

The Daily COVID-19 Literature Surveillance Summary

June 10, 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

Epidemiology

- An epidemiological modeling study that used confirmed COVID-19 cases and deaths from January 31–April 22, estimated [adjusted case fatality rates](#) in both Canada and the US of less than 2% when assuming an estimated reporting rate of less than 50%.
- An observational study of 73 COVID-19 patients, 53 of whom were admitted to the ICU, found that patients who experienced a vascular event were more likely to have a [low serum albumin](#).
- A prospective cohort study in England, Wales, and Scotland reports disease course and demographic data from over [20,000 COVID-19 patients](#), representing 34% of all hospitalized COVID-19 patients in these countries. The authors believe that the rapidity by which this data was collected emphasizes the importance of forward-preparedness planning for pandemics.

Understanding the Pathology

- A prospective cohort study of 5,279 COVID-19 positive patients found that age was the strongest [risk factor for hospitalization](#); however, when looking at patients with critical illness, admission oxygen saturation < 88%, troponin > 1, C-reactive protein > 200, and D-dimer > 2500 exhibited stronger associations than age.

Transmission and Prevention

- An [analysis of human nasal mucus and sputum](#) mixed with SARS-CoV-2 under different environmental conditions found that the viral half-life and viral load were decreased under conditions with warmer temperature and higher humidity, suggesting possible seasonal drive for future outbreaks peaking during cold and dry periods.
- A case series from a skilled nursing facility in California demonstrated successful [prevention of further infections](#) after two residents tested positive for SARS-CoV-2. Their approach included screening all residents and staff members with RT-PCR, serial testing for positive SARS-CoV-2 residents, and cohort isolation for those who tested positive.

Management

- Guidelines and recommendations for caring for COVID-19 patients include:
 - A [novel epidemiological risk score](#) to predict diagnosis of COVID-19
 - [Chest imaging](#)
- A retrospective cohort study in Italy found that among 173 patients admitted to the general or vascular neurology unit with [neurological diseases](#), those who had COVID-19 were more likely to be older, have higher quick Sequential Organ Failure (qSOFA) score on admission, and be admitted with cerebrovascular disease.
- A study of 101 patients hospitalized with COVID-19 found that those on [maintenance hemodialysis](#) were less likely to present with the classic COVID-19 symptoms of fever and cough; though were more likely to develop complications such as shock, acute respiratory distress syndrome, arrhythmia, and acute cardiac injury and had poorer clinical outcomes than controls.

Adjusting Practice During COVID-19

- The European Myeloma Network released a consensus statement to guide treatment decisions for [multiple myeloma](#) patients during the COVID-19 pandemic and urged participation in international registries to record data on multiple myeloma patients and COVID-19 to further guide management.
- An in vitro study conducted by the University of Connecticut Health Center in Farmington, Connecticut in May 2020 found that [povidone-iodine \(aka PVP-I or Betadine\) in concentrations of 0.5% can completely inactivate SARS-CoV-2 in 15 seconds](#) compared to 70% ethanol, which took 30 seconds to inactivate the virus, suggesting that PVP-I oral rinse prior to dental or prosthodontic procedures could decrease the risk of transmission in dental practice.

R&D: Diagnosis and Treatment

- A GRADE-guided systematic review of six studies of [therapeutic convalescent plasma \(CP\)](#), using results from four influenza randomized trials and one non-randomized study of both SARS-CoV and Ebola, found no therapeutic efficacy across patient outcomes, length of hospital or ICU stay, or viral load reduction.
 - Given the use of hemagglutination inhibition to nonspecifically categorize CP in some trials herein, direct study of verified CP from recently recovered COVID-19 patients to gauge its efficacy is recommended.
- A trial of 62 hospitalized COVID-19 patients in China from January to March 2020 compared the control group, treated with Asmeton, Eucalyptol, and Moxifloxacin (n=20), to the intervention group, receiving the same treatment in addition to Arbidol (n=42), and found that the intervention group had a shorter duration of cough and fever, suggesting that COVID-19 [symptom duration may be shortened with the addition of Arbidol](#) to standard treatment.

Mental Health and Resilience Needs

- A cross sectional study of 4,618 [health professionals](#) in the Chinese provinces of Sichuan and Yunnan found a higher Huaxi Emotional Distress Index (HEI) for those exposed to the COVID-19 outbreak with 24.2% experiencing higher levels of anxiety and/or depressive symptoms since the start of the COVID-19 outbreak.

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CLIMATE

DISPARITIES

THE DEMOGRAPHICS AND ECONOMICS OF DIRECT CARE STAFF HIGHLIGHT THEIR VULNERABILITIES AMIDST THE COVID-19 PANDEMIC

Almeida B, Cohen MA, Stone RI, Weller CE. J Aging Soc Policy. 2020 Jun 8:1-7. doi: 10.1080/08959420.2020.1759757. Online ahead of print.

Level of Evidence: Other - Review / Literature Review

BLUF

A group of researchers argue that direct care staff, who provide care for the elderly and disabled, are themselves vulnerable during this pandemic, as they may not have adequate protective equipment, training, insurance, or wages to best care for themselves and others in this time (Figures 1-3). They suggest that these risks can increase the spread of SARS-CoV-2 and greater burden our health care system.

ABSTRACT

An estimated 3.5 million direct care staff working in facilities and people's homes play a critical role during the COVID-19 pandemic. They allow vulnerable care recipients to stay at home and they provide necessary help in facilities. Direct care staff, on average, have decades of experience, often have certifications and licenses, and many have at least some college education to help them perform the myriad of responsibilities to properly care for care recipients. Yet, they are at heightened health and financial risks. They often receive low wages, limited benefits, and have few financial resources to fall back on when they get sick themselves and can no longer work. Furthermore, most direct care staff are parents with children in the house and almost one-fourth are single parents. If they fall ill, both they and their families are put into physical and financial risk.

FIGURES

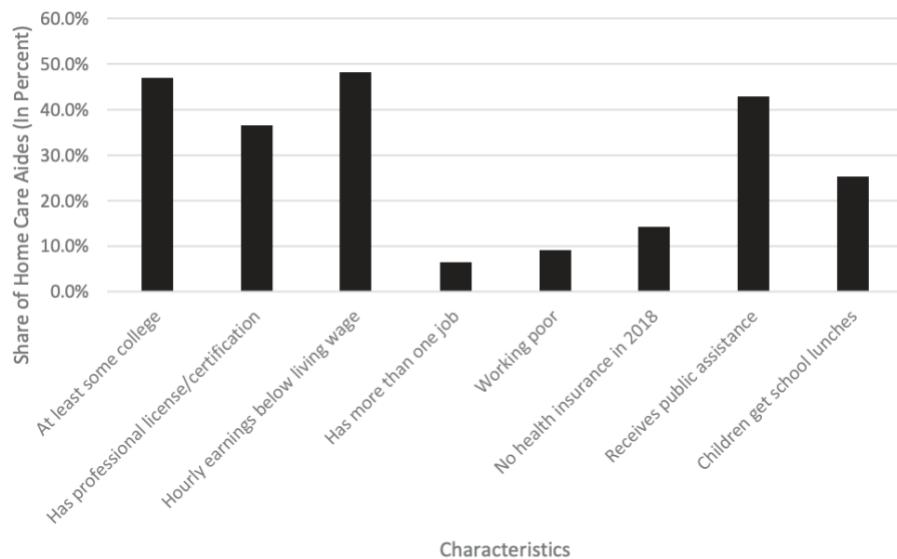


Figure 1. Select Economic Characteristics of Direct Care Staff, 2018/2019.

