these patients once the COVID-19 pandemic is contained.

ABSTRACT

The continuing outbreak of the coronavirus disease 2019 (COVID-19) caused by the novel coronavirus SARS-CoV-2 has inflicted considerable burdens onto the health system of China, the world's most populous country. Remarkably, among spectrum of potential mitigation strategies, the Chinese government has implemented all-out lockdowns on large geographical areas, unprecedented in the modern era. This inevitably undermined the right to healthcare of many who now faced great difficulty in getting treatment, especially those with cancer or other life-threatening issues. We elaborate and discuss the medico-legal and human rights consideration triggered by the lockdowns, the unprecedented mass quarantine of Hubei province in China, and the suspension of normal healthcare services. We argue that the same challenge will now be faced by other countries, particularly the USA, Italy, Spain, and France, as the epicentres of COVID-19 has shifted to Europe and the Americas.

EPIDEMIOLOGY

ESTIMATION OF THE BASIC REPRODUCTION NUMBER, AVERAGE INCUBATION TIME, ASYMPTOMATIC INFECTION RATE, AND CASE FATALITY RATE FOR COVID-19: META-ANALYSIS AND SENSITIVITY ANALYSIS

He W, Yi GY, Zhu Y.. J Med Virol. 2020 May 29. doi: 10.1002/jmv.26041. Online ahead of print.

Level of Evidence: 2

BLUF

Canadian scientists conducted a meta- and sensitivity analysis of 22 articles published between January 24 and April 2, 2020 to explore the virulence of SARS-CoV-2, and found that:

- The basic reproduction number of SARS-CoV-2 is 3.15,
- The average incubation time is 5.08 days,
- The asymptomatic infection rate is 46%, and
- The case fatality rate is 3.34% (when asymptomatic cases are accounted for in a sensitivity analysis, case fatality rate is 1.8%).

ABSTRACT

The coronavirus disease 2019 (COVID-19) has been found to be caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). However, comprehensive knowledge of COVID-19 remains incomplete and many important features are still unknown. This manuscript conducts a meta-analysis and a sensitivity study to answer the questions: What is the basic reproduction number? How long is the incubation time of the disease on average? What portion of infections are asymptomatic? And ultimately, what is the case fatality rate? Our studies estimate the basic reproduction number to be 3.15 with the 95% interval (2.41,3.90), the average incubation time to be 5.08 days with the 95% confidence interval (4.77, 5.39) (in day), the asymptomatic infection rate to be 46% with the 95% confidence interval (18.48%, 73.60%), and the case fatality rate to be 2.72% with 95% confidence interval (1.29%, 4.16%) where asymptomatic infections are accounted for. This article is protected by copyright. All rights reserved.

INTRODUCTIONS AND EARLY SPREAD OF SARS-COV-2 IN THE NEW YORK CITY AREA

Gonzalez-Reiche AS, Hernandez MM, Sullivan MJ, Ciferri B, Alshammary H, Obla A, Fabre S, Kleiner G, Polanco J, Khan Z, Alburquerque B, van de Guchte A, Dutta J, Francoeur N, Melo BS, Ouszenko I, Deikus G, Soto J, Sridhar SH, Wang YC, Twyman K, Kasarskis A, Altman DR, Smith M, Sebra R, Aberg J, Krammer F, García-Sastre A, Luksza M, Patel G, Paniz-Mondolfi A, Gitman M, Sordillo EM, Simon V, van Bakel H.. Science. 2020 May 29:eabc1917. doi: 10.1126/science.abc1917. Online ahead of print.

Level of Evidence: Other

BLUF

This article details an analysis of 84 SARS-CoV-2 sequences obtained from COVID-19 patients at Mount Sinai Health System in New York City between February 29 and March 18 2020 which showed "clear evidence for multiple, independent SARS-CoV-2 introductions into NYC during the first weeks of March." Additionally, the authors suggest that the "NYC SARS-CoV-2 epidemic has been mainly sourced from untracked transmission between the USA and Europe, with limited evidence of direct introductions from China where the virus originated" (figure 1).

ABSTRACT

New York City (NYC) has emerged as one of the epicenters of the current SARS-CoV-2 pandemic. To identify the early transmission events underlying the rapid spread of the virus in the NYC metropolitan area, we sequenced the virus causing COVID-19 in patients seeking care at the Mount Sinai Health System. Phylogenetic analysis of 84 distinct SARS-CoV2 genomes indicates multiple, independent but isolated introductions mainly from Europe and other parts of the United States. Moreover, we find evidence for community transmission of SARS-CoV-2 as suggested by clusters of related viruses found in patients living in different neighborhoods of the city.

FIGURES

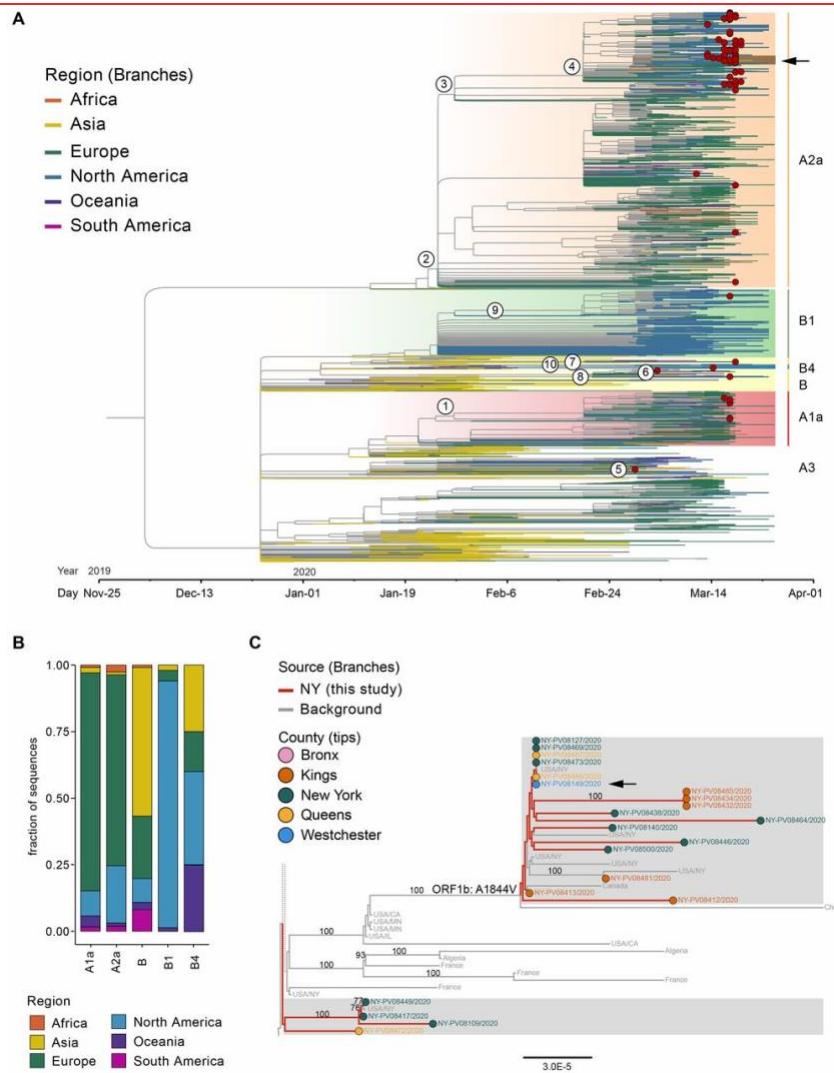


Figure 1: Phylogenetic relationships of SARS-CoV-2 from NY and other global strains.

(A) Maximum Likelihood (ML) phylodynamic inference of 84 SARS-CoV-2 sequences from NY from this study in a global background of 2,363 sequences available in GISAID EpiCoV database as of April 1, 2020. Branches are colored according to the region of origin. Tip circles (red) indicate the position of the 84 NY sequences. Clades that contain NY sequences are highlighted with names shown on the right; the local transmission clusters are indicated by the arrow. The node positions for the transmission events listed in Table 1 are marked by the numbers in white circles. The displayed time tree was inferred under a strict clock model with a fixed substitution rate of 0.8×10^{-3} . (B) Stacked barplot showing the fraction of sequences per region by clade. (C) Local transmission clusters on the ML tree showing the source of cases by county. Bootstrap support values $\geq 70\%$ are shown, sibling clusters are collapsed for easier visualization. The mutation identified specific to the community transmission cluster is indicated. The scale bar at the bottom indicates the number of nucleotide substitutions per site.

MODELING

A NOVEL SIMPLE SCORING MODEL FOR PREDICTING SEVERITY OF PATIENTS WITH SARS-COV-2 INFECTION

Dong Y, Zhou H, Li M, Zhang Z, Guo W, Yu T, Gui Y, Wang Q, Zhao L, Luo S, Fan H, Hu D.. Transbound Emerg Dis. 2020 May 29. doi: 10.1111/tbed.13651. Online ahead of print.

Level of Evidence: 4

BLUF

Authors affiliated with Huazhong University of Science and Technology in Whan, China conducted a retrospective review of 147 COVID-19 patients (94 with non-severe disease and 53 with severe disease), from Feb 10 to Feb 29, 2020, and developed the "COVID-19 index" scoring system to predict disease severity on admission. Three key risk factors (decreased lymphocytes, p=0.001; D-dimer, p=0.001; and ESR, p=0.001) were identified and included in the scoring system where the model was found to be positively correlated with disease severity (ROC=0.843) implicating that a higher risk score may predict more severe COVID-19 disease.

SUMMARY

The article takes into account different variables among which three (lymphocytes, D-dimer, and ESR) are used in developing the formula, " $3 \times \text{D-dimer } (\mu\text{g/L}) + 2 \times \text{lgESR } (\text{mm/h}) - 4 \times \text{lymphocyte } (\times 10^9 / \text{L}) + 8$," for evaluating the severity of COVID-19 in the patients. An "increased level of WBC (p=0.002), neutrophils, D-dimer (p=0.001), fibrinogen, IL-6, CRP, ESR (p=0.001), AST, ALT, alpha hydroxybutyrate dehydrogenase, serum amyloid A and decreased lymphocytes (p=0.001)" was found. The study concludes that with higher risk score levels, the percentage of the severity of COVID-19 increases.

ABSTRACT

An outbreak of pneumonia caused by a novel coronavirus (COVID-19) began in Wuhan, China in December 2019 and quickly spread throughout the country and world. An efficient and convenient method based on clinical characteristics was needed to evaluate the potential deterioration in patients. We aimed to develop a simple and practical risk scoring system to predict the severity of COVID-19 patients on admission. We retrospectively investigated the clinical information of confirmed COVID-19 patients from February 10, 2020 to February 29, 2020 in Wuhan Union Hospital. Predictors of severity were identified by univariate and multivariate logistic regression analysis. A total of 147 patients with confirmed SARS-CoV-2 infection were grouped into non-severe (94 patients) and severe (53 patients) groups. We found that an increased level of white blood cells (WBC), neutrophils, D-dimer, fibrinogen (FIB), IL-6, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), alanine aminotransferase (ALT), aspartate aminotransferase (AST), alpha-hydroxybutyrate dehydrogenase (HBDH), serum amyloid A (SAA) and a decreased level of lymphocytes were important risk factors associated with severity. Furthermore, three variables were used to formulate a clinical risk scoring system named COVID-19 index = $3 \times \text{D-dimer } (\mu\text{g/L}) + 2 \times \text{lgESR } (\text{mm/h}) - 4 \times \text{lymphocyte } (\times 10^9 / \text{L}) + 8$. The area under the receiver operating characteristic (ROC) curve was 0.843 (95% CI, 0.771-0.914). We propose an effective scoring system to predict the severity of COVID-19 patients. This simple prediction model may provide health-care workers with a practical method and could positively impact decision-making with regard to deteriorating patients.

SYMPTOMS AND CLINICAL PRESENTATION

ADULTS

EARLY RISK FACTORS OF THE EXACERBATION OF CORONAVIRUS DISEASE 2019 PNEUMONIA

Wang CZ, Hu SL, Wang L, Li M, Li HT.. J Med Virol. 2020 May 29. doi: 10.1002/jmv.26071. Online ahead of print.
Level of Evidence: 3

BLUF

An international group of researchers in the Hubei Province of China conducted a retrospective analysis of 85 patients with COVID-19 to identify early clinical features and potential early risk factors for pneumonia exacerbation. They found that high neutrophil count and bilateral lung involvement on CT imaging were risk factors for pneumonia progression. Moreover, they identified male sex, older age, and pre-existing heart conditions as risk factors for severe illness, which is consistent with previous reports (Table 1-3).

ABSTRACT

The purpose of this study was to investigate the early risk factors for the exacerbation of coronavirus disease 2019 (COVID-19) pneumonia. Retrospective analysis of clinical data of 85 patients infected with SARS-CoV-2, including gender, age,

comorbidities, symptoms, blood routine, clotting profile, biochemical examination, albumin, myocardial enzyme profile, inflammatory markers, and chest CT. All laboratory examination were measured within first 24 hours after admission, and chest CT were performed before admission. 56 (65.9%) patients had a history of exposure to Huanan seafood market in Wuhan. Fever and dry cough accounted for the highest percentage of all symptoms. Male COVID-2019 patients were more likely to develop severe pneumonia. Patients with severe and critical conditions are older and have higher rates of hypertension ($p=0.003$) and coronary heart disease ($p=0.017$). All severe and critical patients infected with SARS-CoV-2 showed bilateral lung involvement and have more multiple lobes involvement than common patients ($p<0.001$). Severe and critical patients showed higher WBC count ($p=0.006$), NEU count ($p=0.001$), NEU% ($p=0.002$), PCT ($p=0.011$), CRP ($p=0.003$), PT ($p=0.035$), D-dimer ($p=0.025$), AST ($p=0.006$), and lower LYM count ($p=0.019$), LYM% ($p=0.001$), ALB ($p<0.001$). Logistic regression analysis showed NEU count is a independent risk factor for deterioration, with the threshold of 6.5×10^9 L-1 . We concluded that the laboratory independent risk factor for the progression of COVID-19 pneumonia is NEU count. In addition, COVID-19 patients with bilateral lung involvement or multiple lobes involvement should be taken seriously and actively treated to prevent deterioration of the disease. This article is protected by copyright. All rights reserved.

FIGURES

Table1. Clinical features of patients infected with SARS-CoV-2

	Overall (n=85)	General group (n=46)	Severe and critical group (n=39)	p value
Characteristics				
Age, years	59.4 ± 15.3	53.6 ± 13.7	65.1 ± 15.1	0.002
≤ 60	46(54.1%)	32(69.6%)	14(35.9%)	
> 60	39(45.9%)	14(30.4%)	25(64.1%)	
Gender				
Male	45(52.9%)	18(39.1%)	27(69.2%)	0.006
Female	40(47.1%)	28(60.9%)	12(30.8%)	
Comorbidities				
Chronic obstructive pulmonary disease	5(5.9%)	1(2.2%)	4(10.3%)	0.265
Diabetes	10(11.8%)	3(6.5%)	7(17.9%)	0.197
Hypertension	22(25.9%)	6(13.0%)	16(41.0%)	0.003
Chronic kidney disease	4(4.7%)	1(2.2%)	3(7.7%)	0.830
Chronic liver disease	6(7.1%)	2(4.3%)	4(10.3%)	0.526
Coronary heart disease	9(10.6%)	1(2.2%)	8(20.5%)	0.017

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Table 2. The characteristics of chest CT of patients infected with SARS-CoV-2

	Overall (n=85)	General group (n=46)	Severe and critical group (n=39)	p value
Lung				0.010
Unilateral involvement	9(10.6%)	9(19.6%)	0(0)	
Bilateral involvement	76(89.4%)	37(80.4%)	39(100%)	
Lobe				<0.001
1	7(8.2%)	7(15.2%)	0(0)	
2	9(10.6%)	9(19.6%)	0(0)	

Table 3. Laboratory results of patients infected with SARS-CoV-2

	Overall (n=85)	General group (n=46)	Severe and critical group (n=39)	p value
Blood routine				
WBC count, $\times 10^9 \cdot L^{-1}$	3.67(5.16-7.61)	4.58(3.53-6.31)	7.13(4.2-9.03)	0.006
<4	24(28.2%)	15(32.6%)	9(23.1%)	0.035
4-10	50(58.8%)	29(63.0%)	21(53.8%)	
>10	11(12.9%)	2(4.3%)	9(23.1%)	
NEU, %	73.55(62.8-83.08)	67.7(58.0-75.45)	79.3(68.9-87.25)	0.002
NEU count, $\times 10^9 \cdot L^{-1}$	3.81(2.49-6.60)	3.2(2.26-4.06)	5.71(3.05-8.33)	0.001
<6.5	64(75.3%)	43(93.5%)	21(53.8%)	<0.001
≥ 6.5	21(24.7%)	3(6.5%)	18(46.2%)	

REGISTRIES OFFER INSIGHTS ON COVID-19-CANCER CONNECTION

Cancer Discov. 2020 May 29. doi: 10.1158/2159-8290.CD-NB2020-050. Online ahead of print.