Notes: Direct care professionals include nursing, psychiatric, home health aides, and personal care aides from the CPS occupational codes 3600 and 4610. Monthly data are pooled for all months in 2019. Dollar values are in real 2018 dollars. Individual wage income and total family income are taken from the Annual Social and Economic Supplement (ASEC). Those data are collected in March of each year and refer to the previous 12 months and thus reflect mainly data received in 2018. Working poor is defined as having worked at least 27 weeks over the past year and having income below the official federal poverty line. Public assistance includes Medicaid, free and reduced school lunches, housing subsidies, food stamps and earned income tax credits. Wages are deflated using the Consumer Price Index for Clerical Workers (CPI-W) and income is deflated using the Consumer Price Index for Urban Consumers (CPI-U) from the Bureau of Labor Statistics. Wages Source is from Flood et al. (2018)

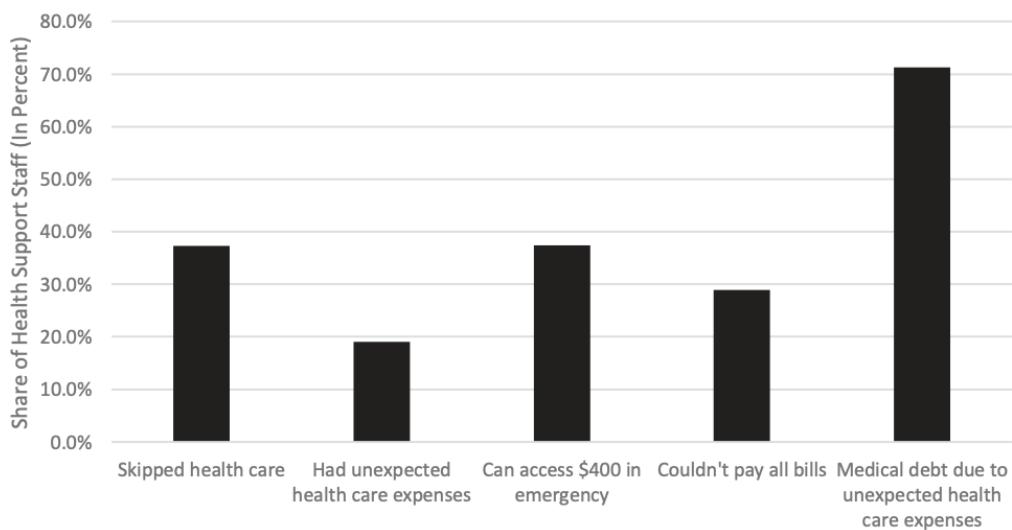


Figure 2. Financial Vulnerability of Health Support Staff, 2018.

Note: Source is Fed. (Federal Reserve, 2019). Skipping health care includes not going to doctor, not taking prescribed medicine, not going to follow up visit. The sample for medical debt includes only those who had unexpected health-care expenses in the previous year.

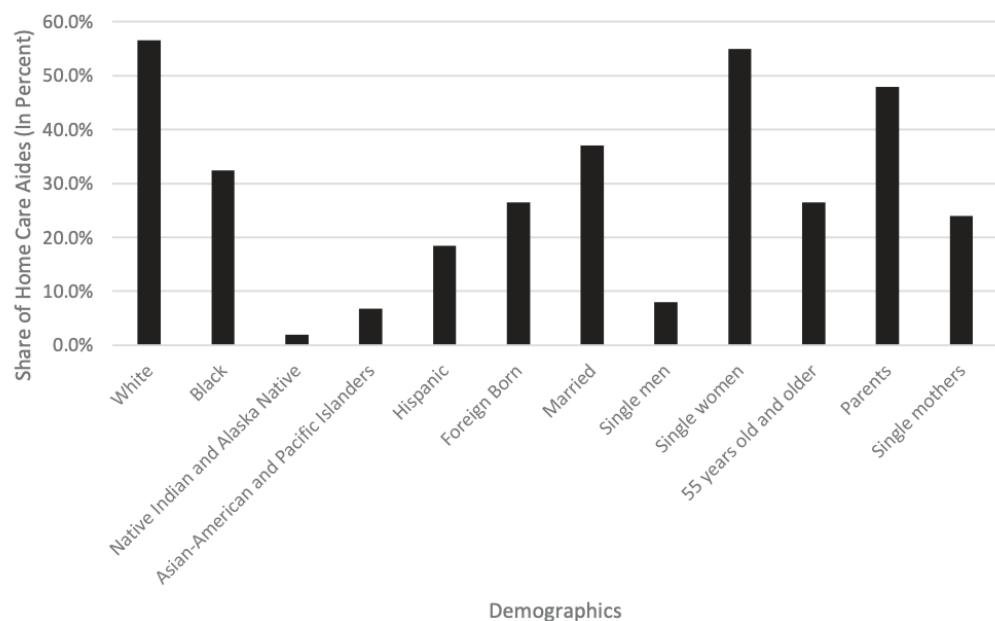


Figure 3. The Demographics of Direct Care Staff.

Note: Direct care staff include nursing, psychiatric, home health aides, and personal care aides from the CPS occupational codes 3600 and 4610. Monthly data are pooled for all months in 2019. Source is Flood et al. (2018).

EPIDEMIOLOGY

MODELING

MALARIA AND PARASITIC NEGLECTED TROPICAL DISEASES: POTENTIAL SYNDEMICS WITH COVID-19?

Gutman JR, Lucchi NW, Cantey PT, Steinhardt LC, Samuels AM, Kamb ML, Kapella BK, McElroy PD, Udhayakumar V, Lindblade KA.. Am J Trop Med Hyg. 2020 Jun 1. doi: 10.4269/ajtmh.20-0516. Online ahead of print.

Level of Evidence: Other - Review / Literature Review

BLUF

This literature review discusses the need to develop additional surveillance modalities to monitor for coinfections of COVID-19 patients with malaria or other neglected tropical diseases in low and middle income countries. Additional testing was deemed necessary in order to better understand and prevent a possible synergistic epidemic.