Level of Evidence: 3

BLUF

Data from two large cancer databases, COVID-19 and Cancer Consortium (CCC19) and Thoracic cancer international coVid 19 cOllaboraTion (TERAVOLT), suggest that the mortality rate of COVID19 in cancer patients is approximately twice that for non-cancer patients. The following potential risk factors for mortality in cancer patients are also highlighted: male gender, former or current smoker, reduced performance status, non-small cell lung cancer diagnoses, current chemo & immunotherapy and being treated with azithromycin in combination with hydroxychloroquine.

SUMMARY

The CCC19 dataset was reviewed and findings included: 928 patients (21% breast cancer, 16% prostate cancer, 12% GI cancer, 11% lymphoma, 10% thoracic cancer, and 43% with active cancer) At 21 days it was found that these patients had a 13% mortality rate, per authors this was "roughly twice the estimated...mortality rate in the general population". This mortality rate increased up to 25% in patients 75-years-old and older in this data set. In the TERAVOLT dataset 400 patients were reviewed and at 33 days, 113 died from COVID-19. 45% of these patients were on chemotherapy and 20% were on immunotherapy.

ABSTRACT

Findings from CCC19 and TERA VOLT suggest that patients with cancer may be more likely to die from COVID-19 than people in the general population. Additional mortality risk factors may include age, performance status, treatment with chemotherapy, and exposure to hydroxychloroquine plus azithromycin.

A CASE SERIES OF FIVE PEOPLE LIVING WITH HIV HOSPITALIZED WITH COVID-19 IN CHICAGO, ILLINOIS

Ridgway JP, Farley B, Benoit JL, Frohne C, Hazra A, Pettit N, Pho M, Pursell K, Saltzman J, Schmitt J, Uvin AZ, Pittrak D, McNulty M.. AIDS Patient Care STDS. 2020 May 29. doi: 10.1089/apc.2020.0103. Online ahead of print.

Level of Evidence: 4

BLUF

A case series of five people living with HIV (PLWH) in Chicago from 3/1/2020–4/7/2020 described the clinical course of COVID-19 infection. All patients presented with classic symptoms of fever and cough, three had diarrhea, and one presented with predominantly cardiac symptoms. The data presented here contributes to the growing literature of PLWH with COVID-19 infection.

SUMMARY

A case series of five patients, all confirmed to be people living with HIV (PLWH), were described by the authors, summarized below:

1. A 38-year-old African American male with a past medical history of uncontrolled type 2 diabetes, obstructive sleep apnea, hypertension, obesity, and hyperlipidemia presented with cough, fever, diarrhea, myalgia, and dyspnea. His treatment included ceftriaxone, azithromycin, and hydroxychloroquine (initiated on day 3). The patient was discharged in stable condition on day 5.
2. A 50-year-old African American female with a past medical history of obesity presented with productive cough, fever, headache and dyspnea. She was admitted inpatient for hypoxia. Her treatment included oxygen via nasal cannula, ceftriaxone, azithromycin, and cefdinir. The patient was discharged in stable condition on day 4.
3. A 51-year-old African American female with a past medical history significant for tuberculosis treated with isoniazid presented with productive cough, myalgia, dyspnea, and diarrhea. She was admitted inpatient out of concern for acute coronary syndrome. Her treatment included ceftriaxone, cefdinir, azithromycin, and hydroxychloroquine. The patient was discharged in stable condition on day 7.
4. A 53-year-old African American female with a past medical history significant for esophageal fistulas presented with productive cough, nausea/vomiting, and diarrhea. She was admitted for hyponatremia with dehydration. Her treatment included azithromycin and cefdinir; the patient was discharged in stable condition on day 3.
5. A 47-year-old African American female with no significant past medical history aside from HIV presented with abdominal pain, dyspnea, nausea/vomiting, and chest pains. The patient was admitted for aberrant ventricular tachycardia. The patient left the hospital against physician advice on day 3.

ABSTRACT

The risk of COVID-19 among people living with HIV (PLWH) is largely unknown and there have been very few reported cases in the literature. We report a case series of five PLWH with COVID-19. We identified all patients with a diagnosis of HIV who tested positive for SARS-CoV-2 at University of Chicago Medicine between March 1, 2020, and April 7, 2020. We retrospectively collected data regarding demographics, comorbidities, medications, laboratory test results, radiology results, and outcomes associated with COVID-19. All five PLWH with COVID-19 were African American; 80% (4/5) were cisgender females. The mean age of patients was 48 years old (range 38–53). The majority of patients presented with cough, fever, and shortness of breath. Three patients had diarrhea. One patient presented with predominantly cardiac symptoms. All were taking antiretroviral therapy (ART) with CD4 count >200 cells/mm³ and suppressed HIV viral loads at the time of COVID-19 diagnosis. All five patients were hospitalized, two required supplemental oxygen, and none required mechanical ventilation. Four patients were treated with azithromycin and a cephalosporin and two were also treated with hydroxychloroquine. The

median length of stay was 3 days (range 2-7). All patients recovered. More research is needed to understand the risks of COVID-19 among PLWH and the impact of ART on outcomes for patients with COVID-19.

CLINICAL CHARACTERISTICS AND OUTCOMES IN PEOPLE LIVING WITH HIV HOSPITALIZED FOR COVID-19

Shalev N, Scherer M, LaSota ED, Antoniou P, Yin MT, Zucker J, Sobieszczyk ME.. Clin Infect Dis. 2020 May 30:ciaa635. doi: 10.1093/cid/ciaa635. Online ahead of print.

Level of Evidence: 4

BLUF

A case series conducted at Allen Hospital and Columbia University Irving Medical Center in New York between March 15 and April 15, 2020 by Columbia University Medical Center found that of 30 patients with HIV (all on antiretroviral therapy prior to admission) who tested positive for COVID-19 and had T cell panel data measured, 80% had CD4 T-cell counts greater than 200 cells/ul, suggesting that patients with uncontrolled HIV are not at greater risk for contraction of SARS-CoV-2. Patient information, presentation, and outcomes are noted in the table.

ABSTRACT

We describe the characteristics of 31 people living with HIV (PLWH) hospitalized for Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) infection. All patients were on antiretroviral therapy and virologically suppressed at the time of admission. Clinical course and outcomes were similar to those reported in other hospitalized cohorts.

FIGURES

HIV-related variables	
CD4+ T cells, cells/ul mean (range)	396 (89-924)
CD4+ T cells % (range)	28.7 (7-49)
HIV-1 viral load <37 copies per ml, n (%)	28 (90.3)
Viral load <200 copies/ml, n (%)	30 (96.8)
Antiretroviral regimen, n (%)	
INSTI+2NRTI	20 (64.5)
NNRTI+2NRTI	3 (9.7)
PI/b+2NRTI	4 (12.9)
Other	4 (12.9)
Contains TDF/TAF	17 (54.8)
Contains PI	7 (22.6)
Fever	
Temperature >38.0°C during admission	23 (74.2)
CXR abnormalities on admission**	20 (64.5)
Pharmacologic treatment n (%)	
None	3 (9.7)
Hydroxychloroquine	24 (77.4)
Azithromycin	16 (51.6)
Corticosteroids	8 (25.8)

IL6 Receptor inhibitor	3 (9.7)
Laboratory values mean (range)	
Lymphocyte % nadir	12.6 (3.8-31.9)
C-reactive protein max, µg/mL	182.2 (1.1->300)
Ferritin max, µg/L	1356.7 (80-7490)
D-dimer max, µg/mL	6.9 (0.3-20)
Procalcitonin max, µg/mL	2.2 (0.04-26.9)
Maximal Oxygenation Support n (%)	
Room air	3 (9.7)
Low flow nasal cannula	13 (41.9)
Non-rebreather mask	7 (22.6)
Mechanical ventilation	8 (25.8)
Vital status	
Alive	23 (74.2)
Discharged	21 (67.7)
Hospitalized	2 (6.5)
Deceased	8 (25.8)

THE NOVEL CORONAVIRUS DISEASE (COVID-19) COMPLICATED BY PULMONARY EMBOLISM AND ACUTE RESPIRATORY DISTRESS SYNDROME

Li T, Cheng GS, Pipavath S, Kicska G, Liu L, Kinahan PE, Wu W.. J Med Virol. 2020 May 29. doi: 10.1002/jmv.26068. Online ahead of print.

Level of Evidence: 5

BLUF

These researchers present two cases of COVID-19 infections in Wuhan, China that resulted in acute pulmonary embolisms (PE): a 57 year old male non-smoker with an unknown medical history and a 70 year old male with a 50 year smoking history and hypertension. The authors indicate that these cases should serve as a reminder to consider PE as a potential source of hypoxemia in COVID-19 patients.

ABSTRACT

Acute respiratory distress syndrome and coagulopathy played an important role in morbidity and mortality of severe COVID-19 patients. A higher frequency of PE than expected in COVID-19 patients was recently reported. The presenting symptoms for PE were atypical including dyspnea, which is one of the major symptoms in severe COVID-19, especially in those patients with ARDS. We reported two COVID-19 cases with coexisting complications of PE and ARDS, aiming to consolidate the emerging knowledge of this global health emergency and raise the awareness that the hypoxemia or severe dyspnea in COVID-19 may be related to PE and not necessarily always due to the parenchymal disease.

UNDERSTANDING THE PATHOLOGY

WITHANONE AND WITHAFERIN-A ARE PREDICTED TO INTERACT WITH TRANSMEMBRANE PROTEASE SERINE 2 (TMPRSS2) AND BLOCK ENTRY OF SARS-COV-2 INTO CELLS

Kumar V, Dhanjal JK, Bhargava P, Kaul A, Wang J, Zhang H, Kaul SC, Wadhwa R, Sundar D.. J Biomol Struct Dyn. 2020 May 29:1-27. doi: 10.1080/07391102.2020.1775704. Online ahead of print.

Level of Evidence: 5

BLUF

This in silico study investigated derivatives from the Ayurvedic plant Ashwagandha, using a modified protein sequence to model transmembrane protease serine 2 (TMPRSS2), which is reportedly the main protease used by SARS-CoV-2 to facilitate viral entry into host cells. The authors found that both Withanone and Withaferin showed stable binding to the active site, while Withanone alone downregulated TMPRSS2 expression during in vitro studies (Figure 2). These bioactive derivatives computationally show promise in preventing viral entry into host cells but require further clinical investigation to determine their role in drug development, prevention, and treatment for COVID-19.

ABSTRACT

Coronavirus disease 2019 (COVID-19) initiated in December 2019 in Wuhan, China, and became pandemic causing high fatality and disrupted normal life calling world almost to a halt. Causative agent is a novel coronavirus called Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2/2019-nCoV). While new line of drug/vaccine development has been initiated world-wide, in the current scenario of high infected numbers, severity of the disease and high morbidity, repurposing of the existing drugs is heavily explored. Here, we used a homology-based structural model of transmembrane protease serine 2 (TMPRSS2), a cell surface receptor, required for entry of virus to the target host cell. Using the strengths of molecular docking and molecular dynamics simulations, we examined the binding potential of Withaferin-A (Wi-A), Withanone (Wi-N) and Caffeic Acid Phenethyl Ester to TMPRSS2 in comparison to its known inhibitor, Camostat mesylate. We found that both Wi-A and Wi-N could bind and stably interact at the catalytic site of TMPRSS2. Wi-N showed stronger interactions with TMPRSS2 catalytic residues than Wi-A, and also able to induce changes in its allosteric site. Furthermore, we investigated the effect of Wi-N on TMPRSS2 expression in MCF7 cells and found remarkable downregulation of TMPRSS2 mRNA in treated cells predicting dual action of Wi-N to block SARS-CoV-2 entry to the host cells. Since the natural compounds are easily available/affordable, they may even offer a timely therapeutic/preventive value for the management of SARS-CoV-2 pandemic. We also report that Wi-A/Wi-N content varies in different parts of Ashwagandha and warrants careful attention for their use.

FIGURES

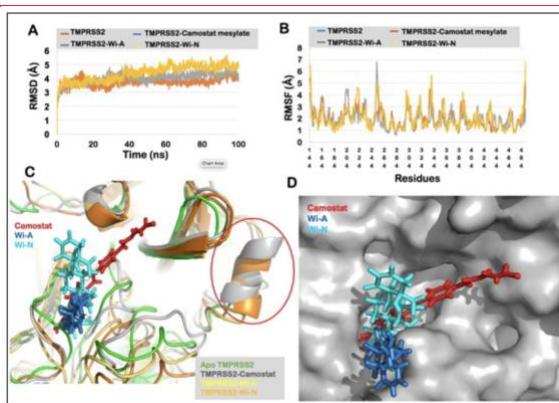


Figure 2. (A) RMSD of the protein backbone along the simulation trajectory for the protein alone and all the docked complexes.

The overall structure of TMPRSS2 did not change much after the binding of Wi-N or Wi-A when compared to Camostat mesylate. (B) RMSF of the amino acids comprising the interacting domain of TMPRSS2. No abrupt fluctuations were observed in any region of the protein with or without the three ligands. (C) Superimposition of the three docked complexes with Apo-TMPRSS2. All the three small molecules- Camostat mesylate, Wi-N and Wi-A were bound in the same site suggesting their similar mechanism of action. Conformational change from loop to helix was observed in region Arg316 to Tyr322 in case of Camostat mesylate and Wi-N. (D) Surface representation of TMPRSS2 showing all the ligands embedded in its catalytic pocket.

COVID-19 AND THE IMMUNE SYSTEM

Paces J, Strizova Z, Smrz D, Cerny J.. Physiol Res. 2020 May 29. Online ahead of print.

Level of Evidence: Other

BLUF

Researchers from Charles University, Czech Republic discuss the immunological aspects of COVID-19. They find the following and emphasize that deeper understanding of the pathophysiology can accelerate vaccine development efforts.

- Both innate and adaptive immune systems are crucial in mounting a response, but it is unknown whether failure to mobilize the adaptive immune system leads to severe disease
- IgA response is stronger than the other antibodies generated and more persistent
- Interleukin(IL)-6 is elevated in greater than 50% of patients
- "Macrophage Activation Syndrome" may explain the unusual finding of elevated CRP in some COVID-19 patients.

ABSTRACT

A close interaction between the virus SARS-CoV-2 and the immune system of an individual results in a diverse clinical manifestation of the COVID-19 disease. While adaptive immune responses are essential for SARS-CoV-2 virus clearance, the innate immune cells, such as macrophages, may contribute, in some cases, to the disease progression. Macrophages have shown a significant production of IL-6 suggesting they may contribute to the excessive inflammation in COVID-19 disease. Macrophage Activation Syndrome may further explain the high serum levels of CRP, which are normally lacking in viral infections. In adaptive immune responses, it has been revealed that cytotoxic CD8+ T cells exhibit functional exhaustion patterns, such as the expression of NKG2A, PD-1, and TIM-3. Since SARS-CoV-2 restrains antigen presentation by downregulating MHC class I and II molecules and, therefore, inhibits the T cell-mediated immune responses, humoral immune responses also play a substantial role. Specific IgA response appears to be stronger and more persistent than IgM response. Moreover, IgM and IgG antibodies show similar dynamics in COVID-19 disease.

SARS-COV-2 PERTURBS THE RENIN-ANGIOTENSIN SYSTEM AND ENERGY METABOLISM

Mori J, Oudit GY, Lopaschuk GD.. Am J Physiol Endocrinol Metab. 2020 May 29. doi: 10.1152/ajpendo.00219.2020. Online ahead of print.

Level of Evidence: Other

BLUF

This review article discusses the mechanisms which may put persons with obesity and diabetes at increased risk for severe COVID-19 disease, which include a chronic inflammatory state and impaired T cell function. Additionally, the authors suggest that SARS-CoV-2 infections can disrupt the renin-angiotensin system (RAS) which decreases the activity of the pyruvate dehydrogenase complex and impairs energy metabolism. The authors conclude by arguing that "restoring the balance in the RAS and energy metabolism could be crucial to reducing disease severity and mortality of patients with COVID-19, and especially obese patients, with or without diabetes."

ABSTRACT

The COVID-19 pandemic, caused by the novel coronavirus, SARS-CoV-2, is threatening our health systems and daily lives, and is responsible for causing substantial morbidity and mortality. In particular, aged individuals, and individuals with comorbidities, including obesity, diabetes mellitus, and hypertension, have significantly higher risks of hospitalization and death than normal individuals. The renin-angiotensin system (RAS) plays a pivotal role in the pathogenesis of diabetes mellitus, obesity, and hypertension. Angiotensin converting enzyme 2 (ACE2), belonging to the RAS family, has received much attention during this COVID-19 pandemic, owing to the fact that SARS-CoV-2 uses ACE2 as a receptor for cellular entry. Additionally, the RAS greatly affects energy metabolism in certain pathological conditions, including cardiac failure, diabetes mellitus, and viral infections. This article discusses the potential mechanisms by which SARS-CoV-2 modulates the RAS and energy metabolism in individuals with obesity and diabetes mellitus. The article aims to highlight the appropriate strategies for combating the COVID-19 pandemic in the clinical setting and emphasize on the areas that require further investigation in relation to COVID-19 infections in patients with obesity and diabetes mellitus, from the viewpoint of endocrinology and metabolism.

NOVEL IMMUNOGLOBULIN DOMAIN PROTEINS PROVIDE INSIGHTS INTO EVOLUTION AND PATHOGENESIS OF SARS-COV-2-RELATED VIRUSES

Tan Y, Schneider T, Leong M, Aravind L, Zhang D.. mBio. 2020 May 29;11(3):e00760-20. doi: 10.1128/mBio.00760-20.

Level of Evidence: 5

BLUF

Researchers in Missouri conducted genomic and structural analysis of the SARS-CoV-2 proteome focusing on fast-evolving genomic regions that may be the result of an evolutionary arms race between virus and host. They describe the receptor binding domain of the Spike protein, three tandem Macro fold domains in ORF1, and a previously uncharacterized protein encoded by ORF8. They note that the ORF8 protein possesses a hypervariable position in its predicted binding groove and propose that this, along with the aforementioned proteins, plays a significant role in pathogenicity through modulation of host immunity (figures 1-3) and should be investigated further for this application.

ABSTRACT

A novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was recently identified as the causative agent for the coronavirus disease 2019 (COVID-19) outbreak that has generated a global health crisis. We use a combination of genomic analysis and sensitive profile-based sequence and structure analysis to understand the potential pathogenesis determinants of this virus. As a result, we identify several fast-evolving genomic regions that might be at the interface of virus-host interactions, corresponding to the receptor binding domain of the Spike protein, the three tandem Macro fold domains in ORF1a, and the uncharacterized protein ORF8. Further, we show that ORF8 and several other proteins from alpha- and beta-CoVs belong to novel families of immunoglobulin (Ig) proteins. Among them, ORF8 is distinguished by being rapidly evolving, possessing a unique insert, and having a hypervariable position among SARS-CoV-2 genomes in its predicted ligand-binding groove. We also uncover numerous Ig domain proteins from several unrelated metazoan viruses, which are distinct in sequence and structure but share comparable architectures to those of the CoV Ig domain proteins. Hence, we propose that SARS-CoV-2 ORF8 and other previously unidentified CoV Ig domain proteins fall under the umbrella of a widespread strategy of deployment of Ig domain proteins in animal viruses as pathogenicity factors that modulate host immunity. The rapid evolution of the ORF8 Ig domain proteins points to a potential evolutionary arms race between viruses and hosts, likely arising from immune pressure, and suggests a role in transmission between distinct host species.

IMPORTANCE The ongoing COVID-19 pandemic strongly emphasizes the need for a more complete understanding of the biology and pathogenesis of its causative agent SARS-CoV-2. Despite intense scrutiny, several proteins encoded by the genomes of SARS-CoV-2 and other SARS-like coronaviruses remain enigmatic. Moreover, the high infectivity and severity of SARS-CoV-2 in certain individuals make wet-lab studies currently challenging. In this study, we used a series of computational strategies to identify several fast-evolving regions of SARS-CoV-2 proteins which are potentially under host immune pressure. Most notably, the hitherto-uncharacterized protein encoded by ORF8 is one of them. Using sensitive sequence and structural analysis methods, we show that ORF8 and several other proteins from alpha- and beta-coronavirus comprise novel families of immunoglobulin domain proteins, which might function as potential immune modulators to delay or attenuate the host immune response against the viruses.

FIGURES



Figure 1: Genome similarity analysis of SARS-CoV-2-related viruses. The similarity plot of SARS-CoV-2-related CoVs compared to the human SARS-CoV-2 Wuhan-Hu-1 genome (GenBank accession no. NC_045512.2) is drawn based on a multiple-sequence alignment of the whole genomes. Each point represents percent identity of a 200-bp window of the alignment with a 50-bp step size between the points in each pair. The open reading frames of the SARS-CoV-2 genome (NC_045512.2) are shown above the plot. Each colored line corresponds to the nucleotide similarity between the human SARS-CoV-2 genome and the respective other CoV genome. The recombination events are represented by dispersed regions (indicated by red arrows), which deviate from the overall pattern of similarity between genomes, while the fast-evolving regions are represented by valleys where there is low similarity between genome regions (R1, R2, and R3). An in-depth analysis performed with various sizes of similarity windows is shown in Fig. S1. For detailed information about the genomes that were used in this study, refer to Table S1.

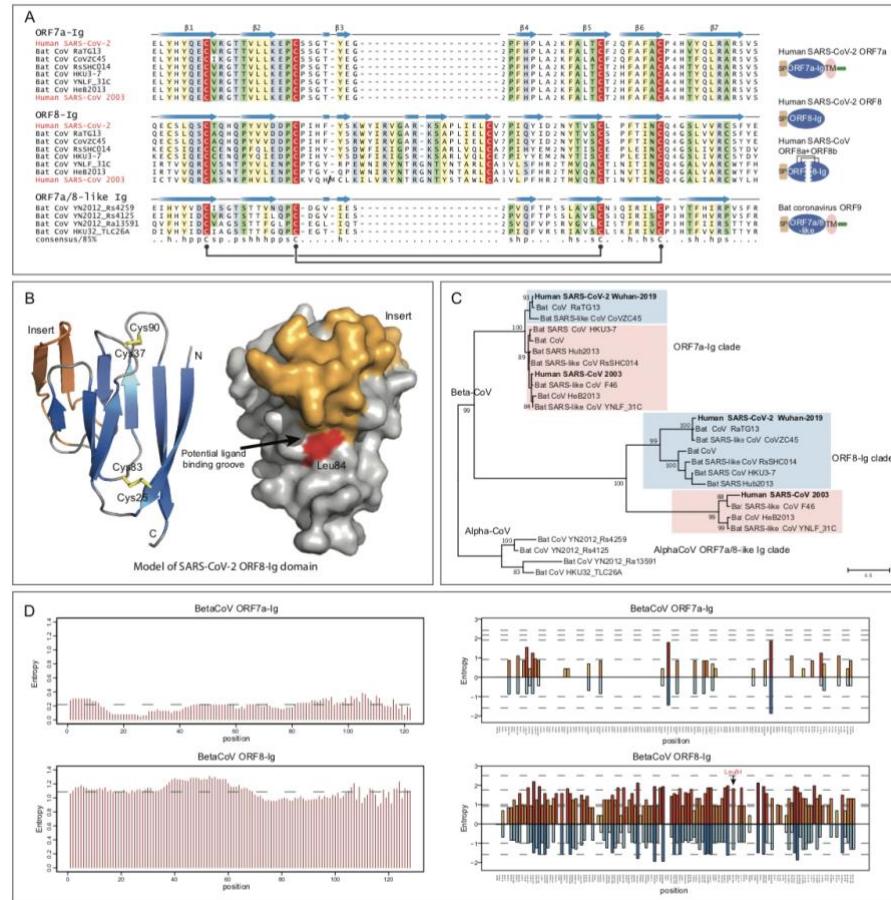


Figure 2: Sequence, structure, and evolutionary analysis of novel Ig domain proteins in SARS-CoV-2-related CoVs. (A) Multiple-sequence alignment (MSA) and representative domain architectures of ORF7a-Ig, ORF8-Ig, and ORF7a/8-like Ig domain families. Each sequence in the MSA is labeled by its species abbreviation followed by its source. The predicted secondary structure is shown above each alignment, and the consensus is shown below the superalignment, where “h” stands for hydrophobic residues, “s” for small residues, and “p” for polar residues. Two pairs of conserved cysteines that form disulfide bonds are highlighted in red. (B) Homology model of the SARS-CoV-2 ORF8-Ig domain (GenBank accession no. YP_009724396.1) and the location of the hypervariable position corresponding to Leu84 in the predicted ligand-binding groove. The β -sheets of the common core of the Ig fold are colored in blue, the insertion in ORF8-Ig in orange, and the loops in gray. The characteristic disulfide bonds are highlighted in yellow. (C) Maximum likelihood phylogenetic analysis of CoV Ig domain families. Supporting values from 100 bootstraps are shown for the major branches only. (D) Entropy plot for the ORF7a and ORF8 proteins in betacoronavirus. (Left) Shannon entropy data were computed for each column for a character space of 20 amino acids and are presented as mean entropy in a sliding window of 30 residues. The mean entropy across the entire length of the protein is indicated as a green horizontal line. (Right) Shannon entropy data computed based on regular amino acid alphabet (20 amino acids) are shown above the zero line in shades of orange. Shannon entropy data computed based on a reduced alphabet of 8 residues are shown below the zero line in shades of blue. Where a position shows high entropy in both alphabets, it is a sign of potential positive selection at those positions for amino acids of different chemical characters.

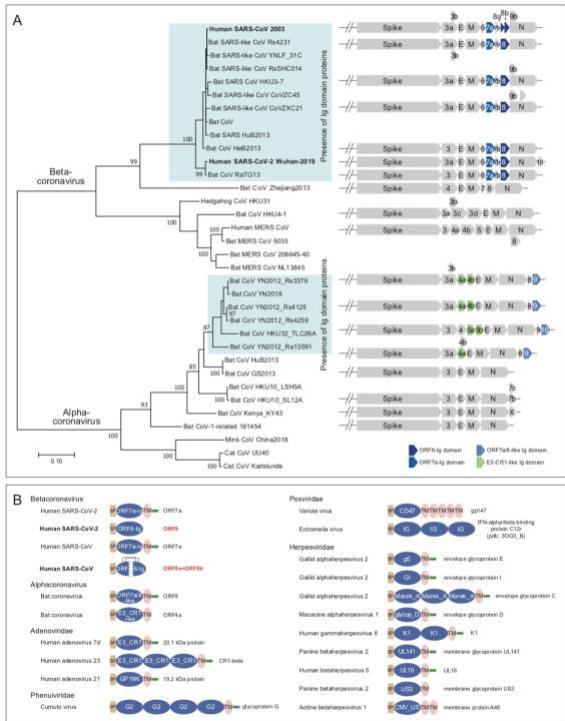


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COVID-19: TWO THIRDS OF PEOPLE CONTACTED THROUGH TRACING DID NOT FULLY COOPERATE, PILOT SCHEME FINDS

Mahase E.. BMJ. 2020 May 29;369:m2169. doi: 10.1136/bmj.m2169.

Level of Evidence: Other

BLUF

A pilot COVID-19 tracing scheme in Sheffield, UK by the Sheffield Community Contact Tracers team reports underwhelming cooperation with contact tracing. Only 19 out of 58 cases provided contact information while others were unable or unwilling to cooperate. In the author's opinion, they there is a need for a better contact tracing system that emphasizes the notion of civic duty.

MANAGEMENT

ACUTE CARE

DIAGNOSTIC RADIOLOGY

THE SPECTRUM OF CARDIAC MANIFESTATIONS IN CORONAVIRUS DISEASE 2019 (COVID-19) - A SYSTEMATIC ECHOCARDIOGRAPHIC STUDY

Szekely Y, Lichter Y, Taieb P, Banai A, Hochstadt A, Merdler I, Gal Oz A, Rothschild E, Baruch G, Peri Y, Arbel Y, Topilsky Y..

Circulation. 2020 May 29. doi: 10.1161/CIRCULATIONAHA.120.047971. Online ahead of print.

Level of Evidence: 4

BLUF

A prospective cohort study evaluated cardiac abnormalities in COVID-19 by conducting comprehensive echocardiographic (Echo) examinations of 100 adult COVID-19 patients (RT-PCR confirmed) enrolled between March 21-April 16, 2020 at the Tel Aviv Medical Center. They found that 32% had a normal Echo, while 20% had clinical deterioration with right ventricular deterioration more common than left. The authors conclude that to reduce the risk of COVID-19 transmission transthoracic Echo should be restricted to patients with clinical deterioration in cardiac function, where it can help in the determination of the mechanics of the cardiac injury and guide management.

ABSTRACT

Background: Information regarding the cardiac manifestations of COVID-19 is scarce. We performed a systematic and comprehensive echocardiographic evaluation of consecutive patients hospitalized with COVID-19 infection. **Methods:** 100 consecutive patients diagnosed with COVID-19 infection underwent complete echocardiographic evaluation within 24 hours of admission and were compared to reference values. Echocardiographic studies included left ventricular (LV) systolic and diastolic function, valve hemodynamics and right ventricular (RV) assessment, as well as lung ultrasound. A second exam was performed in case of clinical deterioration. **Results:** Thirty two patients (32%) had a normal echocardiogram at baseline. The most common cardiac pathology was RV dilatation and dysfunction (observed in 39% of patients), followed by LV diastolic dysfunction (16%) and LV systolic dysfunction (10%). Patients with elevated troponin (20%) or worse clinical condition did not demonstrate any significant difference in LV systolic function compared to patients with normal troponin or better clinical condition, but had worse RV function. Clinical deterioration occurred in 20% of patients. In these patients, the most common echocardiographic abnormality at follow-up was RV function deterioration (12 patients), followed by LV systolic and diastolic deterioration (in 5 patients). Femoral vein thrombosis (DVT) was diagnosed in 5 of 12 patients with RV failure. **Conclusions:** In COVID-19 infection, LV systolic function is preserved in the majority of patients, but LV diastolic and RV function are impaired. Elevated troponin and poorer clinical grade are associated with worse RV function. In patients presenting with clinical deterioration at follow-up, acute RV dysfunction, with or without DVT, is more common, but acute LV systolic dysfunction was noted in 20%.

MEDICAL SUBSPECIALTIES

NEWLY DIAGNOSED DIABETES IS ASSOCIATED WITH A HIGHER RISK OF MORTALITY THAN KNOWN DIABETES IN HOSPITALIZED PATIENTS WITH COVID-19

Li H, Tian S, Chen T, Cui Z, Shi N, Zhong X, Qiu K, Zhang J, Zeng T, Chen L, Zheng J.. Diabetes Obes Metab. 2020 May 29. doi: 10.1111/dom.14099. Online ahead of print.

Level of Evidence: 3

BLUF

A retrospective study involving 453 COVID-19 patients located at Union Hospital in Wuhan, China from 22 January and 17 March 2020 found that patients with "newly diagnosed diabetes at the first measurement of hospital admission and a history of diabetes were associated with an increased risk of all-cause mortality in hospitalized patients with COVID-19." The authors suggest that "patients with COVID-19 need to be under surveillance for blood glucose screening, and COVID-19 patients with newly diagnosed diabetes should be paid more attention to the combination therapy for all COVID-19-related complications."

ABSTRACT

CONTEXT: No studies evaluated the prospective association between hyperglycemia assessed by laboratory measurements and the risk of mortality among patients with coronavirus disease 2019 (COVID-19).

OBJECTIVE: We aimed to evaluate the association between different degrees of hyperglycemia and the risk of all-cause mortality among hospitalized patients with COVID-19.

DESIGN: A retrospective study.

SETTING: Union Hospital in Wuhan, China.

PARTICIPANTS: 453 patients were admitted to the hospital with laboratory-confirmed SARS-CoV-2 infection from January 22, 2020 to March 17, 2020.

MAIN OUTCOMES AND MEASURES: Patients were classified into four categories: normal glucose, hyperglycemia (fasting glucose 5.6-6.9 mmol/L and/or HbA1c 5.7-6.4%), newly diagnosed diabetes (fasting glucose ≥ 7 mmol/L and/or HbA1c $\geq 6.5\%$), and known diabetes. The major outcomes included in-hospital mortality, intensive care unit (ICU) admission, and invasive mechanical ventilation (IMV).

RESULTS: Patients with newly diagnosed diabetes had the highest percentage to be admitted to the ICU (11.7%) and require IMV (11.7%), followed by patients with known diabetes (4.1%; 9.2%) and patients with hyperglycemia (6.2%; 4.7%), compared with patients with normal glucose (1.5%; 2.3%), respectively. The multivariable-adjusted hazard ratios of mortality among COVID-19 patients with normal glucose, hyperglycemia, newly diagnosed diabetes, and known diabetes were 1.00, 3.29 (95% confidence interval [CI] 0.65-16.6), 9.42 (95% CI 2.18-40.7), and 4.63 (95% CI 1.02-21.0), respectively.

CONCLUSION: We firstly showed that COVID-19 patients with newly diagnosed diabetes had the highest risk of all-cause mortality compared with COVID-19 patients with known diabetes, hyperglycemia and normal glucose. Patients with COVID-19 need to be under surveillance for blood glucose screening.

SURGICAL SUBSPECIALTIES

OTOLARYNGOLOGY

MANAGEMENT OF UPPER AIRWAY BLEEDING IN COVID-19 PATIENTS ON EXTRACORPOREAL MEMBRANE OXYGENATION

LoSavio PS, Patel T, Urban MJ, Tajudeen B, Papagiannopoulos P, Revenaugh PC, Husain I, Batra PS.. Laryngoscope. 2020 May 29. doi: 10.1002/lary.28846. Online ahead of print.

Level of Evidence: 4

BLUF

Authors from Rush University Medical Center present a case series of three COVID-19 patients requiring otolaryngology intervention during veno-venous extracorporeal membrane oxygenation (V-V ECMO) (Table I) and found that patients on ECMO are at high risk for airway hemorrhage. While anti-coagulation prophylaxis contributed to bleeding in these cases, the authors caution that it should be resumed as soon as bleeding is controlled to avoid COVID-19 related thrombotic complications.

FIGURES

Case	Age	Sex	Hgb (g/dL)	Platelets (K/ μ L)	INR/PTT (s)	Anticoagulant	Method of hemostasis	Length of time anticoagulation held (days)
1	53	M	11.8	146	1.85/71.4	bivalirudin	Oropharyngeal gauze, absorbable nasal (gelatin/thrombin matrix, gelatin sponge)	5
2	46	M	13.2	103	1.38/61.8	bivalirudin	Absorbable nasal (cellulose hemostat, gelatin sponge)	1
3	34	M	12.4	144	1.66/65.8	bivalirudin	Absorbable nasal (gelatin sponge, gelatin/thrombin matrix)	3

Table I. Summary of COVID-19 patients on ECMO requiring otolaryngology intervention for airway bleeding. Hgb=hemoglobin, INR=international normalized ratio, PTT=partial thromboplastin time.