ABSTRACT

The COVID-19 pandemic, caused by SARS-CoV-2, have surpassed 5 million cases globally. Current models suggest that low-and middle-income countries (LMICs) will have a similar incidence but substantially lower mortality rate than high-income countries. However, malaria and neglected tropical diseases (NTDs) are prevalent in LMICs, and coinfections are likely. Both malaria and parasitic NTDs can alter immunologic responses to other infectious agents. Malaria can induce a cytokine storm and pro-coagulant state similar to that seen in severe COVID-19. Consequently, coinfections with malaria parasites and SARS-CoV-2 could result in substantially worse outcomes than mono-infections with either pathogen, and could shift the age pattern of severe COVID-19 to younger age-groups. Enhancing surveillance platforms could provide signals that indicate whether malaria, NTDs, and COVID-19 are syndemics (synergistic epidemics). Based on the prevalence of malaria and NTDs in specific localities, efforts to characterize COVID-19 in LMICs could be expanded by adding testing for malaria and NTDs. Such additional testing would allow the determination of the rates of coinfection and comparison of severity of outcomes by infection status, greatly improving the understanding of the epidemiology of COVID-19 in LMICs and potentially helping to mitigate its impact.

TEMPORAL ESTIMATES OF CASE-FATALITY RATE FOR COVID-19 OUTBREAKS IN CANADA AND THE UNITED STATES

Abdollahi E, Champredon D, Langley JM, Galvani AP, Moghadas SM.. CMAJ. 2020 May 22:cmaj.200711. doi: 10.1503/cmaj.200711. Online ahead of print.

Level of Evidence: Other -

BLUF

An epidemiology modeling study, performed using confirmed COVID-19 cases and deaths from January 31–April 22, 2020, found that adjusted case fatality rates (CFR) in both Canada (5.1%; credible interval 4.9%–6.4%) and the US (6.1%; credible interval 5.4%–6.9%) to actually be less than 2% when factoring in estimated reporting rates less than 50% (Figures 1 and 2). These results, when compared to other studies with CFR anywhere from 13.5% to 67%, highlight how accounting for bias, in this case the lag time between infection and death, can have drastic effects on quantifying epidemiological variables.

SUMMARY

The authors highlight two biases when calculating case fatality rates: the lag time between infection and death and the under-reporting of COVID-19 cases. To account for these two biases, the authors applied a statistical method that implemented a probability distribution with a wide range of survival intervals and assumed the reporting rates to be less than 50% (95% CI 10–50%). Their analysis reports adjusted CFR for Canada (CFR = 5.5%; credible interval 4.9%–6.4%) and US (CFR = 6.1%; credible interval 5.4%–6.9%).

ABSTRACT

BACKGROUND: Estimates of the casefatality rate (CFR) associated with coronavirus disease 2019 (COVID-19) vary widely in different population settings. We sought to estimate and compare the COVID-19 CFR in Canada and the United States while adjusting for 2 potential biases in crude CFR.

METHODS: We used the daily incidence of confirmed COVID-19 cases and deaths in Canada and the US from Jan. 31 to Apr. 22, 2020. We applied a statistical method to minimize bias in the crude CFR by accounting for the survival interval as the lag time between disease onset and death, while considering reporting rates of COVID-19 cases less than 50% (95% confidence interval 10%-50%).

RESULTS: Using data for confirmed cases in Canada, we estimated the crude CFR to be 4.9% on Apr. 22, 2020, and the adjusted CFR to be 5.5% (credible interval [CrI] 4.9%-6.4%). After we accounted for various reporting rates less than 50%, the adjusted CFR was estimated at 1.6% (CrI 0.7%-3.1%). The US crude CFR was estimated to be 5.4% on Apr. 20, 2020, with an adjusted CFR of 6.1% (CrI 5.4%-6.9%). With reporting rates of less than 50%, the adjusted CFR for the US was 1.78 (CrI 0.8%-3.6%).

INTERPRETATION: Our estimates suggest that, if the reporting rate is less than 50%, the adjusted CFR of COVID-19 in Canada is likely to be less than 2%. The CFR estimates for the US were higher than those for Canada, but the adjusted CFR still remained below 2%. Quantification of case reporting can provide a more accurate measure of the virulence and disease burden of severe acute respiratory syndrome coronavirus 2.