TRANSPLANT SURGERY

LOW PREVALENCE AND DISEASE SEVERITY OF COVID-19 IN POST LIVER TRANSPLANT RECIPIENTS - A SINGLE CENTRE EXPERIENCE

Verma A, Khorsandi SE, Dolcet A, Prachalias A, Suddle A, Heaton N, Jassem W.. Liver Int. 2020 May 29. doi: 10.1111/liv.14552. Online ahead of print.

Level of Evidence: 4

BLUF

A case-series conducted at a single high volume UK liver transplant unit identified 5 liver transplant recipients with reported COVID-19 out of about 4,500 post-transplant cases, for a relatively low incidence of known COVID-19 infection at about 0.1%. Each of the 5 patients who contracted the disease had a mild course of illness that improved with supportive care and required minimal change to their immunosuppressive regimen. The authors conclude that liver transplant patients have a low prevalence of COVID-19 and speculate that this may be due in part to strong recommendations of social isolation for this high-risk group and/or a beneficial effect of their immune suppression.

ABSTRACT

Coronavirus disease 2019 (COVID-19) caused by a novel coronavirus called severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is driving a present day global pandemic. Immunosuppressed patients are regarded as a high risk cohort. The following is a short report on COVID-19 in liver transplant recipients (n=5) from a high volume UK liver transplant unit with a large follow up cohort (n=4500). Based on this limited data, liver transplant recipients appear to have a low incidence of COVID-19, with less severe symptoms than expected, when compared to the general population and other solid organ recipients. This possibly could be related to self-isolation adherence and/or the "ideal" level of immunosuppression that favourably modulates the immune response to COVID-19.

ADJUSTING PRACTICE DURING COVID-19

FOR HEALTHCARE PROFESSIONALS

LETTER TO THE EDITOR: IN RESPONSE TO "ROLE OF TELEHEALTH IN THE MANAGEMENT OF COVID-19: LESSONS LEARNED FROM PREVIOUS SARS, MERS, AND EBOLA OUTBREAKS"

Dunnigan A.. Telemed J E Health. 2020 May 29. doi: 10.1089/tmj.2020.0141. Online ahead of print.

Level of Evidence: Other

BLUF

This commentary details how the National Health Service (NHS) in the United Kingdom lagged behind the rest of the world when it came to implementation of telemedicine. The author discuss the successes of telemedicine both in previous outbreaks as well as the current COVID-19 pandemic but explain that the NHS's reluctance stemmed from concerns about data protection and privacy.

ACUTE CARE

NEUROLOGY

NEUROPATHOGENESIS AND NEUROLOGIC MANIFESTATIONS OF THE CORONAVIRUSES IN THE AGE OF CORONAVIRUS DISEASE 2019: A REVIEW

Zubair AS, McAlpine LS, Gardin T, Farhadian S, Kuruvilla DE, Spudich S.. JAMA Neurol. 2020 May 29. doi: 10.1001/jamaneurol.2020.2065. Online ahead of print.

Level of Evidence: Other

BLUF

This review discusses neurologic manifestations and complications of COVID-19 infection. Common neurologic symptoms include headaches, anosmia (loss of smell) and ageusia (loss of taste) with other complications listed as strokes, seizures and encephalopathy. Proposed mechanisms of symptoms include transsynaptic transfer, infection via olfactory nerve, and infection or inflammation of vascular endothelium (Figures 1-3), but additional studies are needed to better understand the pathophysiology as well as potential treatments.

ABSTRACT

Importance: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in December 2019, causing human coronavirus disease 2019 (COVID-19), which has now spread into a worldwide pandemic. The pulmonary manifestations of COVID-19 have been well described in the literature. Two similar human coronaviruses that cause Middle East respiratory syndrome (MERS-CoV) and severe acute respiratory syndrome (SARS-CoV-1) are known to cause disease in the central and peripheral nervous systems. Emerging evidence suggests COVID-19 has neurologic consequences as well. **Observations:** This review serves to summarize available information regarding coronaviruses in the nervous system, identify the potential tissue targets and routes of entry of SARS-CoV-2 into the central nervous system, and describe the range of clinical neurological complications that have been reported thus far in COVID-19 and their potential pathogenesis. Viral neuroinvasion may be achieved by several routes, including transsynaptic transfer across infected neurons, entry via the olfactory nerve, infection of vascular endothelium, or leukocyte migration across the blood-brain barrier. The most common neurologic complaints in COVID-19 are anosmia, ageusia, and headache, but other diseases, such as stroke, impairment of consciousness, seizure, and encephalopathy, have also been reported. **Conclusions and Relevance:** Recognition and understanding of the range of neurological disorders associated with COVID-19 may lead to improved clinical outcomes and better treatment algorithms. Further neuropathological studies will be crucial to understanding the pathogenesis of the disease in the central nervous system, and longitudinal neurologic and cognitive assessment of individuals after recovery from COVID-19 will be crucial to understand the natural history of COVID-19 in the central nervous system and monitor for any long-term neurologic sequelae.

FIGURES

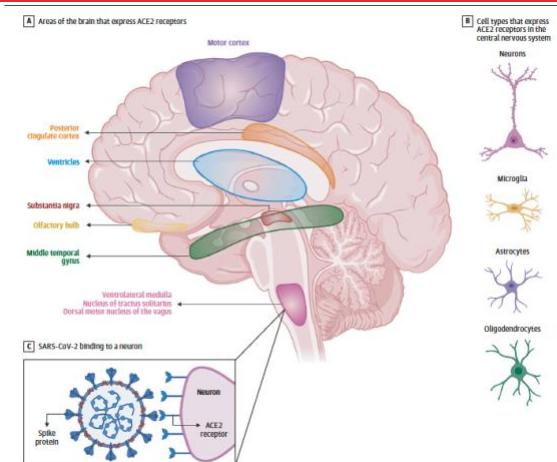


Figure 1. Angiotensin-Converting Enzyme 2 (ACE2) Expression in the Brain. Emerging data suggest that ACE2 receptors are expressed in multiple regions of the human and mouse brain, including the motor cortex, posterior cingulate cortex, ventricles, substantia nigra, olfactory bulb, middle temporal gyrus, ventrolateral medulla, nucleus of tractus solitarius, and dorsal motor nucleus of the vagus nerve (A) and on several key cell types that make up the central nervous system, including neurons, microglia, astrocytes, and oligodendrocytes (B).³⁵⁻³⁷ C, ACE2 receptors on a medullary neuron binding to the SPIKE protein on severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). This figure was created by an author (L.S.M.) using the website <https://app.biorender.com>.

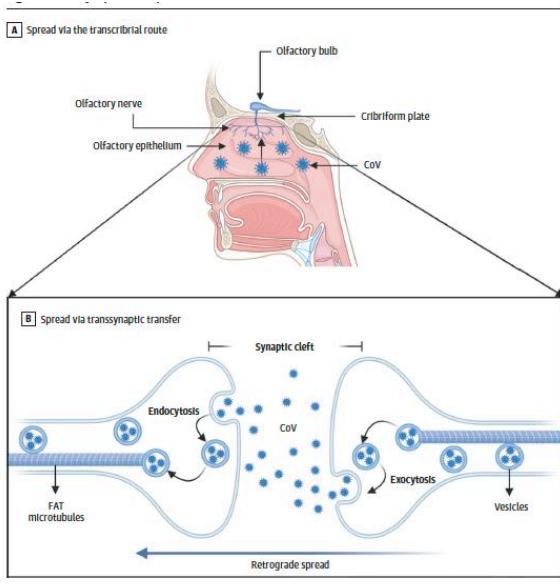


Figure 2. Transsynaptic Viral Spread. A, Coronavirus (CoV) has been shown to spread via the transcribral route from the olfactory epithelium along the olfactory nerve to the olfactory bulb within the central nervous system. B, CoV has been shown to spread retrograde via transsynaptic transfer using an endocytosis or exocytosis mechanism and a fast axonal transport (FAT) mechanism of vesicle transport to move virus along microtubules back to neuronal cell bodies. This figure was created by an author (L.S.M.) using the website <https://app.biorender.com>.

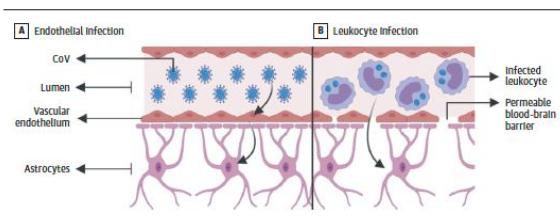


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MEDICAL SUBSPECIALTIES

INPATIENT MEDICINE

DECEASES IN ACUTE HEART FAILURE HOSPITALIZATIONS DURING COVID-19

Cox ZL, Lai P, Lindenfeld J.. Eur J Heart Fail. 2020 May 29. doi: 10.1002/ejhf.1921. Online ahead of print.

Level of Evidence: 3

BLUF

A chart review conducted by authors affiliated with Vanderbilt University Medical Center comparing acute heart failure (AHF) patient admissions between 2019 and 2020 found a mean decrease in AHF hospitalizations of 62% from March 22nd to April 20th. They indicate that findings suggest heart failure patients may be delaying care to avoid potential COVID-19 infection.

FIGURES

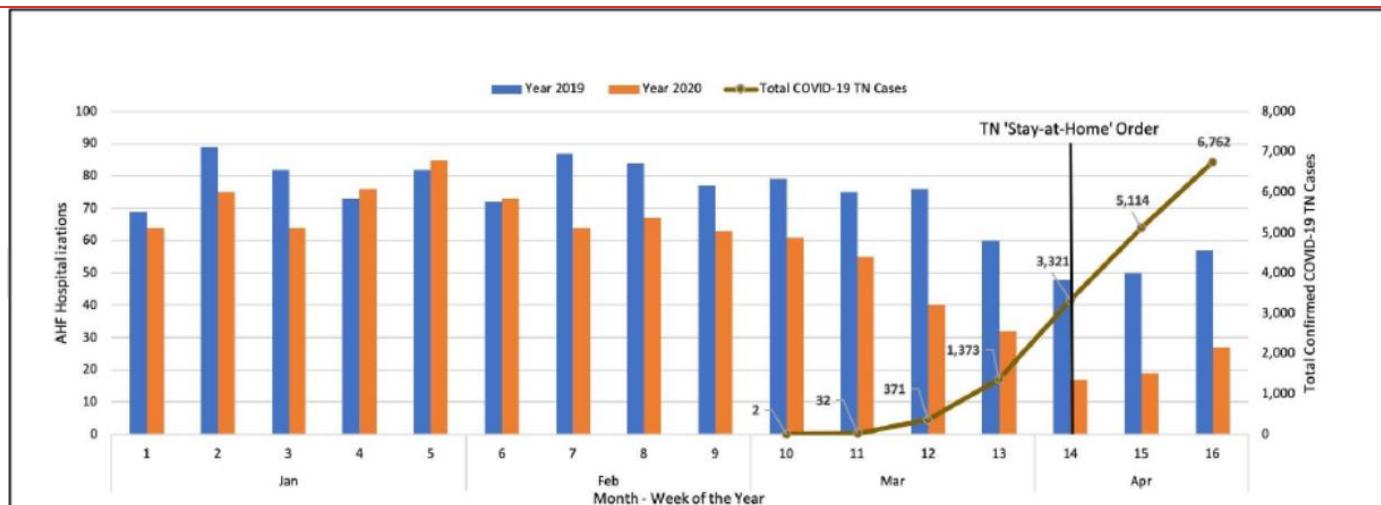


Figure 1: The number of hospital admissions for acute heart failure (y-axis) in weekly intervals (x-axis) to Vanderbilt University Medical Center decreased both compared to the same time period in 2019 (blue bars) and in current year (orange bars) as confirmed cases of COVID-19 (brown line) began to rise. The 'stay-at-home' order for the state of Tennessee was signed on April 2, 2020. TN = Tennessee; AHF = acute heart failure

DERMATOLOGY

VIRTUAL MELANOMA CHECKS DURING A PANDEMIC

Janda M, Swetter SM, Horsham C, Soyer HP.. Br J Dermatol. 2020 May 29. doi: 10.1111/bjd.19255. Online ahead of print.

Level of Evidence: Other

BLUF

In this research letter, the authors propose the benefit and efficacy of whole-body skin self-examinations (SSE) by teledermatology (guide in Table 1) to continue screening patients for early detection and monitoring of melanoma during the

COVID-19 pandemic. The authors cite recent studies showing at-home SSE have a high degree of sensitivity (>75%) and specificity (>87%) in detecting suspicious lesions, suggesting this electronic adaptation of dermatology is a sufficient platform for melanoma checks while the increased threat of contracting SARS-CoV-2 persists.

ABSTRACT

Healthcare services internationally are experiencing unprecedented strain due to the COVID-19 pandemic. Governments mandate strict social distancing to reduce the spread of SARS-CoV-2 infection, and as a result, people are avoiding health services for less urgent issues. In this crisis, it is important that patients continue to receive preventive and surveillance care without compromising their safety or that of healthcare workers.

FIGURES

Virtual melanoma checks at home: a guide for patients to take standardised images
To provide an accurate diagnosis, the image needs to be high-quality:
<ol style="list-style-type: none">1. Use natural daylight, or a brightly lit space. Use a plain, neutral coloured background.2. Remove any jewellery.3. Move anything creating a shadow out of the way, including your hair.4. If your photos are coming out blurry, ask a second person to help you with photo taking, especially in hard-to-reach body locations.5. Take two photos of each skin spot or mole<ul style="list-style-type: none">— The first photo is an overview image of the skin spot or mole. Hold the camera approximately 20cm from the skin spot or mole. Point to the skin spot or mole if there are multiple skin spots visible in the photo. Move the camera until you have a clear photo, then hold the camera still and take the image.— The second photo is a dermoscopic image (if applicable). Dermoscopic images are magnified close-up images. When using the dermatoscope place the lens directly contacting the skin.6. When photographing the lesion hold the camera horizontally each time to ensure the same orientation.7. Ensure the skin spot or mole is in the centre of the image.8. Record the body location.9. In the notes or comments section select any symptoms that may describe the skin spot or mole photographed such as:<ul style="list-style-type: none">— change in size or shape— more raised— change in colour— more than 2 colours— itchy— bleeding— scaly or rough surface— sore or painful— duration of lesion.
Patients should provide a brief medical history including DOB, gender, skin type and previous skin cancer history.

Table 1.

HEMATOLOGY AND ONCOLOGY

CHALLENGES IN EARLY PHASE CLINICAL TRIALS FOR CHILDHOOD CANCER DURING THE COVID-19 PANDEMIC: A REPORT FROM THE NEW AGENTS GROUP

OF THE SPANISH SOCIETY OF PAEDIATRIC HAEMATOLOGY AND ONCOLOGY (SEHOP)

Rubio-San-Simón A, Verdú-Amorós J, Hladun R, Juan-Ribelles A, Molero M, Guerra-García P, Pérez-Martínez A, Castañeda A, Cañete A, de Rojas T, Moreno L, Bautista F.. Clin Transl Oncol. 2020 May 29. doi: 10.1007/s12094-020-02399-3. Online ahead of print.

Level of Evidence: 3

BLUF

A 93-item questionnaire provided at 5 ITCC-accredited Spanish Paediatric Oncology Early Phase Clinical Trial Units during April 13 - 19, 2020 found common barriers to practicing clinical pediatric cancer trials during the COVID-19 pandemic. Based on these results, the authors discuss the need for developing a standard strategy for future restrictions in pediatric cancer clinical trial and offer recommendations for continuing safe, efficient research (Figure 1). Notable barriers include:

- staff shortages: a median personnel decrease of 59% across all units
- disrupted patient recruitment: 49% of trials on average discontinued recruitment
- patient enrollment issues: 7 patients were unable to enroll due to interrupted recruitment by the sponsor or patient safety considerations
- problems with supplying medical treatments or research devices to patients
- inability to conduct proper trial assessments
- delayed monitoring visits: 73% of trials postponed monitoring activity

ABSTRACT

PURPOSE: The COVID-19 pandemic has forced healthcare stakeholders towards challenging decisions. We analyse the impact of the pandemic on the conduct of phase I-II trials for paediatric cancer during the first month of state of alarm in Spain.

METHODS: A questionnaire was sent to all five ITCC-accredited Spanish Paediatric Oncology Early Phase Clinical Trial Units, including questions about impact on staff activities, recruitment, patient care, supply of investigational products, and legal aspects.

RESULTS: All units suffered personnel shortages and difficulties in enrolling patients, treatment continuity, or performing trial assessments. Monitoring activity was frequently postponed (73%), and 49% of on-going trials interrupted recruitment. Only two patients could be recruited during this period (75% reduction in the expected rate). **CONCLUSIONS:** The COVID-19 crisis has significantly impacted clinical research practice and access to innovation for children with cancer. Structural and functional changes are under way to better cope with the expected future restrictions.