FIGURES

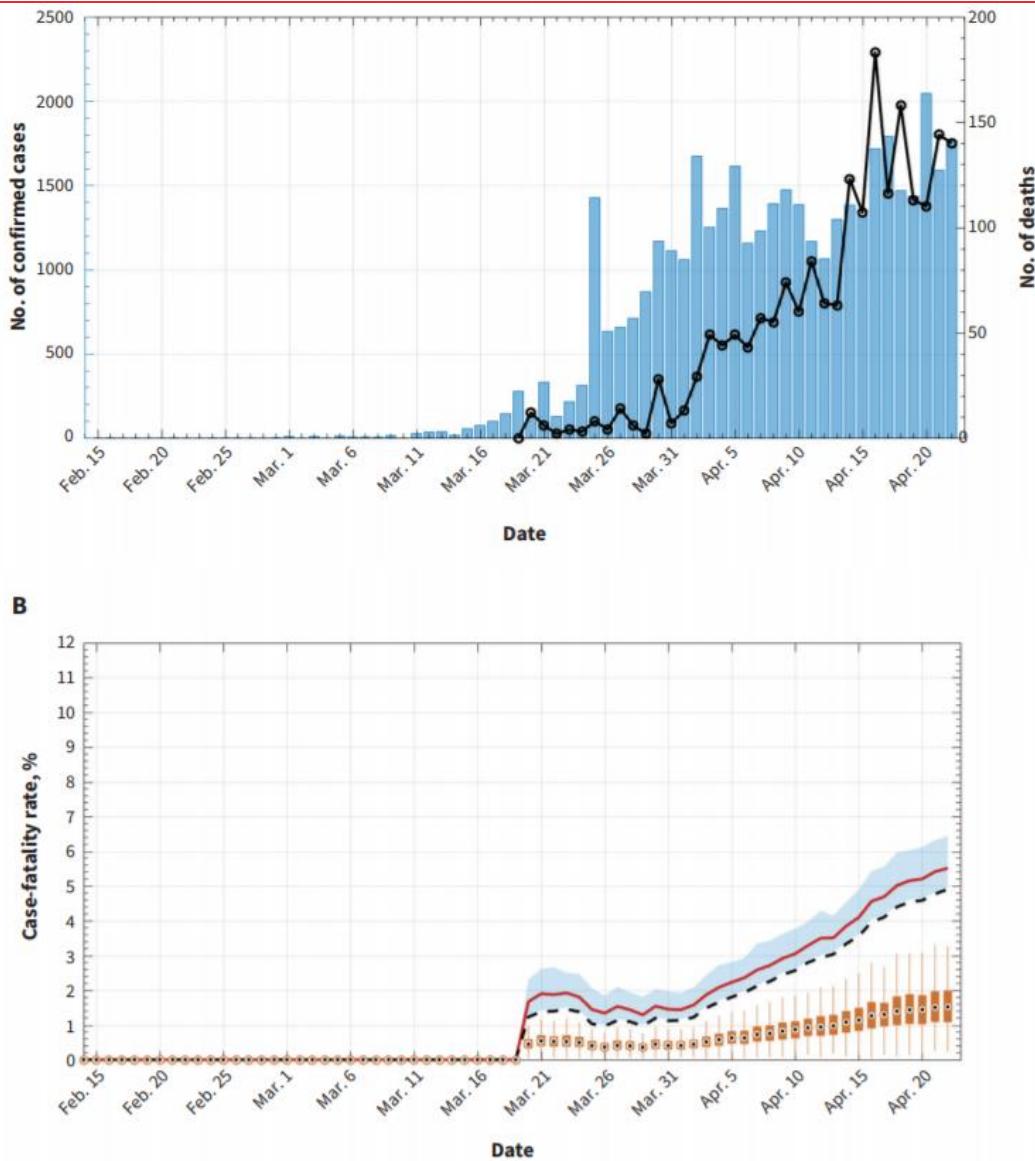
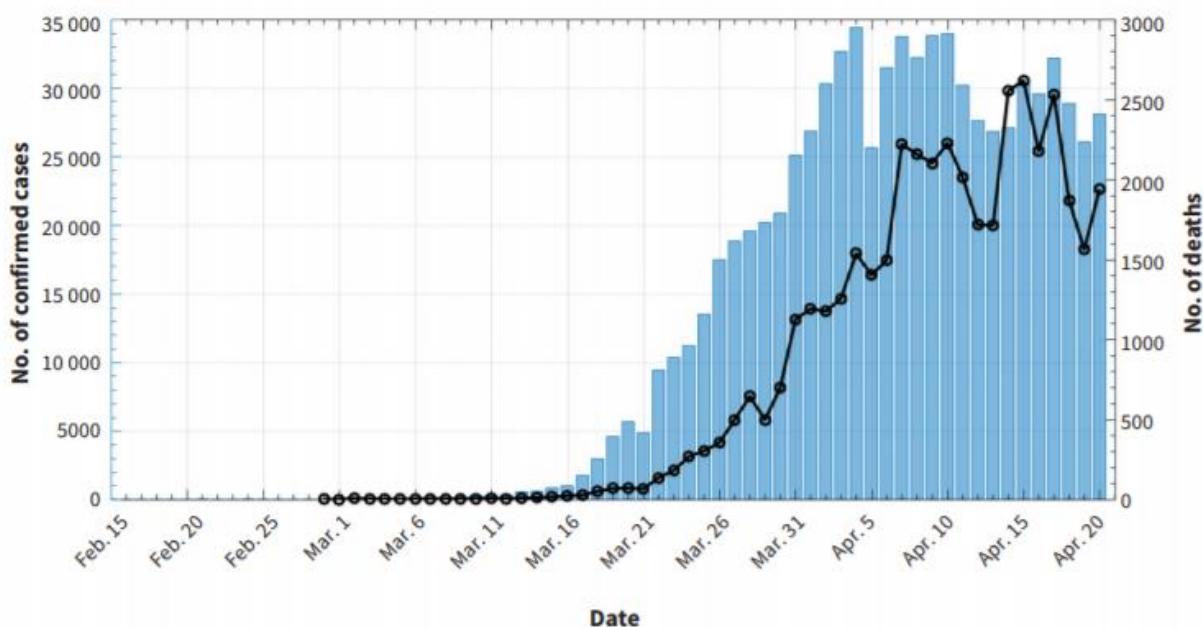
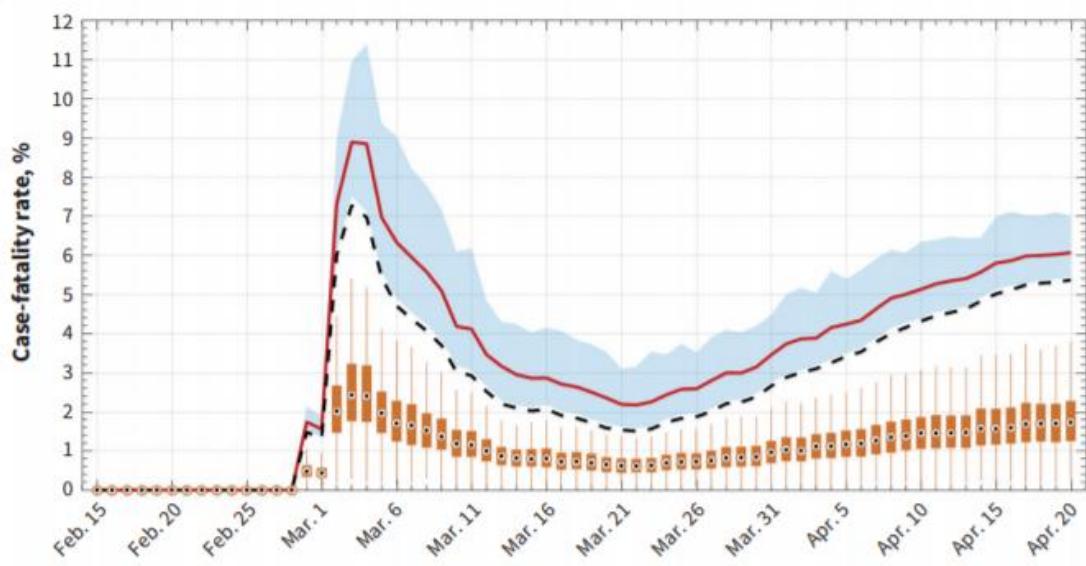


Figure 1: Canada (March 19–April 22, 2020)

(A) Bar graph represents COVID-19 incidence. Dashed line represents confirmed deaths.

(B) Dashed line represents crude CFR. Red line represents adjusted CFR. Blue area around red line represents 95% credible interval for adjusted CFR. Box plots represent range of values when assuming less than 50% COVID-19 reporting levels. Boxes represent interquartile range.

A**B**

SYMPTOMS AND CLINICAL PRESENTATION

HYPOALBUMINEMIA, COAGULOPATHY AND VASCULAR DISEASE IN COVID-19

Violi F, Ceccarelli G, Cangemi R, Alessandri F, d'Ettorre G, Oliva A, Pastori D, Loffredo L, Pignatelli P, Ruberto F, Venditti M, Pugliese F, Mastrianni CM.. Circ Res. 2020 Jun 8. doi: 10.1161/CIRCRESAHA.120.317173. Online ahead of print.

Level of Evidence: 3 - Local non-random sample

BLUF

An observational study by Italian authors included 73 COVID-19 patients with 53 admitted to the ICU and found that patients who experienced a vascular event were more likely to have a low serum albumin, with serum levels less than 35 g/L in 94% of vascular patients compared to 68% in non-vascular patients. The authors also found higher D-dimer levels in vascular patients (4610 ng/mL [1814-4700]) versus non-vascular patients (2154 ng/mL [853-4610]). The authors suggest that hypoalbuminemia and coagulopathy in combination may negatively impact patient outcomes, and urge additional research on a potential cause-effect relationship between hypoalbuminemia and hypercoagulopathy.

FIGURES

	All patients	Non-ICU	ICU	p	Albumin <35 g/L	Albumin ≥35g/L	p
N.	73	20	53		54	19	-
Age	67.1±13.8	66.8±15.2	67.2±13.4	0.932 ^a	66.9±12.9	68.0±16.2	0.780 ^a
Men	81%	75%	83%	0.509	78%	90%	0.331
Creatinine (mg/dl)	1.25±0.82	1.01±0.33	1.34±0.93	0.028 ^a	1.29±0.9	1.13±0.41	0.028 ^a
high sensitivity C-Reactive Protein (mg/L)	100 [35-193]	47 [15-94]	114 [67-207]	0.001 ^b	115 [55-214]	45 [21-103]	0.002 ^b
sPO₂ (%)	92±8	94±4	83±12	0.007 ^a	91±7	84±15	0.736 ^a
White blood cells (x1000/mm³)	6.9±3.0	6.8±2.1	7.9±4.3	0.034 ^a	6.9±2.9	6.8±3.4	0.908 ^a
D-dimer (ng/ml)	3166[992-4655]	1218 [750-4020]	4610 [1385-4700]	0.005 ^b	4610 [1519-4700]	965 [654-3377]	0.002 ^b
Albumin (g/L)	31.7±5.1	33.6±5.9	30.9±4.5	0.041 ^a	-	-	-
Albumin < 35 g/L	74%	55%	81%	0.036	-	-	-

Table 1. Clinical and laboratory characteristics of study patients, according to the intensive care unit (ICU) admission.

Differences between percentages were assessed by Fisher exact tests. All continuous variables were tested for normality with the Shapiro-Wilk test. aStudent unpaired t-test was used for normally distributed continuous variables (expressed as mean±SD). bMann-Whitney U test was used for not-normally distributed continuous variables (expressed as median[interquartile range]).



FEATURES OF 20 133 UK PATIENTS IN HOSPITAL WITH COVID-19 USING THE ISARIC WHO CLINICAL CHARACTERISATION PROTOCOL: PROSPECTIVE OBSERVATIONAL COHORT STUDY

Docherty AB, Harrison EM, Green CA, Hardwick HE, Pius R, Norman L, Holden KA, Read JM, Dondelinger F, Carson G, Merson L, Lee J, Plotkin D, Sigfrid L, Halpin S, Jackson C, Gamble C, Horby PW, Nguyen-Van-Tam JS, Ho A, Russell CD, Dunning J, Openshaw PJ, Baillie JK, Semple MG; ISARIC4C investigators.. BMJ. 2020 May 22;369:m1985. doi: 10.1136/bmj.m1985.

Level of Evidence: 3 -

BLUF

This prospective cohort study reports the characteristics and mortality data of 20,133 COVID-19 patients (see Figures 3, 4, and 5) admitted to 208 hospitals in England, Wales, and Scotland, representing 34% of all COVID-19 patients in these countries. This study was created as part of the United Kingdom's pandemic preparedness plan, following the Influenza A H1N1 pandemic in 2009 and MERS epidemic in 2012. The authors believe that the rapidity by which this data was collected emphasizes the importance of forward-preparedness planning for pandemics.

SUMMARY

This is a prospective cohort study reporting the characteristics and outcomes of 20,133 COVID-19 patients admitted to 208 hospitals in England, Wales and Scotland. This study, known as the International Severe Acute Respiratory and Emerging Infections Consortium (ISARIC) WHO Clinical Characterisation Protocol (CCP-UK) study, is still actively enrolling patients and was created as part of the United Kingdom's pandemic preparedness plan, following the Influenza A H1N1 pandemic in 2009 and MERS epidemic in 2012. The study was activated once the first known case of COVID-19 was reported in the UK on January 31, 2020, and started enrolling patients by February 6. The data showed that 17% of hospitalized patients required admission to the ICU and 10% required invasive ventilation (see Figure 3). 26% of total patients admitted to the hospital died, 32% of patients admitted to critical care died, and 37% of patients receiving invasive ventilation died (see Figure 4). Multivariable analysis showed that increasing age and major comorbidities conferred significantly greater risk of mortality, while female gender was protective (see Figure 5). The ISARIC CCP-UK study enrolled and collected data on a large number of patients (34% of all COVID-19 hospitalized patients in England, Wales and Scotland) in an exceedingly timely manner. The authors believe that this study emphasizes the importance of forward preparedness planning for pandemics.

ABSTRACT

OBJECTIVE: To characterise the clinical features of patients admitted to hospital with coronavirus disease 2019 (covid-19) in the United Kingdom during the growth phase of the first wave of this outbreak who were enrolled in the International Severe Acute Respiratory and emerging Infections Consortium (ISARIC) World Health Organization (WHO) Clinical Characterisation Protocol UK (CCP-UK) study, and to explore risk factors associated with mortality in hospital.

DESIGN: Prospective observational cohort study with rapid data gathering and near real time analysis.

SETTING: 208 acute care hospitals in England, Wales, and Scotland between 6 February and 19 April 2020. A case report form developed by ISARIC and WHO was used to collect clinical data. A minimal follow-up time of two weeks (to 3 May 2020) allowed most patients to complete their hospital admission.

PARTICIPANTS: 20 133 hospital inpatients with covid-19.

MAIN OUTCOME MEASURES: Admission to critical care (high dependency unit or intensive care unit) and mortality in hospital.

RESULTS: The median age of patients admitted to hospital with covid-19, or with a diagnosis of covid-19 made in hospital, was 73 years (interquartile range 58-82, range 0-104). More men were admitted than women (men 60%, n=12 068; women 40%, n=8065). The median duration of symptoms before admission was 4 days (interquartile range 1-8). The commonest comorbidities were chronic cardiac disease (31%, 5469/17 702), uncomplicated diabetes (21%, 3650/17 599), non-asthmatic chronic pulmonary disease (18%, 3128/17 634), and chronic kidney disease (16%, 2830/17 506); 23% (4161/18 525) had no reported major comorbidity. Overall, 41% (8199/20 133) of patients were discharged alive, 26% (5165/20 133) died, and 34% (6769/20 133) continued to receive care at the reporting date. 17% (3001/18 183) required admission to high dependency or intensive care units; of these, 28% (826/3001) were discharged alive, 32% (958/3001) died, and 41% (1217/3001) continued to receive care at the reporting date. Of those receiving mechanical ventilation, 17% (276/1658) were discharged alive, 37% (618/1658) died, and 46% (764/1658) remained in hospital. Increasing age, male sex, and comorbidities including chronic cardiac disease, non-asthmatic chronic pulmonary disease, chronic kidney disease, liver disease and obesity were associated with higher mortality in hospital.

CONCLUSIONS: ISARIC WHO CCP-UK is a large prospective cohort study of patients in hospital with covid-19. The study continues to enrol at the time of this report. In study participants, mortality was high, independent risk factors were increasing age, male sex, and chronic comorbidity, including obesity. This study has shown the importance of pandemic preparedness and the need to maintain readiness to launch research studies in response to outbreaks.

STUDY REGISTRATION: ISRCTN66726260.