FIGURES

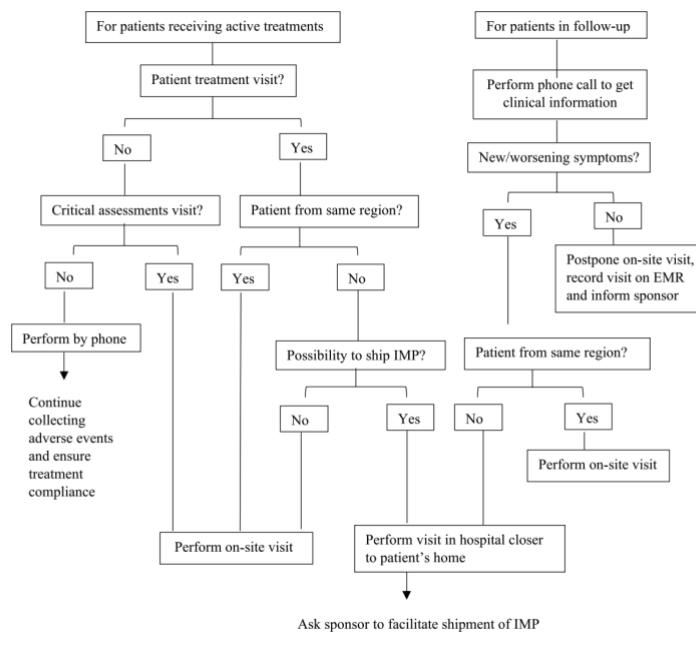


Figure 1. Set of recommendations to preserve patient safety, scientific integrity and research value

THE FUTURE OF CANCER RESEARCH AFTER COVID-19 PANDEMIC: RECESSION?

Kourie HR, Eid R, Haddad F, Ghosn M, Sarkis DK.. Future Oncol. 2020 May 29. doi: 10.2217/fon-2020-0397. Online ahead of print.

Level of Evidence: Other

BLUF

An editorial by faculty at Saint Joseph University of Beirut in Lebanon details their growing concerns about the short- and long-term future of cancer research on an international scale in the context of the COVID-19 pandemic due to the necessities of social distancing, the refocusing of research towards COVID-19, and the detrimental effects of this pandemic on the economy and donations. They call for increased unity and sharing of resources amongst cancer researchers as well as new protocols for publishing that consider the aforementioned realities.

SUMMARY

"... the load of research, publications and new trials in oncology will most probably decrease on short and long-term due to this pandemic. Cancer researchers, although stuck in the middle of this pandemic, should counter this impending recession by combining their efforts to establish a clear road map to ensure a smooth and effective revival of cancer research immediately after the lockdown ends and new recommendations for trials, that will start, should be added to the protocols concerning the period."

RHEUMATOLOGY

CHARACTERISTICS ASSOCIATED WITH HOSPITALISATION FOR COVID-19 IN PEOPLE WITH RHEUMATIC DISEASE: DATA FROM THE COVID-19 GLOBAL RHEUMATOLOGY ALLIANCE PHYSICIAN-REPORTED REGISTRY

Gianfrancesco M, Hyrich KL, Al-Adely S, Carmona L, Danila MI, Gossec L, Izadi Z, Jacobsohn L, Katz P, Lawson-Tovey S, Mateus EF, Rush S, Schmajuk G, Simard J, Strangfeld A, Trupin L, Wysham KD, Bhana S, Costello W, Grainger R, Hausmann JS, Liew JW, Sirotich E, Sufka P, Wallace ZS, Yazdany J, Machado PM, Robinson PC; COVID-19 Global Rheumatology Alliance.. Ann Rheum Dis. 2020 May 29:annrheumdis-2020-217871. doi: 10.1136/annrheumdis-2020-217871. Online ahead of print.

Level of Evidence: 4

BLUF

Researchers present findings from a case series of 600 patients across 40 countries with rheumatic diseases to analyze characteristics associated with COVID-19 hospitalization. Their findings (summarized below) support previous guidelines proposed by the American College of Rheumatology and the European League Against Rheumatism to continue rheumatic medications in the absence of COVID-19 infection or SARS-CoV-2 exposure.

SUMMARY

Patient data were gathered from the COVID-19 Global Rheumatology Alliance physician-reported registry, which indicated whether the diagnosis of COVID-19 was made via RT-PCR, metagenomic testing, CT scan, laboratory assay, or from clinical symptoms alone. Of 600 patients, the most common rheumatic disease was rheumatoid arthritis (230, 38%), followed by SLE (85, 14%) and psoriatic arthritis (74, 12%). 277 patients, or 46%, were hospitalized and 55 patients (9%) passed away. Glucocorticoid use at a prednisone-equivalent dose ≥ 10 mg/day was associated with increased risk of hospitalization, while TNF-inhibitors were associated with decreased risk of hospitalization. There was no correlation with hospitalization with biologic agents (such as JAK inhibitors), although the sample size was small for this category. There was also no correlation with NSAIDS (although the authors note that since these are available OTC, reporting may not be as accurate as the other therapies), or antimalarials including hydroxychloroquine and chloroquine.

ABSTRACT

OBJECTIVES: COVID-19 outcomes in people with rheumatic diseases remain poorly understood. The aim was to examine demographic and clinical factors associated with COVID-19 hospitalisation status in people with rheumatic disease.
METHODS: Case series of individuals with rheumatic disease and COVID-19 from the COVID-19 Global Rheumatology Alliance registry: 24 March 2020 to 20 April 2020. Multivariable logistic regression was used to estimate ORs and 95% CIs of

hospitalisation. Age, sex, smoking status, rheumatic disease diagnosis, comorbidities and rheumatic disease medications taken immediately prior to infection were analysed. RESULTS: A total of 600 cases from 40 countries were included. Nearly half of the cases were hospitalised (277, 46%) and 55 (9%) died. In multivariable-adjusted models, prednisone dose ≥ 10 mg/day was associated with higher odds of hospitalisation (OR 2.05, 95% CI 1.06 to 3.96). Use of conventional disease-modifying antirheumatic drug (DMARD) alone or in combination with biologics/Janus Kinase inhibitors was not associated with hospitalisation (OR 1.23, 95% CI 0.70 to 2.17 and OR 0.74, 95% CI 0.37 to 1.46, respectively). Non-steroidal anti-inflammatory drug (NSAID) use was not associated with hospitalisation status (OR 0.64, 95% CI 0.39 to 1.06). Tumour necrosis factor inhibitor (anti-TNF) use was associated with a reduced odds of hospitalisation (OR 0.40, 95% CI 0.19 to 0.81), while no association with antimalarial use (OR 0.94, 95% CI 0.57 to 1.57) was observed. CONCLUSIONS: We found that glucocorticoid exposure of ≥ 10 mg/day is associated with a higher odds of hospitalisation and anti-TNF with a decreased odds of hospitalisation in patients with rheumatic disease. Neither exposure to DMARDs nor NSAIDs were associated with increased odds of hospitalisation.

SURGICAL SUBSPECIALTIES

GENERAL SURGERY

PERSPECTIVES FROM ITALY DURING THE COVID-19 PANDEMIC: NATIONWIDE SURVEY-BASED FOCUS ON MINIMALLY INVASIVE HPB SURGERY

Aldrighetti L, Boggi U, Falconi M, Giulante F, Cipriani F, Ratti F, Torzilli G; Italian Association of HepatoBilioPancreatic Surgeons-AICEP.. Updates Surg. 2020 May 29. doi: 10.1007/s13304-020-00815-5. Online ahead of print.

Level of Evidence: 3

BLUF

A survey conducted by the Italian Association of HepatoBilioPancreatic Surgeons (AICEP) during April 2020 found that 72.8% of hepato-pancreato-biliary (HPB) surgery centers reported a decrease in routine elective HPB operations by 50% or greater and 66.2% of minimally invasive surgery centers reported a 50% or greater reduction of minimally invasive liver resections. Additionally, 70.3% of centers reported a considerable or severe impact on the waiting time because of the pandemic, which the authors indicate suggests a need for a national standardization process to prioritize patients who need HPB surgery.

ABSTRACT

The safety of minimally invasive procedures during COVID pandemic remains hotly debated, especially in a country, like Italy, where minimally invasive techniques have progressively and pervasively entered clinical practice, in both the hepatobiliary and pancreatic community. A nationwide snapshot of the management of HPB minimally invasive surgery activity during COVID-19 pandemic is provided: a survey was developed and conducted within AICEP (Italian Association of HepatoBilioPancreatic Surgeons) with the final aim of conveying the experience, knowledge, and opinions into a unitary report enabling more efficient crisis management. Results from the survey (81 respondents) show that, in Italian hospitals, minimally invasive surgery maintains its role despite the COVID-19 pandemic, with the registered reduction of cases being proportional to the overall reduction of the HPB surgical activity. Respondents agree that the switch from minimally invasive to open technique can be considered as a valid option for cases with a high technical complexity. Several issues merit specific attention: screening for virus positivity should be universally performed; only expert surgical teams should operate on positive patients and specific technical measures to lower the biological risk of contamination during surgery must be followed. Future studies specifically designed to establish the true risks in minimally invasive surgery are suggested. Furthermore, a standard and univocal process of prioritization of patients from Regional Healthcare Systems is advisable.

A MANUAL REDUCTION OF HERNIA UNDER ANALGESIA/SEDATION (TAXIS) IN THE ACUTE INGUINAL HERNIA: A USEFUL TECHNIQUE IN COVID-19 TIMES TO REDUCE THE NEED FOR EMERGENCY SURGERY-A LITERATURE REVIEW

East B, Pawlak M, de Beaux AC.. Hernia. 2020 May 29. doi: 10.1007/s10029-020-02227-1. Online ahead of print.

Level of Evidence: Other

BLUF

In this review of 9 papers, a group of researchers evaluated the management of emergency inguinal hernia using manual reduction of the hernia under analgesia (taxis method). They found that taxis is effective in about 70% of patients and is a useful first-line treatment in situations with limited surgical availability, as it is currently in the COVID-19 pandemic. The authors acknowledge the need for future studies to better elucidate the long-term implications of taxis usage.

ABSTRACT

BACKGROUND: Acute IH is a common surgical presentation. Despite new guidelines being published recently, a number of important questions remained unanswered including the role of taxis, as initial non-operative management. This is particularly relevant now due to the possibility of a lack of immediate surgical care as a result of COVID-19. The aim of this review is to assess the role of taxis in the management of emergency inguinal hernias.

METHODS: A review of the literature was undertaken. Available literature published until March 2019 was obtained and reviewed. 32,021 papers were identified, only 9 were of sufficient value to be used. **RESULTS:** There was a large discrepancy in the terminology of incarcerated/strangulated used. Taxis can be safely attempted early after the onset of symptoms and is effective in about 70% of patients. The possibility of reduction en-mass should be kept in mind. Definitive surgery to repair the hernia can be delayed by weeks until such time as surgery can be safely arranged. **CONCLUSIONS:** The use of taxis in emergency inguinal hernia is a useful first line of treatment in areas or situations where surgical care is not immediately available, including the COVID-19 pandemic. Emergency surgery remains the mainstay of management in the strangulated hernia setting.

OTOLARYNGOLOGY

MINIMIZING CONTAGION RISKS OF COVID-19 DURING TRANS ORAL ROBOTIC SURGERY

Meccariello G, Cammaroto G, Iannella G, Capaccio P, Pelucchi S, Vicini C.. Laryngoscope. 2020 May 29. doi: 10.1002/lary.28847. Online ahead of print.

Level of Evidence: Other

BLUF

A team of otolaryngologists from Morgagni Pierantoni Hospital in Italy offer recommendations to minimize the aerosol transmission risk of SARS-CoV-2 while performing Trans Oral Robotic Surgery (TORS) for oropharyngeal carcinoma.

SUMMARY

Recommendations include:

- Prepare and intubate the patient in a separate room from the operating room to reduce the chance of aerosol transmission into the operating room during intubation. Wrap the nose and mouth in plastic dressing before transferring into the operating room.
- Use a Davis-Meyer mouth gag with aspirating blade to reduce aerosol transmission.
- Once surgical field exposure has been achieved, use a transparent plastic bag to cover the whole face, with holes in the bag that permit instrument placement. Additional holes can be cut to insert suction devices to further decrease aerosol transmission.

ABSTRACT

In this communication we would like to share our experience in managing TORS patients during COVID-19 pandemic.

OBGYN

THE GENDERED IMPACT OF CORONAVIRUS DISEASE (COVID-19): DO ESTROGENS PLAY A ROLE?

Grandi G, Facchinetti F, Bitzer J.. Eur J Contracept Reprod Health Care. 2020 May 29:1-2. doi: 10.1080/13625187.2020.1766017. Online ahead of print.

Level of Evidence: Other

BLUF

This letter from physicians in Italy addresses potential effects that estrogens can have on risk of severe COVID-19 due to the immune-stimulating properties of estradiol (E2) and the immune-suppressant properties of progesterone. Use of combined hormonal contraception (CHC) during the COVID-19 pandemic could convey protective benefits earlier in the disease course, but could also promote adverse events, such as DIC and thromboembolism later in the disease course. Overall, these authors recommend that the benefits of CHC outweigh the risks and it should not be discontinued during the current pandemic.

ABSTRACT

Objective: Although sex-disaggregated data for COVID-19 show equal numbers of cases between men and women, there seem to be sex differences in mortality rate and vulnerability to the disease: more men than women are dying. **Methods:** We have explored the potential role of estrogens in this COVID-19 gendered impact. **Results:** Estrogens stimulate the humoral response to viral infections, while testosterone and progesterone give an immune suppression of both innate and cell-mediated immune responses. We hypothesise that estrogens, in particular estradiol but also synthetic estrogen such as ethinylestradiol, could protect women from the most serious complications of COVID-19. The use of medications that keep hormonal levels high and stable, such as combined hormonal contraceptive, could therefore play a protective role. These potential benefits overtake the thrombotic risk in healthy women. As stated by the World Health Organization, all modern methods of contraception were safe to use during the COVID-19 pandemic.

CHALLENGES AND SOLUTIONS FOR MATERNITY AND GYNECOLOGY SERVICES DURING THE COVID-19 CRISIS IN JORDAN

Alsharaydeh I, Rawashdeh H, Saadeh N, Obeidat B, Obeidat N.. Int J Gynaecol Obstet. 2020 May 29. doi: 10.1002/ijgo.13240. Online ahead of print.

Level of Evidence: Other

BLUF

This descriptive study conducted at a large tertiary referral center in Jordan details the multidisciplinary approach and local measures to sustain a maternity and gynecology service amid the COVID-19 pandemic. Successful operation hinged on changes to patient care, staff governance, residency programs, and medical student teaching programs.

SUMMARY

Changes for successful operation in the maternity and gynecology services at King Abdullah University Hospital (which serves five cities with a total population of 3-4 million people) amid the COVID-19 pandemic:

1. **Patient changes:** Those with acute obstetric and gynecologic complaints were seen in the emergency department, while routine procedures were deferred. The hospital cancelled all visiting hours and restricted family and friends' access to the hospital. Urgent questions regarding pregnancy were fielded via teleconference. A triage system based on COVID-19 risk of exposure was implemented.
2. **Staff governance:** Staffing was minimized to reduce the number of providers at risk of infection. Fewer duties were assigned to residents.
3. **Residency programs:** To avoid gathering, morning report was cancelled and messaging applications were leveraged to communicate among residents.
4. **Medical student teaching program:** Course materials were uploaded to an online platform for fifth and sixth year medical students. Telemedicine was leveraged to communicate with patients from home.

ABSTRACT

OBJECTIVE: To describe regional experiences and measures implemented to safely maintain obstetrics and gynecology services during the COVID-19 pandemic at King Abdullah University Hospital in Jordan.

METHODS: All policies and measures were implemented in keeping with World Health Organization and other international recommendations and guidelines.

RESULTS: With concerted effort and a multidisciplinary approach, most maternity and gynecology services were provided and all other training and educating responsibilities were maintained.

CONCLUSION: COVID-19 caused an unprecedented global healthcare crisis. Our institution addressed the challenges and implemented several measures at different levels to maintain services and facilitate the training and teaching of trainees and medical students.

PEDIATRICS

ETHICAL CONSIDERATIONS FOR PAEDIATRICS DURING THE COVID-19 PANDEMIC: A DISCUSSION PAPER FROM THE AUSTRALIAN PAEDIATRIC CLINICAL ETHICS COLLABORATION

Jansen M, Irving H, Gillam L, Sharwood E, Preisz A, Basu S, Delaney C, McDougall R, Johnston C, Isaacs D, Lister P.. J Paediatr Child Health. 2020 May 29. doi: 10.1111/jpc.14946. Online ahead of print.

Level of Evidence: Other

BLUF

A group of Australian physicians and ethicists consider the disproportionate infection of adults with SARS-CoV-2 when compared to children, and they discuss the ethical concerns around topics of redistribution of pediatric resources to adult ICUs, ICU admission criteria, and decreased routine healthcare visits. They present a set of recommendations on how to best distribute resources during the COVID-19 pandemic in an equitable way and optimize care for both adult and pediatric patients, though they acknowledge that redistribution is a complex process requiring frequent reevaluation.