FIGURES

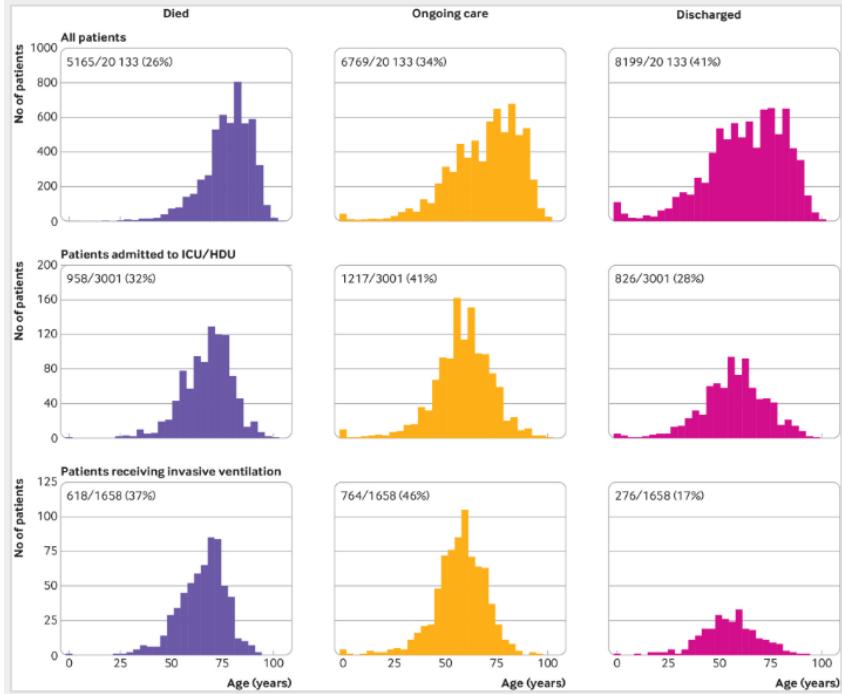


Figure 4. Status of patients at time of reporting stratified by level of care. Top panel: all patients in hospital with coronavirus disease 2019 (covid-19); middle panel: all patients admitted to intensive care unit (ICU) or high dependency unit (HDU); lower panel: patients receiving invasive mechanical ventilation

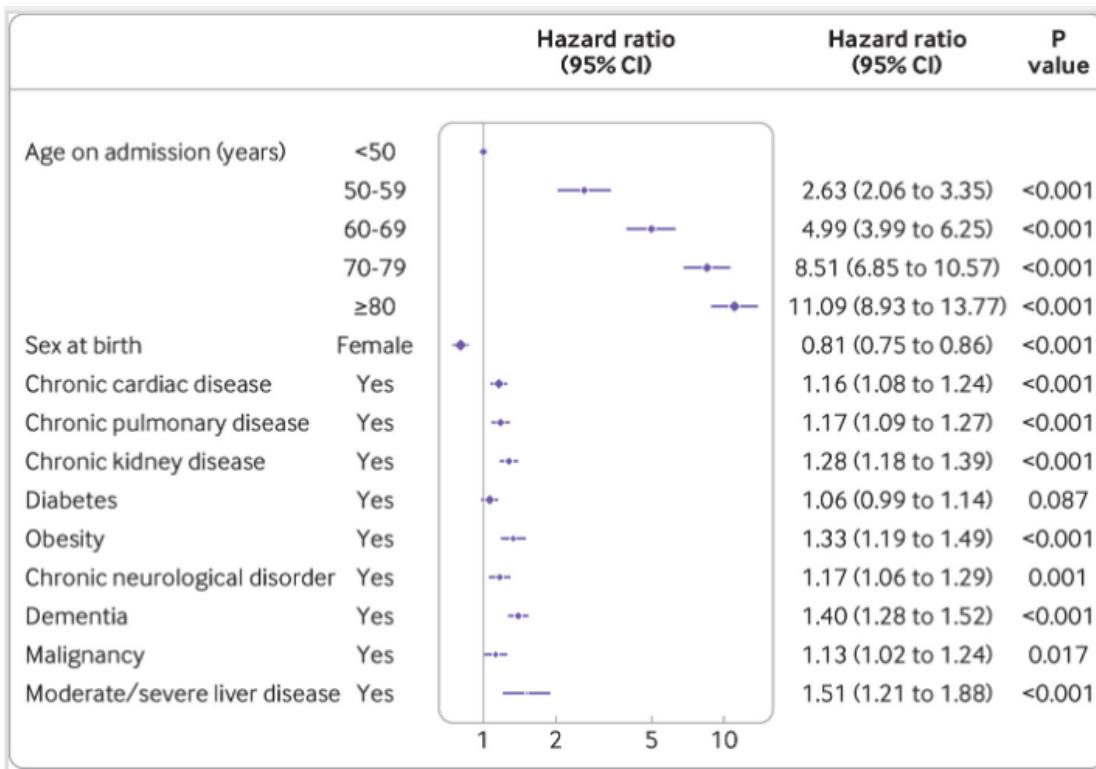


Figure 3. Level of care stratified by age: admitted to intensive care unit (ICU) or high dependency unit (HDU), high flow oxygen, non-invasive ventilation, and invasive ventilation

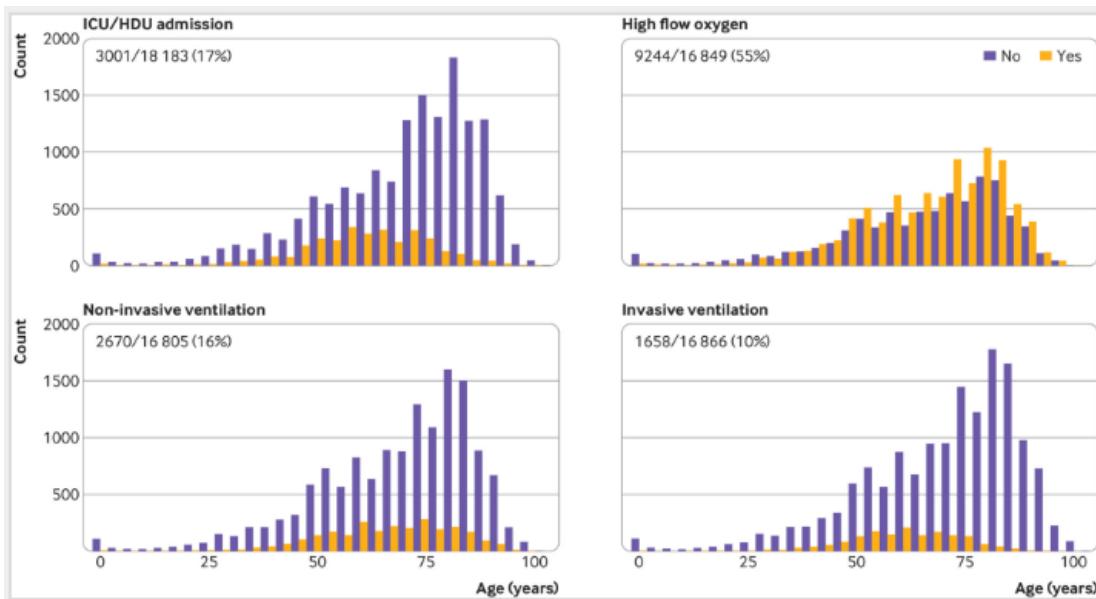


Figure 3. Level of care stratified by age: admitted to intensive care unit (ICU) or high dependency unit (HDU), high flow oxygen, non-invasive ventilation, and invasive ventilation

INCIDENTAL COVID-19 ON PET/CT IMAGING

Amin R, Grinblat L, Husain M.. CMAJ. 2020 May 22:cmaj.200831. doi: 10.1503/cmaj.200831. Online ahead of print.
Level of Evidence: Other -

BLUF

This case study involves a 58-year-old asymptomatic woman with a history of diabetes and morbid obesity who presented to the hospital for PET/CT screening and was noted to have stage 2 pelvic adenopathy as well as incidental findings of bilateral peripheral lung opacities. RT-PCR showed that the patient was positive for SARS-CoV-2 infection suggesting that patients who pass pre-screening for COVID-19 may still present with SARS-CoV-2 infection.