SUMMARY

The following recommendations are promoted by authors:

- "1. There should be frequent review of routine health service curtailment, specifically considering the short-term and long-term detriments to children. Services should be reinstated as soon as is safe.
2. Triage criteria for paediatric elective and outpatient care should include psychosocial and developmental considerations.
3. Guidelines written for adult patients should clearly direct clinicians to the corresponding paediatric guidelines and paediatric guidelines should be actively promoted to general and paediatric clinicians.
4. Paediatric critical care services, in conjunction with adult services, should locally assess the most effective ways to support the adult sector.
5. Clinicians working in general hospitals should have 24-h access to specialist paediatric input for prioritisation decisions involving children, and should make the need for this explicit in their local guidelines.
6. In prioritising intensive care resources, it is ethically reasonable to consider according children some priority.
7. PICU should work closely with general paediatrics, palliative care, and other subspecialty services to optimise timely goals of care discussions and parallel planning. Palliative care surge capacity should be part of the overall strategy to address intensive care resource limitation.
8. Decision-making processes for determining ICU eligibility and priority should be designed in a transparent and consultative way. All decisions should be clearly documented and reviewed.
9. The health professions and health organisations should actively reflect on the benefits arising from pandemic preparation and practice changes and harness these to improve health-care service delivery in the future."

R&D: DIAGNOSIS & TREATMENTS

CURRENT DIAGNOSTICS

PERFORMANCE OF ABBOTT ID NOW COVID-19 RAPID NUCLEIC ACID AMPLIFICATION TEST IN NASOPHARYNGEAL SWABS TRANSPORTED IN VIRAL MEDIA AND DRY NASAL SWABS, IN A NEW YORK CITY ACADEMIC INSTITUTION

Basu A, Zinger T, Inglima K, Woo KM, Atie O, Yurasits L, See B, Aguero-Rosenfeld ME.. J Clin Microbiol. 2020 May 29;JCM.01136-20. doi: 10.1128/JCM.01136-20. Online ahead of print.

Level of Evidence: 4

BLUF

Clinical microbiologists at NYU in April found the new 5-minute Abbott ID NOW COVID-19 test had a positive predictive value of 94.4% and a negative predictive value of 83.1% (n=101) when compared to the Xpert Xpress SARS-CoV-2 test, suggesting this test may be useful as a rule-in. However, they posited that a single negative result may not be useful as a rule-out.

ABSTRACT

The recent emergence of the SARS-CoV-2 pandemic has posed formidable challenges for clinical laboratories seeking reliable laboratory diagnostic confirmation. The swift advance of the crisis in the United States has led to Emergency Use Authorization (EUA) facilitating the availability of molecular diagnostic assays without the more rigorous examination to which tests are normally subjected prior to FDA approval. Our laboratory currently uses two real time RT-PCR platforms, the Roche Cobas SARS-CoV2 and the Cepheid Xpert Xpress SARS-CoV-2. Both platforms demonstrate comparable performance; however, the run times for each assay are 3.5 hours and 45 minutes, respectively. In search for a platform with shorter turnaround time, we sought to evaluate the recently released Abbott ID NOW COVID-19 assay which is capable of producing positive results in as little as 5 minutes. We present here the results of comparisons between Abbott ID NOW COVID-19 and Cepheid Xpert Xpress SARS-CoV-2 using nasopharyngeal swabs transported in viral transport media and comparisons between Abbott ID NOW COVID-19 and Cepheid Xpert Xpress SARS-CoV-2 using nasopharyngeal swabs transported in viral transport media for Cepheid and dry nasal swabs for Abbott ID NOW. Regardless of method of collection and sample type, Abbott ID NOW COVID-19 had negative results in a third of the samples that tested positive by Cepheid Xpert Xpress when using nasopharyngeal swabs in viral transport media and 45% when using dry nasal swabs.

FIGURES

	Positive Xpert Xpress	Negative Xpert Xpress	Total
Positive ID NOW	17	1	18
Negative ID NOW	14	69	83
Total	31	70	101

Table 2. Comparison of ID NOW using dry nasal swabs and Xpert Xpress using NPS in VTM on 101 paired samples.

DEVELOPMENTS IN DIAGNOSTICS

DETECTION OF SARS-COV-2 IN HUMAN RETINAL BIOPSIES OF DECEASED COVID-19 PATIENTS

Casagrande M, Fitzek A, Püschel K, Aleshcheva G, Schultheiss HP, Berneking L, Spitzer MS, Schultheiss M.. Ocul Immunol Inflamm. 2020 May 29:1-5. doi: 10.1080/09273948.2020.1770301. Online ahead of print.

Level of Evidence: 4

BLUF

This pilot study conducted at the University Medical Center Hamburg-Eppendorf in Germany conducted autopsies on 14 deceased patients (table 1) with confirmed COVID-19, and found three patients with SARS-CoV-2 viral RNA detected in the retina via reverse transcriptase-polymerase chain reaction (RT-PCR). The results suggest that SARS-CoV-2 can be present in the intraocular tissue of COVID-19 patients and further build upon previous studies reporting that the ophthalmic involvement in COVID-19 was limited to conjunctivitis. Further research investigating whether SARS-CoV-2 can be present in various ocular structures is warranted.

ABSTRACT

PURPOSE: To report the presence of viral ribonucleic acid (RNA) of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in human retina in deceased patients with confirmed novel coronavirus disease 2019 (COVID-19). **PATIENTS AND METHODS:** Fourteen eyes of 14 deceased patients with confirmed COVID-19 disease were enucleated during autopsy. A sample of human retina was secured and fixed in RNAlater. Real-time reverse transcriptase-polymerase chain reaction (RT-PCR) was performed to detect three different viral RNA sequences (RdRp-gene, E-gene and Orf1 gene) of SARS-CoV-2.

RESULTS: In three out of 14 eyes SARS-CoV-2 viral RNA was detected in the retina of deceased COVID-19 patients. As analysis for three different sequences (RdRp-gene, E-gene and Orf1 gene) revealed positive results in RT-PCR, the existence of SARS-CoV-2 viral RNA in human retina is proven according to the standards of the World-Health-Organization. **CONCLUSION:** Viral RNA of SARS-CoV-2 is detectable in the retina of COVID-19 patients.

FIGURES

Table 1. Patient characteristics.

Patient characteristics	
Sex, male ^a	10 (71.4%)
Age, years ^b	77 ± 13.9
Post-mortem interval, days ^b	4 ± 3.0
Invasive ventilation, yes ^a	2 (14.29%)
Body-mass-index ^b	24.4 ± 6.6
Fatal COVID-19 deaths ^a	12 (85.71%)
Number of comorbidities ^b	5.2 ± 2.0
CT value from nasopharyngeal swabs ^c	22.5 (14.6–32.2)
Cause of death	
Pneumonia ^d	12
Cardiac arrhythmia ^d	1
Pericardial tamponade following myocardial rupture ^d	1
Place of death	
Unknown ^a	1 (7.14%)
Own home ^a	6 (42.86%)
Normal ward ^a	5 (35.71%)
Intensive Care Unit ^a	2 (14.29%)
Comorbidity ^e	
Coronary heart disease ^a	12 (85.71%)
Arteriosclerosis ^a	7 (50%)
Chronic obstructive pulmonary disease ^a	6 (42.86%)
Mycardial infarction ^a	4 (33.33%)
Dementia ^a	3 (25%)
Arterial hypertension ^a	5 (41.64%)
Acute or chronic renal failure ^a	6 (50%)
Diabetes mellitus type 2 ^a	3 (25%)
Ischemic cardiomyopathy ^a	2 (16.67%)
Anemia ^a	2 (16.67%)
Heart failure ^a	5 (35.71%)
Atrial fibrillation ^a	5 (41.64%)
Pulmonary embolism ^a	1 (8.33%)
Stroke ^a	2 (16.67%)
Trisomy 21 ^a	1 (8.33%)
Ethyl-toxic liver cirrhosis ^a	1 (8.33%)
Cancer (prostate, colon) ^a	1 (8.33%)
Polycythemia vera ^a	1 (8.33%)

^anumber (%)

^bmean ± standard deviation

^cmedian (range)

^dnumber of patients

^emultiple inclusion of one patient in the various categories possible

This table displays patient characteristics, cause of death, place of death and comorbidities.

DEVELOPMENTS IN TREATMENTS

POTENTIAL RNA-DEPENDENT RNA POLYMERASE INHIBITORS AS PROSPECTIVE THERAPEUTICS AGAINST SARS-COV-2

Pokhrel R, Chapagain P, Siltberg-Liberles J.. J Med Microbiol. 2020 May 29. doi: 10.1099/jmm.0.001203. Online ahead of print.
Level of Evidence: 5

BLUF

In this research study, the authors performed sequencing, structural analysis, and molecular docking using in silico models to determine if RNA-dependent RNA polymerase (RdRP) from SARS-CoV could act as an acceptable binding site for known antiviral targets (Table 1). They concluded the top five hits of FDA-approved drugs against RdRP from SARS-CoV are Quinupristin, Dactinomycin, Sirolimus, Cetrorelix, Rifampin (Tables 2,3), suggesting potential therapeutics to consider when treating COVID-19 patients.

ABSTRACT

Introduction. The emergence of SARS-CoV-2 has taken humanity off guard. Following an outbreak of SARS-CoV in 2002, and MERS-CoV about 10 years later, SARS-CoV-2 is the third coronavirus in less than 20 years to cross the species barrier and start spreading by human-to-human transmission. It is the most infectious of the three, currently causing the COVID-19 pandemic. No treatment has been approved for COVID-19. We previously proposed targets that can serve as binding sites for antiviral drugs for multiple coronaviruses, and here we set out to find current drugs that can be repurposed as COVID-19 therapeutics.

Aim. To identify drugs against COVID-19, we performed an in silico virtual screen with the US Food and Drug Administration (FDA)-approved drugs targeting the RNA-dependent RNA polymerase (RdRP), a critical enzyme for coronavirus replication.

Methodology. Initially, no RdRP structure of SARS-CoV-2 was available. We performed basic sequence and structural analysis to determine if RdRP from SARS-CoV was a suitable replacement. We performed molecular dynamics simulations to generate multiple starting conformations that were used for the in silico virtual screen. During this work, a structure of RdRP from SARS-CoV-2 became available and was also included in the in silico virtual screen.

Results. The virtual screen identified several drugs predicted to bind in the conserved RNA tunnel of RdRP, where many of the proposed targets were located. Among these candidates, quinupristin is particularly interesting because it is expected to bind across the RNA tunnel, blocking access from both sides and suggesting that it has the potential to arrest viral replication by preventing viral RNA synthesis. Quinupristin is an antibiotic that has been in clinical use for two decades and is known to cause relatively minor side effects.

Conclusion. Quinupristin represents a potential anti-SARS-CoV-2 therapeutic. At present, we have no evidence that this drug is effective against SARS-CoV-2 but expect that the biomedical community will expeditiously follow up on our in silico findings.

FIGURES

Table 1. Antiviral targets

Protein	Target	Sequence motif ^a and SARS-CoV-2 numbering ^b	PDB ID ^c , range
Protease	NSP5:1	3406-GSCGS-3387	1UJ1:143-147
Protease	NSP5:2	346-AWLYAA-3474	1UJ1:206-211
Replicase	NSP7:1	3866-KCTSWLL-3873	6NUR_C: 7-14
Replicase	NSP7:2	3875-VLQQL-3879	6NUR_C: 16-20
RdRP	NSP12:1	4599-LDNQDNG-4606	6NUR_A: 207-214
RdRP	NSP12:2	4610-DFGDF-4614	6NUR_A: 218-222
RdRP	NSP12:3	4891-DKSAG-4895	6NUR_A: 499-503
RdRP	NSP12:4	4958-MTNRQ-4962	6NUR_A: 566-570
RdRP	NSP12:5	5047-LANECA <u>Q</u> VL-5055	6NUR_A: 655-663
RdRP	NSP12:6	5070-GGTSSGD-5076	6NUR_A: 678-684
RdRP	NSP12:7	5223-YPDPSR-5228	6NUR_A: 831-836
RdRP	NSP12:8	5241-KTDGT-5245	6NUR_A: 849-853
RdRP	NSP12:9	5259-YPLTK-5263	6NUR_A: 867-871
Helicase	NSP13:1	5334-SQTSLR-5339	6JYT: 10-15
Helicase	NSP13:2	5685-NALPE-5689	6JYT: 361-365
Helicase	NSP13:3	5725-DPAQLP-5730	6JYT: 401-406
Helicase	NSP13:4	5859-SSQGS-5863	6JYT: 535-539
Exonuclease	NSP14:1	6192-AHVAS-6196	5C8S_B: 267-271
Exonuclease	NSP14:2	6201-MTRCLA-6206	5C8S_B: 276-280
Exonuclease	NSP14:3	6349-H <u>A</u> FHT-6353	5C8S_B: 424-428
Exonuclease	NSP14:4	6402-CNLGG-6406	5C8S_B: 477-481

^aSequence motifs in the targets provided by Rahaman and Siltberg-Liberies [7].^bResidues shown in bold are surface accessible. Residues that are not 100% conserved across the SARS-CoV-2 strains are underlined.^cPDB ID is given with chain if appropriate, e.g. 6NUR_A means chain A from PDB ID 6NUR. References for PDB IDs: 1UJ1 [19], 6NUR [9], 6JYT [20] and 5C8S [21].**Table 3.** Top five hits from virtual screening with FDA-approved drugs against RdRP

Final rank and Best score*	Drug name	DrugBank† description
1 Score: -12.3	Quinupristin	An antibiotic effective against Gram-positive bacteria; commonly used in combination with dalfopristin
2 Score: -12.2	Dactinomycin	An antibiotic that inhibits bacterial transcription; has cytotoxic properties; used for chemotherapy
3 Score: -12.2	Sirolimus	A macrolide from <i>Streptomyces hygroscopicus</i> with immunosuppressive, antifungal and antineoplastic properties
4 Score: -11.5	Cetorelix	A man-made hormone that blocks the effects of gonadotropin-releasing hormone
5 Score: -11.4	Rifampin	A broad-spectrum antibiotic known to inhibit DNA-dependent RNA polymerase activity by forming a stable complex with the enzyme

*Best score based on the virtual screens (Table 2).

†DrugBank [36, 37].

Table 2. Top-scoring drugs from the different docking rounds*

Ensemble		Rigid		Flexible based on rigid		Flexible based on ensemble	
Drug	Score	Drug	Score	Drug	Score	Drug	Score
Sirolimus	-12.2	Quinupristin	-10.7	Quinupristin	-12.3	Dactinomycin	-12.2
Cetorelix	-11.5	Cetorelix	-10.5	Dactinomycin	-12.1	Sirolimus	-11.5
Quinupristin	-11.3	Dactinomycin	-10.1	Cetorelix	-11.4	Quinupristin	-11.4
Dactinomycin	-11.3	Ledipasvir	-9.9	Rifampin	-11.4	Eptifibatide	-11.3
Anidulafungin	-10.6	Rifampin	-9.8	Grazoprevir	-10.6	Cetorelix	-11.3

*The lowest (best) score for the five top-ranked drugs are shown in green.

DOCKING STUDY OF CHLOROQUINE AND HYDROXYCHLOROQUINE INTERACTION WITH SARS-COV-2 SPIKE GLYCOPROTEIN-AN IN SILICO INSIGHT INTO THE COMPARATIVE EFFICACY OF REPURPOSING ANTIVIRAL DRUGS

Amin M, Abbas G.. J Biomol Struct Dyn. 2020 May 29:1-11. doi: 10.1080/07391102.2020.1775703. Online ahead of print.

Level of Evidence: Other

BLUF

An in-silico computational drug repurposing study conducted at the University of Sargodha in Pakistan found that hydroxychloroquine potentially exhibited inhibitory effects on the SARS-CoV-2 S-protein (crucial for host cell invasion) with a binding energy of -7.28 kcal/mol compared to a value of -6.30 kcal/mol value for chloroquine (Table 4). This work suggests hydroxychloroquine could function to reduce SARS-CoV-2 infectivity, but further in vivo studies are needed to see if the benefit outweighs the possible side effects.

ABSTRACT

Recent outbreak of novel Coronavirus disease (Covid-19) pandemic around the world is associated with severe acute respiratory syndrome. The death toll associated with the pandemic is increasing day by day. SARS-CoV-2 is an enveloped virus and there are ample evidences that its Spike protein (S-protein) is mainly associated with pathogenesis as it is surface-exposed and mediates entry into host cells by binding to angiotensin-converting enzyme-2 (ACE-2) receptor. Therefore, it is the main target of neutralizing antibodies upon infection and there is always a quest to inhibit the S-protein which in turn may help in controlling diseases caused by SARS-CoV-2 in humans. The role of Chloroquine and Hydroxychloroquine as potential treatments for Covid-19 is still under debate globally because of some side effects associated with it. This study involves the In silico interactions of Chloroquine and Hydroxychloroquine with the S-protein of SARS-CoV-2. With the help of various computational methods, we have re-explored the potential role of both of these antiviral drugs for the treatment of Covid-19 patients by comparing the efficacy of both of the drugs to bind to S-protein at its host receptor region. In our research Hydroxychloroquine exhibited potential inhibitory effects of S-protein with binding energy -7.28 kcal/mol than Chloroquine (-6.30 kcal/mol) at SARS-CoV-2 receptor recognition of susceptible cells. The outcomes of this research strongly appeal for in vivo trials of Hydroxychloroquine for the patients infected with Covid-19. Furthermore, the recommended doses of Hydroxychloroquine may reduce the chances of catching Covid-19 to the healthcare workers and staff who are in contact with or delivering direct care to coronavirus patients as long as they have not been diagnosed with Covid-19. We further hypothesize that the comparative S-protein-drug docking interactions may help to understand the comparative efficacy of other candidate repurposing drugs until discovery of a proper vaccine.