ADULTS

RISK FACTORS FOR MORTALITY IN PATIENTS WITH CORONAVIRUS DISEASE 2019 (COVID-19) INFECTION: A SYSTEMATIC REVIEW AND META-ANALYSIS OF OBSERVATIONAL STUDIES

Parohani M, Yaghoubi S, Seraji A, Javanbakht MH, Sarraf P, Djalali M.. Aging Male. 2020 Jun 8:1-9. doi: 10.1080/13685538.2020.1774748. Online ahead of print.

Level of Evidence: 2 - Systematic review of inception cohort studies

BLUF

This systematic review and meta-analysis pooled 14 observational studies of 29,909 COVID-19 infected patients to identify risk factors associated with death from COVID-19. The authors found that age ≥ 65 years, male gender, cardiovascular diseases, hypertension, diabetes, COPD, and cancer were associated with increased risk of death from COVID-19 (Figures 1-3). Other potential risk factors such as smoking history, body mass index were not included in this meta-analysis.

ABSTRACT

Purpose: Coronavirus disease 2019 (COVID-19) is an emerging disease that was first reported in Wuhan city, the capital of Hubei province in China, and has subsequently spread worldwide. Risk factors for mortality have not been well summarized. Current meta-analysis of retrospective cohort studies was done to summarize available findings on the association between age, gender, comorbidities and risk of death from COVID-19 infection.

Methods: Online databases including Web of Science, PubMed, Scopus, Cochrane Library and Google scholar were searched to detect relevant publications up to 1 May 2020, using relevant keywords. To pool data, random-effects model was used. Furthermore, sensitivity analysis and publication bias test were also done.

Results: In total, 14 studies with 29,909 COVID-19 infected patients and 1445 cases of death were included in the current meta-analysis. Significant associations were found between older age ($>=65$ vs <65 years old) (pooled ORs = 4.59, 95% CIs = 2.61-8.04, $p < .001$), gender (male vs female) (pooled ORs = 1.50, 95% CIs = 1.06-2.12, $p = .021$) and risk of death from COVID-19 infection. In addition, hypertension (pooled ORs = 2.70, 95% CIs = 1.40-5.24, $p = .003$), cardiovascular diseases (CVDs) (pooled ORs = 3.72, 95% CIs = 1.77-7.83, $p = .001$), diabetes (pooled ORs = 2.41, 95% CIs = 1.05-5.51, $p = .037$), chronic obstructive pulmonary disease (COPD) (pooled ORs = 3.53, 95% CIs = 1.79-6.96, $p < .001$) and cancer (pooled ORs = 3.04, 95% CIs = 1.80-5.14, $p < .001$), were associated with higher risk of mortality.

Conclusions: Older age ($>=65$ years old), male gender, hypertension, CVDs, diabetes, COPD and malignancies were associated with greater risk of death from COVID-19 infection. These findings could help clinicians to identify patients with poor prognosis at an early stage.

FIGURES

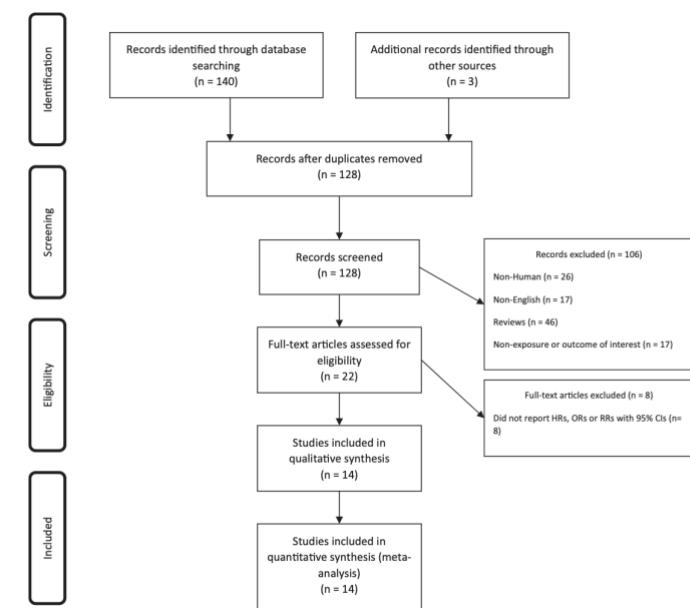


Figure 1. Flow chart of study selection.

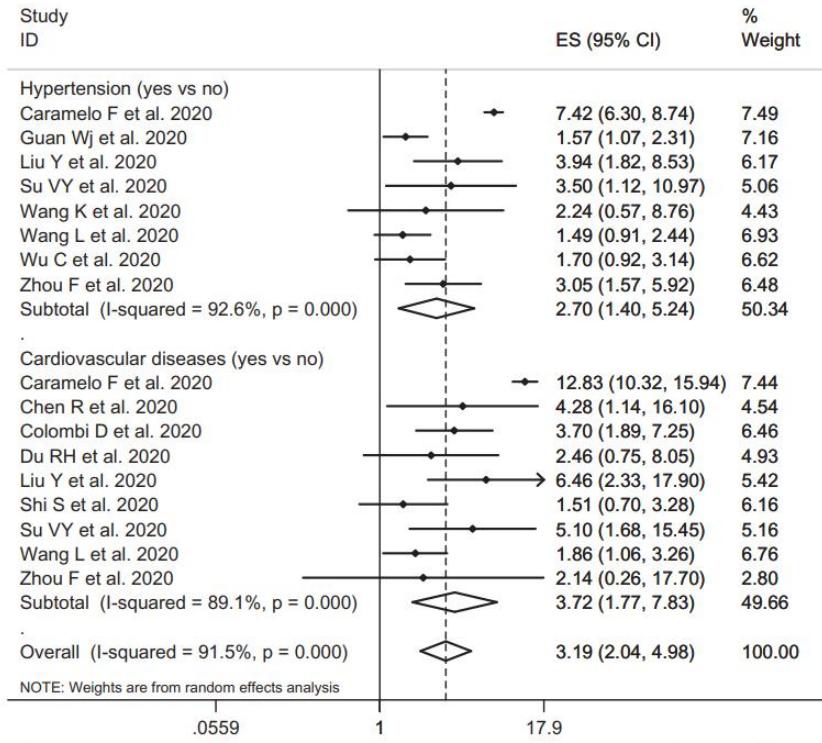


Figure 3. Forest plot for the association between hypertension, cardiovascular diseases and risk of mortality from COVID-19 using random-effects model.