FIGURES

Table 4. Free binding energy ((kcal/mol)) scores of ten conformation of Hydroxychloroquine interaction with ‘SARS-CoV-2’ Spike Protein (pdb 6VY) determined by flexible ligand-rigid receptor method

Conformation#	Inhibition Constant (uM)	Final Intermolecular Energy	vdW+ Hbond + desolv Energy	Electrostatic Energy	Final Total Internal Energy	Torsional Free Energy	Unbound System's Energy
1	135.12	-8.26	-8.45	+0.19	-0.94	+2.98	-0.94
2	182.19	-8.08	-8.12	+0.04	-1.55	+2.98	-1.55
3	218.61	-7.98	-8.01	+0.03	-0.78	+2.98	-0.78
4	359.95	-7.68	-7.63	-0.05	-0.84	+2.98	0.84
5	512.16	-7.47	-7.28	-0.19	-1.01	+2.98	-1.01
6	549.05	-7.43	-7.68	+0.24	-1.55	+2.98	-1.55
7	639.90	-7.34	-7.69	+0.35	-1.58	+2.98	-1.58
8	795.93	-7.21	-7.10	-0.11	-1.29	+2.98	-1.29
9	815.99	-6.78	-6.81	+0.03	-1.10	+2.98	-1.10
10	830.25	-6.18	-6.02	-0.17	-1.64	+2.98	-1.64

Table 4: Free binding energy ((kcal/mol)) scores of ten conformation of Hydroxychloroquine interaction with ‘SARS-CoV-2’ Spike Protein (pdb 6VY) determined by flexible ligand-rigid receptor method

MENTAL HEALTH & RESILIENCE NEEDS

BEHAVIORAL HEALTH AND RESPONSE FOR COVID-19

Hansel TC, Saltzman LY, Bordnick PS.. Disaster Med Public Health Prep. 2020 May 29:1-23. doi: 10.1017/dmp.2020.180.

Online ahead of print.

Level of Evidence: Other

BLUF

Authors from the Tulane University School of Social Work argue that behavioral health interventions are needed now and will continue to be needed after the pandemic recedes. Specifically, the authors propose a four-step plan of 1) outreach, 2) screening, 3) brief interventions, and 4) referral for more intensive treatment. Clinicians should be attentive to behavioral changes in patients, particularly in those with previous substance use problems or additional life stressors.

ABSTRACT

Research from financial stress, disasters, pandemics and other extreme events, suggests that behavioral health will suffer, including anxiety, depression, and posttraumatic stress symptoms. Further these symptoms are likely to exacerbate alcohol or drug use, especially for those vulnerable to relapse. The nature of COVID-19 and vast reach of the virus, leave many unknowns for the repercussions on behavioral health, yet existing research suggests that behavioral health concerns should take a primary role in response to the pandemic. We propose a four-step services system designed for implementation with a variety of different groups and reserves limited clinical services for the most extreme reactions. While we can expect symptoms to remit overtime, many will also have longer-term or more severe concerns. Behavioral health interventions will likely need to change overtime and different types of interventions should be considered for different target groups, such as for those that recover from COVID-19, healthcare professionals and essential personnel; and the general public either due to loss of loved ones or significant life disruption. The important thing is to have a systematic plan to support behavioral health and to engage citizens in the prevention and doing their part in recovery by staying home and protecting others.

COVID-19'S IMPACT ON HEALTHCARE WORKFORCE

SOCIAL SUPPORT AND MENTAL HEALTH AMONG HEALTH CARE WORKERS DURING CORONAVIRUS DISEASE 2019 OUTBREAK: A MODERATED MEDINATION MODEL

Hou T, Zhang T, Cai W, Song X, Chen A, Deng G, Ni C.. PLoS One. 2020 May 29;15(5):e0233831. doi: 10.1371/journal.pone.0233831. eCollection 2020.

Level of Evidence: 3

BLUF

A cross-sectional study of 1472 health care workers aged 18-50 years old from Jiangsu Province, China from February 1-7, 2020 found that social support was positively associated with younger age group (18-30), and associated with increased resilience and better mental health (lower SCL-90 scores, see figure 2). These findings propose that resiliency-focused training and increased social support may improve mental health, particularly among younger health care workers during COVID-19 (Figure 1).

ABSTRACT

PURPOSES: During the outbreak of Coronavirus Disease 2019 (COVID-19) all over the world, the mental health conditions of health care workers are of great importance to ensure the efficiency of rescue operations. The current study examined the effect of social support on mental health of health care workers and its underlying mechanisms regarding the mediating role of resilience and moderating role of age during the epidemic. **METHODS:** Social Support Rating Scale (SSRS), Connor-Davidson Resilience scale (CD-RISC) and Symptom Checklist 90 (SCL-90) were administrated among 1472 health care workers from Jiangsu Province, China during the peak period of COVID-19 outbreak. Structural equation modeling (SEM) was used to examine the mediation effect of resilience on the relation between social support and mental health, whereas moderated

mediation analysis was performed by Hayes PROCESS macro. RESULTS: The findings showed that resilience could partially mediate the effect of social support on mental health among health care workers. Age group moderated the indirect relationship between social support and mental health via resilience. Specifically, compared with younger health care workers, the association between resilience and mental health would be attenuated in the middle-aged workers. CONCLUSIONS: The results add knowledge to previous literature by uncovering the underlying mechanisms between social support and mental health. The present study has profound implications for mental health services for health care workers during the peak period of COVID-19.

FIGURES

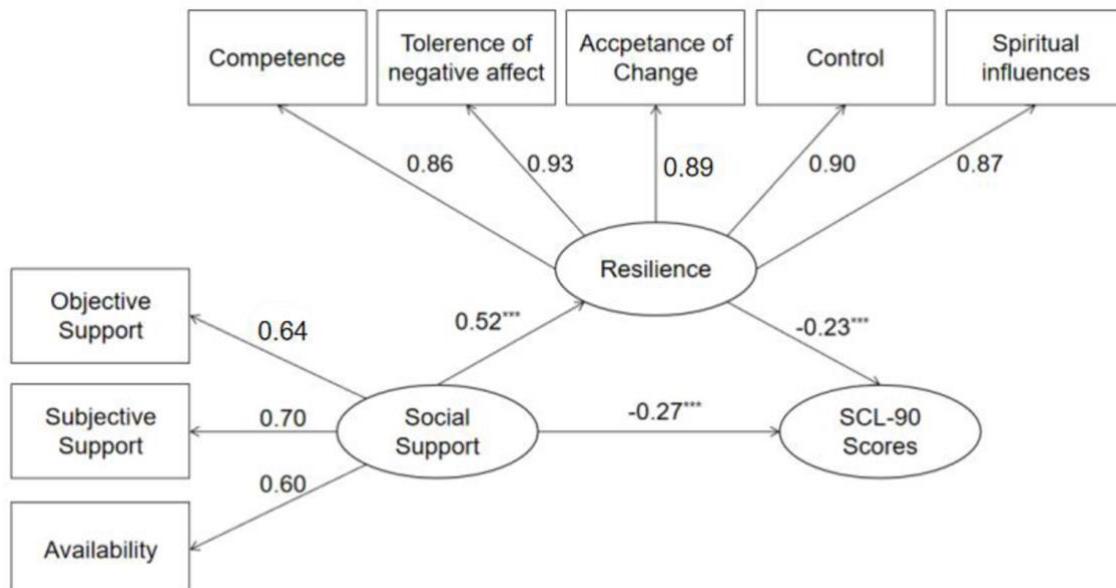


Figure 1. The mediating role of resilience in the association between social support and SCL-90 scores.

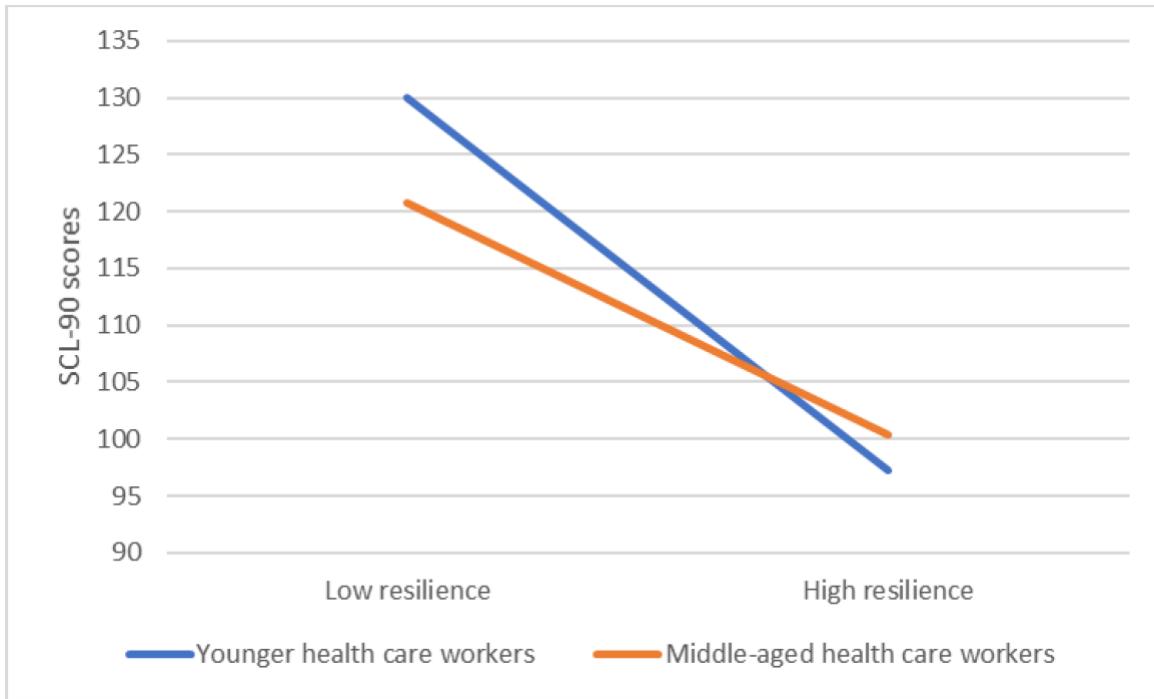


Figure 2. The interaction between resilience and age group on SCL-90 scores.

IMPACT ON PUBLIC MENTAL HEALTH

COMPLIANCE AND PSYCHOLOGICAL IMPACT OF QUARANTINE IN CHILDREN AND ADOLESCENTS DUE TO COVID-19 PANDEMIC

Saurabh K, Ranjan S.. Indian J Pediatr. 2020 May 29. doi: 10.1007/s12098-020-03347-3. Online ahead of print.

Level of Evidence: 3

BLUF

Researchers in India assessed the understanding of quarantine and level of compliance in a cohort of 121 children (ages 9-18) and compared their psychological well-being to a cohort of 131 non-quarantined children. They found that while the majority of the quarantined children (73.55%) understand the reasoning behind quarantine, there was variable compliance to protection measures (only 7.43% correctly following all measures) and that feelings of worry, helplessness, and fear were more commonly reported in the quarantined cohort.

ABSTRACT

OBJECTIVES: To examine a cohort of children and adolescents quarantined during Coronavirus disease 2019 outbreak in India and to describe their understanding of, compliance with and the psychological impact of quarantine experience. **METHODS:** One hundred twenty one children and adolescents along with their parents were interviewed regarding their compliance and psychological distress during the quarantine period. A comparable data was also obtained from 131 children and adolescents who were not quarantined. **RESULTS:** Most of the children and adolescents were non-compliant as compliance with all requirements was low (7.43%), though compliance with community protective measures (17.35%) was better than compliance with household protective measures (10.71%). Quarantined children and adolescents experienced greater psychological distress than non-quarantined children and adolescents ($p < 0.001$). Worry (68.59%), helplessness (66.11%) and fear (61.98%) were the most common feelings experienced under quarantine. **CONCLUSIONS:** The low compliance with quarantine requirements as seen in this study raises a serious concern about the effectiveness of quarantine as a preventive measure of disease transmission. Compliance and mental health problems can be improved by providing adequate financial support and enhanced knowledge about pandemic planning.

FIGURES

1. Understanding of rationale for quarantine	Number (n) = 121	Percentage (%)
1a. Quarantine protects self	67	55.37
1b. Quarantine protects household	62	51.23
1c. Quarantine protects community	89	73.55
1d. All correct	20	16.52
Compliance		
2. Compliant with all household protective measures	13	10.71
2a. Used separate towels	41	33.88
2b. Used separate plates for eating	39	32.23
2c. Slept in separate room	31	25.61
2d. Used mask when family members present	31	25.61
3. Compliant with all community protective measures	21	17.35
3a. Did not go out of house to socialise	112	92.56
3b. Did not run errands outside of home	101	83.47
3c. Used mask for home healthcare visits	51	42.14
3d. Used mask when answer door	48	39.66
3e. Did not allow visitors into home	81	66.94
4. Compliant with all protective measures	9	7.43
5. Most common difficulties		
5a. Not going out of house to socialise	79	65.26
5b. Not going out of house to errands	78	64.46
5c. Using mask when family member present	71	58.67
5d. Staying in room by self with door closed	59	48.76

Table 1. Understanding the rationale, compliance, and difficulties associated with quarantine among adolescents and children.

AMERICANS' COVID-19 STRESS, COPING, AND ADHERENCE TO CDC GUIDELINES

Park CL, Russell BS, Fendrich M, Finkelstein-Fox L, Hutchison M, Becker J.. J Gen Intern Med. 2020 May 29. doi: 10.1007/s11606-020-05898-9. Online ahead of print.

Level of Evidence: 3

BLUF

A cross-sectional, national study that included 1,015 individuals was conducted across the United States of America from April 7-9, 2020 by the University of Connecticut and sought to understand American adults' experiences in social isolation, particularly their specific stressors, coping strategies, and adherence to CDC guidelines. Stress was reported to be common, with the greatest stressor being reading/hearing about the severity and contagiousness of COVID-19 (96.6%).

SUMMARY

A cross-sectional, national study conducted across the United States of America from April 7-9, 2020 by the University of Connecticut sought to understand American adults' experiences in social isolation, particularly their specific stressors, coping strategies, and adherence to CDC guidelines. 1,015 individuals participated in completing the national survey (Amazon's Mechanical Turk). Stress was extremely common, and the greatest stressor was reading/hearing about the severity and contagiousness of COVID-19 (96.6%). The most common coping strategies were distraction, active coping, and seeking emotional support. Lastly, most participants adhered selectively to CDC guidelines, demonstrating varying amounts of social distancing. These findings should inform policy-makers and guide appropriate mental health interventions for the American public.

ABSTRACT

IMPORTANCE: Documenting Americans' stress responses to an unprecedented pandemic and their degree of adherence to CDC guidelines is essential for mental health interventions and policy-making.

OBJECTIVE: To provide the first snapshot of immediate impact of COVID-19 on Americans' stress, coping, and guideline adherence.

DESIGN: Data were collected from an online workers' platform for survey research (Amazon's Mechanical Turk) from April 7 to 9, 2020. The current data represents the baseline of a longitudinal study. Best practices for ensuring high-quality data were employed.

PARTICIPANTS: Individuals who are 18 years of age or older, living in the USA, and English-speaking were eligible for the study. Of 1086 unique responses, 1015 completed responses are included.

SETTING: Population-based.

MAIN OUTCOMES: Exposure to and stressfulness of COVID-19 stressors, coping strategies, and adherence to CDC guidelines.

RESULTS: The sample was 53.9% women ($n = 547$), with an average age of 38.9 years ($SD = 13.50$, range = 18-88), most of whom were White ($n = 836$, 82.4%), non-Hispanic ($n = 929$, 91.5%), and straight/heterosexual ($n = 895$, 88.2%); 40% were currently married ($n = 407$), and 21.6% ($n = 219$) were caregivers. About half (50.5%) endorsed having at least "mostly" enough money to meet their needs. Respondents' locations across the USA ranged from 18.5% in the Northeast to 37.8% in the South. The most commonly experienced stressors were reading/hearing about the severity and contagiousness of COVID-19, uncertainty about length of quarantine and social distancing requirements, and changes to social and daily personal care routines. Financial concerns were rated most stressful. Younger age, female gender, and caregiver status increased risk for stressor exposure and greater degree of stressfulness. The most frequently reported strategies to manage stress were distraction, active coping, and seeking emotional social support. CDC guideline adherence was generally high, but several key social distancing and hygiene behaviors showed suboptimal adherence, particularly for men and younger adults.

CONCLUSIONS AND RELEVANCE: Americans have high COVID-19 stress exposure and some demographic subgroups appear particularly vulnerable to stress effects. Subgroups less likely to adhere to CDC guidelines may benefit from targeted information campaigns. These findings may guide mental health interventions and inform policy-making regarding implications of specific public health measures.

FIGURES

Demographic Characteristics of the Sample

Demographic	
Age (years), M (SD)	38.9 (13.5)

Demographic

Gender, N (%)	
Male	453 (44.6%)
Female	547 (53.9%)
Non-binary/third gender	3 (0.3%)
Transgender	4 (0.4%)
Prefer to self-describe	4 (0.4%)
Prefer not to say	4 (0.4%)
Race, N (%)	
Black/African American	122 (12.0%)
Asian/Asian American	121 (11.9%)
Native Hawaiian/other Pacific Islander	50 (4.9%)
American Indian/Alaska Native	70 (6.9%)
White	836 (82.4%)
Ethnicity, N (%)	
Hispanic	86 (8.5%)
Non-Hispanic	929 (91.5%)
Sexual orientation, N (%)	
Straight/heterosexual	895 (88.2%)
Gay or lesbian	40 (3.9%)
Bisexual	64 (6.3%)
Prefer to self-describe	7 (0.7%)
Prefer not to say	9 (0.9%)
Geographic state, N (%)	
West	244 (24.1%)
Midwest	199 (19.6%)
South	383 (37.7%)
Northeast	188 (18.5%)
Marital status, N (%)	
Married	407 (40.1%)
Single	359 (35.4%)
Divorced	73 (7.2%)
Separated	14 (1.4%)
Widowed	18 (1.8%)
Living with but not married	144 (14.2%)
Current living arrangement, N (%)	
In parent/guardian home	158 (15.6%)
With others (no relation)	214 (21.1%)
With others (related)	468 (46.1%)
By yourself	172 (16.9%)
Residence location, N (%)	
House	614 (60.5%)
Apartment	243 (23.9%)
Caregiver status, N (%)	
Yes	219 (21.6%)
No	796 (78.4%)
Type of caregiver, N (%)	
Child (under 18 years old)	182 (83.1%)
Same age relative/friend	12 (5.5%)
Parent	19 (8.7%)
Grandparent	4 (1.8%)
Other	2 (0.9%)
Current student status, N (%)	
No	890 (87.7%)
Yes, part-time	60 (5.9%)

Demographic	
Yes, full-time	65 (6.4%)
Type of school, N (%)	
Residential	44 (35.2%)
Commuter	51 (40.8%)
Online-only	30 (24.0%)
Prior to COVID-19 employment status, N (%)	
No	180 (17.7%)
Yes, part-time	185 (18.2%)
Yes, full-time	650 (64.0%)
Current employment status, N (%)	
No	286 (28.2%)
Yes, part-time	198 (19.5%)
Yes, full-time	531 (52.3%)
Finances sufficient to meet needs, N (%)	
Not at all	74 (7.3%)
A little	209 (20.6%)
Moderately	219 (21.6%)
Mostly	276 (27.2%)
Completely	237 (23.3%)

Table 1. Demographic Characteristics of the Sample

Prevalence and Stressfulness of COVID-19-Related Stressors

	N endorsed (%)	Group differences in stressor prevalence	Mean stress appraisal (SD)	Group differences in stress appraisal
Infection-related				
1. Risk of becoming infected	576 (56.8%)	e1 ($r = -.09$)	3.06 (1.03)	a1 ($d = -0.26$); b ($d = 0.20$); e1 ($r = -.09$)
2. Self-monitoring of symptoms	440 (43.4%)	c1 ($h = 0.36$); e1 ($r = -.07$)	2.43 (1.13)	b ($d = 0.36$); d1 ($r = -.18$); e1 ($r = -.18$); f ($d = 0.28$)
3. Risk of loved ones becoming infected	622 (61.3%)	a1 ($h = -0.14$)	3.65 (1.01)	a1 ($d = -0.23$); b ($d = 0.21$); e1 ($r = -.21$)
4. Risk of unintentionally infecting other people	246 (24.3%)	d1 ($r = -.12$); e1 ($r = -.07$)	3.26 (1.08)	e1 ($r = -.16$)
5. Read or heard others talk about the severity and contagiousness of COVID-19	980 (96.6%)	d2 ($r = .07$)	3.07 (1.08)	a1 ($d = -0.23$); d1 ($r = -.09$); e1 ($r = -.15$)
6. Stigma, shame, discrimination, or social exile related to quarantine or working in a high-risk area (e.g., others shunning you because you work in healthcare)?	66 (6.5%)	b ($h = 0.23$); d1 ($r = -.12$)	3.53 (0.96)	b ($d = 0.53$)
7. Stigma, shame, or discrimination related to being in a certain age group (e.g., negative statements about Millennials or Generation Z)	158 (15.6%)	c1 ($h = 0.20$); d1 ($r = -.22$); e1 ($r = -.10$)	2.57 (1.13)	b ($d = 0.40$)
8. Uncertainty about how long quarantine and/or social distancing requirements will last?	896 (88.3%)	a1 ($h = -0.13$)	3.26 (1.08)	a1 ($d = -0.25$); d1 ($r = -.20$); e1 ($r = -.17$)
Activity-related				
9. Changes to daily personal care routines (e.g., cooking, cleaning, exercise/relaxation, hobbies)	811 (80.1%)	d1 ($r = -.08$)	2.76 (1.12)	a1 ($d = -0.15$); b ($d = 0.17$); d1 ($r = -.20$); e1 ($r = -.22$)
10. Changes to daily work routines (e.g., unable to earn money, attend full- or part-time work schedule)	608 (60.3%)	d1 ($r = -.18$); e1 ($r = -.15$)	3.46 (1.16)	a1 ($d = -0.32$); d1 ($r = -.17$); e1 ($r = -.39$)
11. Changes to daily education routines (e.g., online instruction)	233 (23.0%)	a1 ($h = -0.25$); b ($h = 0.43$); d1 ($r = -.20$)	3.16 (1.13)	d1 ($r = -.13$)
12. Changes to social routines (e.g., spending free time with friends/loved ones)	849 (83.7%)	-	2.91 (1.12)	a1 ($d = -0.22$); d1 ($r = -.10$); e1 ($r = -.13$)
13. Changed responsibilities to care for dependents (e.g., childcare, eldercare)	246 (24.3%)	b ($h = 1.02$); c2 ($h = -0.26$)	2.10 (1.17)	d1 ($r = -.23$); e1 ($r = -.18$)

	N endorsed (%)	Group differences in stressor prevalence	Mean stress appraisal (SD)	Group differences in stress appraisal
14. Cancelation of planned or scheduled celebrations, entertainment, vacations, or trips (e.g., graduations, birthdays, concerts)	696 (68.7%)	a1 ($h = -0.27$); b ($h = 0.25$); d1 ($r = -.07$)	2.95 (1.15)	d1 ($r = -.11$)
15. Cancelation of meaningful personal or religious rituals (e.g., funerals, religious services)	266 (26.3%)	b ($h = 0.32$); c2 ($h = -0.42$); d2 ($r = .08$); f ($h = 0.16$)	2.94 (1.19)	a1 ($d = -0.34$); e1 ($r = -.18$)
16. Inability to travel (e.g., cancelation of vacations, weekend trips)	565 (55.8%)	e2 ($r = .07$)	2.90 (1.12)	d1 ($r = -.12$)
17. Increased contact with close others or loved ones (e.g., increased conflict, co-worrying)	438 (43.3%)	b ($h = 0.20$); c1 ($h = 0.24$)	2.60 (1.17)	a1 ($d = -0.28$); c1 ($d = 0.27$); d1 ($r = -.19$); e1 ($r = -.22$)
18. Pressure to “make the most of” COVID-19 or “find a silver lining” while quarantining (e.g., social media fitness challenges, encouragement to increase productivity)	502 (49.7%)	a1 ($h = -0.24$); b ($h = 0.18$); c1 ($h = 0.20$); d1 ($r = -.11$)	2.41 (1.20)	a1 ($d = -0.28$); d1 ($r = -.19$); e1 ($r = -.18$)
Financial/resource-related				
19. Loss of current job security or income (e.g., inability to earn money)?	339 (33.6%)	a1 ($h = -0.11$); c1 ($h = 0.20$); d1 ($r = -.11$); e1 ($r = -.37$)	4.09 (0.96)	d1 ($r = -.16$); e1 ($r = -.32$)
20. Loss of current job training opportunities or education benchmarks (e.g., certification, apprenticeship, internship or degree completion)	121 (12.0%)	d1 ($r = -.22$); e1 ($r = -.13$)	3.52 (1.18)	a1 ($d = -0.42$); e1 ($r = -.33$)
21. Potential changes to the national or global economy (e.g., future job prospects, loss of investments)	643 (63.6%)	-	3.45 (1.05)	a1 ($d = -0.20$); d1 ($r = -.12$); e1 ($r = -.19$)
22. Difficulty accessing important resources for daily life (e.g., healthcare, food, clothes, water, housing, medical supplies or prescriptions)	501 (49.5%)	a1 ($h = -0.21$); e1 ($r = -.23$)	3.36 (1.04)	a1 ($d = -0.28$); d1 ($r = -.18$); e1 ($r = -.20$)
23. Inadequate access to reliable information about COVID-19 (including your personal risk of illness)	176 (17.4%)	d1 ($r = -.10$); e1 ($r = -.15$)	3.50 (1.09)	e1 ($r = -.23$)

a1, reported more by women vs. men; *a2*, reported more by men vs. women; *b*, reported more by caregivers vs. non-caregivers; *c1*, reported more by non-heterosexual participants; *c2*, reported more by heterosexual participants; *d1*, negatively associated with older age; *d2*, positively associated with older age; *e1*, negatively associated with having needs met; *e2*, positively associated with having needs met; *f*, reported more often by non-White participants (all two-tailed p 's < .05). Two-tailed independent samples *t* tests were used for categorical group comparisons; bivariate correlations were used for continuous predictors (age and financial needs met) to retain maximal variance. Average stress appraisals apply only for participants who endorsed experiencing each item; participants who did not endorse a given item did not report on stress appraisals. Standardized effect sizes differ by statistical test used (h = Cohen's h (0.20 = small, 0.50 = medium, 0.80 = large); d = Cohen's d (0.20 = small, 0.50 = medium, 0.80 = large); r = bivariate correlation (0.1 = small, 0.3 = medium, 0.5 = large))

Table 2. Prevalence and Stressfulness of COVID-19-Related Stressors

Coping with COVID-Related Stress

	Mean (SD)	Range	Cronbach's alpha	Demographic predictors
COPE subscales				
1. Substance use (4 items)	1.45 (0.78)	1-4	0.96	c1 ($D = 0.24$), d1 ($R = -.20$), e1 ($R = -.12$)
2. Active (2 items)	2.43 (0.83)	1-4	0.77	b ($D = 0.18$), c2 ($D = -0.19$)
3. Distraction (2 items)	2.70 (0.80)	1-4	0.48	a1 ($D = -0.31$), d1 ($R = -.10$)
4. Behavioral disengagement (2 items)	1.40 (0.66)	1-4	0.74	c1 ($D = 0.24$), d1 ($R = -.24$), e1 ($R = -.15$)
5. Humor (2 items)	1.86 (0.89)	1-4	0.88	a2 ($D = 0.22$), c1 ($D = 0.24$), d1 ($R = -.18$)
6. Seeking instrumental social support (2 items)	1.91 (0.83)	1-4	0.83	b ($D = 0.19$), d1 ($R = -.15$)
7. Seeking emotional social support (2 items)	2.23 (0.89)	1-4	0.84	a1 ($D = -0.24$), b ($D = 0.16$)
8. Religious support (2 items)	1.78 (1.00)	1-4	0.90	a1 ($D = -0.30$), b ($D = 0.21$), c2 ($D = -0.31$), d2 ($R = .13$), f ($D = 0.27$)

a1, reported more by women vs. men; *A2*, reported more by men vs. women; *B*, reported more by caregivers vs. non-caregivers; *C1*, reported more by non-heterosexual participants; *C2*, reported more by heterosexual participants; *D1*, negatively associated with older age; *D2*, positively associated with older age; *E1*, negatively associated with having needs met; *E2*, positively associated with having needs met; *F*, reported more often by non-White participants (all two-tailed P 's < .05). Two-tailed independent samples *T* tests were used for categorical group comparisons; bivariate correlations were used for continuous predictors (age and financial needs met). Mean response values were calculated for each subscale to facilitate comparison and interpretability. Standardized effect sizes differ by statistical test used (D = Cohen's D (0.20 = small, 0.50 = medium, 0.80 = large); R = bivariate correlation (0.1 = small, 0.3 = medium, 0.5 = large))

Table 2. Prevalence and Stressfulness of COVID-19-Related Stressors

RESOURCES

A COMPREHENSIVE UPDATED REVIEW ON SARS-COV-2 AND COVID-19

Ren YR, Golding A, Sorbello A, Ji P, Chen J, Bhawana S, Witzmann K, Arya V, Reynolds KS, Choi SY, Nikolov N, Sahajwalla C.. *J Clin Pharmacol.* 2020 May 29. doi: 10.1002/jcph.1673. Online ahead of print.

Level of Evidence: Other

BLUF

A literature review conducted by members of the U.S. Food and Drug Administration summarizes clinicopathologic features of COVID-19 infections and reviews current investigational treatments to facilitate future research on treatments and protocols.

ABSTRACT

This literature review aims to provide a comprehensive current summary of the pathogenesis, clinical features, disease course, host immune responses, and current investigational antiviral and immunomodulatory pharmacotherapies, in order to facilitate the development of future therapies and measures for prevention and control. This article is protected by copyright. All rights reserved.

FIGURES

Table 1 Baseline Clinical Symptoms and Signs of Patients with COVID-19 on Hospital Admission					
Symptom	Wang D et al. ⁸	Deng Y et al. ⁹	Zhou F et al. ¹¹	Wu J et al. ¹⁰	Guan W et.al ⁷
Source	Zhongnan Hospital, Wuhan	Tongji Hospital, Wuhan	Jinyintan and Wuhan Pulmonary Hospital, Wuhan	Multiple Hospitals in Provinces Zhejiang and Jiangsu	Multiple Hospitals across China
Patient N	138	225	191	280	1099
Fever	98.6%	87.2%	94%	84.6%	43.8% ³
Myalgia	34.8%	27.5%	15%	25.4%	14.9% ⁴
Fatigue	69.6%		23%	N/A	38.1%
Headache	6.5%	5.5%	N/A	15.4% ²	13.6%
Cough	59.4%	43.1%	79%	70.4%	67.8%
Sputum	26.8%	32.1%	23%	N/A	33.7%
Sore Throat	17.4% ¹	N/A	N/A	11.1%	13.9%
Hemoptysis	N/A	4.6%	N/A	N/A	0.9%
Dyspnea	31.2%	70.6%	N/A	53.6%	18.7%
Diarrhea	10.1%	17.4%	5%	2.5%	3.8%
Nausea	10.1%	N/A		4%	1.1%
Vomiting	3.6%	N/A			5%
Days from symptom onset to admission ⁵	7.0 (4.0 – 8.0)	7.0 (5.0 – 10.0) ⁶ 10.0 (6.5 – 12.0) ⁷	N/A	N/A	N/A

¹ pharyngalgia

² including mental disorder

³ 88.7% patients experienced fever during hospitalization

⁴ including arthralgia

⁵ median (range)

⁶ recovered patients

⁷ deceased patients

Table 2 Major Demographic Differences between Mild/Moderate Cases and Severe Cases

	Wang D et al. ⁸	Deng Y et al. ⁹	Zhou F et al. ¹¹	Wu J et al. ¹⁰	Guan W et.al ⁷
Severity Definition	Non-ICU vs. ICU	Recovered vs. Death	Survivor vs. non-survivor	Mild/moderate vs. severe/critical ⁵	Non-severe vs. severe ⁶
Patient N	102 vs. 36	116 vs. 109	137 vs. 54	197 vs. 83	1099
Median age (years)	51 vs. 66 ¹	40 vs. 69 ¹	52 vs. 69 ¹	38 vs. 63 ¹	45 vs 52
Sex (male %)	52% vs. 61%	44% vs. 67% ¹	59% vs. 70%	54% vs. 54%	58% vs. 58%
Comorbidities (%)	37% vs. 72% ¹	41% vs. 73% ¹	40% vs. 67% ¹	N/A	21% vs. 39%
Hypertension	22% vs. 58% ¹	16% vs. 37% ¹	23% vs. 48%	N/A	13% vs. 24%
Cardiovascular disease	11% vs. 25%	3% vs. 12% ³	1% vs. 24% ^{1,4}		1.8% vs. 5.8% ⁴
Cerebrovascular disease	1% vs. 17% ¹	N/A	N/A		1.2% vs. 2.3%
Diabetes	6% vs 22% ¹	8% vs. 16%	14% vs. 31%	3% vs. 34% ²	6% vs. 12%
Pulmonary disease	N/A	3% vs. 20% ¹	N/A	1.5% vs. 3.6%	N/A
COPD	1% vs. 8%	N/A	1% vs. 7%	0% vs. 1.2%	0.6% vs. 3.5%

¹p≤0.001

²counted as endocrine system disease

³counted as heart disease

⁴counted as coronary heart disease

⁵patients experienced severe acute respiratory syndrome

⁶the degree of severity at the time of admission using the American Thoracic Society guidelines for community-acquired pneumonia

ACKNOWLEDGEMENTS

CONTRIBUTORS

Carter Butuk
Danika Scott
Dax Cvancara
Dean Cataldo
Diep Nguyen
Jeremiah Sims
Jesse Abelson
John Michael Sherman
Julia Ghering
Kate Buhrke
Kinza Sultan
Krithika Kumarasan
Kylie Jenkins
Maggie Donovan
Maryam Naushab
Maya Patel
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