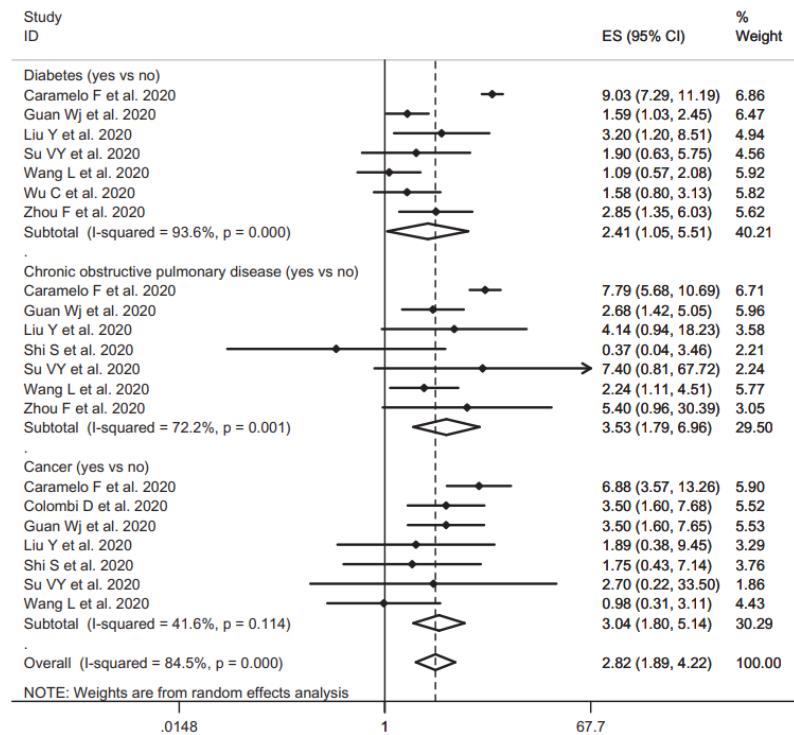


Figure 4. Forest plot for the association between diabetes, chronic obstructive pulmonary disease, cancer and risk of mortality from COVID-19 using random-effects model.

UNDERSTANDING THE PATHOLOGY

FACTORS ASSOCIATED WITH HOSPITAL ADMISSION AND CRITICAL ILLNESS AMONG 5279 PEOPLE WITH CORONAVIRUS DISEASE 2019 IN NEW YORK CITY: PROSPECTIVE COHORT STUDY

Petrilli CM, Jones SA, Yang J, Rajagopalan H, O'Donnell L, Chernyak Y, Tobin KA, Cerfolio RJ, Francois F, Horwitz LI.. BMJ. 2020 May 22;369:m1966. doi: 10.1136/bmj.m1966.

Level of Evidence: 3 -

BLUF

A prospective cohort study of 5,279 COVID-19 positive patients conducted at NYU Langone Health by NYU physicians and professors from 1 March 2020 to 8 April 2020 found that age was the strongest risk factor for hospitalization, while other factors that increase risk include heart failure, male sex, chronic kidney disease, and any increase in BMI. However, some diagnostic information collected upon admission had higher correlation with critical illness than age, including admission oxygen saturation < 88%, troponin > 1, C-reactive protein > 200, and D-dimer > 2500. These findings provide additional tools for clinicians to evaluate potential severity of COVID-19 in patients at an early stage.

SUMMARY

This cohort included all patients (5,279 included in total of 11,544 tested) who tested positive for COVID-19 at NYU Langone Health from 1 March 2020 to 8 April 2020, excluding 287 people not admitted to the hospital for whom key information was missing. Age (odds ratio greater than 2 at age 44 and 37.9 for ages 75 and older), heart failure (4.4), male sex (2.8), chronic kidney disease (2.6), and a high BMI (BMI above 40 carries 2.5 risk factor) were associated with a higher chance of hospital admission. Initial markers including less than 88% oxygen saturation (3.7), troponin level greater than 1 (4.8), C reactive protein level greater than 200 (5.1), and D-dimer level greater than 2500 (3.9) were more strongly associated with critical disease and death than age and comorbidities. Outcomes improved over time, suggesting improvements in care over the course of the study.

ABSTRACT

OBJECTIVE: To describe outcomes of people admitted to hospital with coronavirus disease 2019 (covid-19) in the United States, and the clinical and laboratory characteristics associated with severity of illness.

DESIGN: Prospective cohort study.

SETTING: Single academic medical center in New York City and Long Island.

PARTICIPANTS: 5279 patients with laboratory confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection between 1 March 2020 and 8 April 2020. The final date of follow up was 5 May 2020. **MAIN OUTCOME MEASURES:** Outcomes were admission to hospital, critical illness (intensive care, mechanical ventilation, discharge to hospice care, or death), and discharge to hospice care or death. Predictors included patient characteristics, medical history, vital signs, and laboratory results. Multivariable logistic regression was conducted to identify risk factors for adverse outcomes, and competing risk survival analysis for mortality.

RESULTS: Of 11 544 people tested for SARS-CoV-2, 5566 (48.2%) were positive. After exclusions, 5279 were included. 2741 of these 5279 (51.9%) were admitted to hospital, of whom 1904 (69.5%) were discharged alive without hospice care and 665 (24.3%) were discharged to hospice care or died. Of 647 (23.6%) patients requiring mechanical ventilation, 391 (60.4%) died and 170 (26.2%) were extubated or discharged. The strongest risk for hospital admission was associated with age, with an odds ratio of >2 for all age groups older than 44 years and 37.9 (95% confidence interval 26.1 to 56.0) for ages 75 years and older. Other risks were heart failure (4.4, 2.6 to 8.0), male sex (2.8, 2.4 to 3.2), chronic kidney disease (2.6, 1.9 to 3.6), and any increase in body mass index (BMI) (eg, for BMI >40: 2.5, 1.8 to 3.4). The strongest risks for critical illness besides age were associated with heart failure (1.9, 1.4 to 2.5), BMI >40 (1.5, 1.0 to 2.2), and male sex (1.5, 1.3 to 1.8). Admission oxygen saturation of <88% (3.7, 2.8 to 4.8), troponin level >1 (4.8, 2.1 to 10.9), C reactive protein level >200 (5.1, 2.8 to 9.2), and D-dimer level >2500 (3.9, 2.6 to 6.0) were, however, more strongly associated with critical illness than age or comorbidities. Risk of critical illness decreased significantly over the study period. Similar associations were found for mortality alone.

CONCLUSIONS: Age and comorbidities were found to be strong predictors of hospital admission and to a lesser extent of critical illness and mortality in people with covid-19; however, impairment of oxygen on admission and markers of inflammation were most strongly associated with critical illness and mortality. Outcomes seem to be improving over time, potentially suggesting improvements in care.

FIGURES

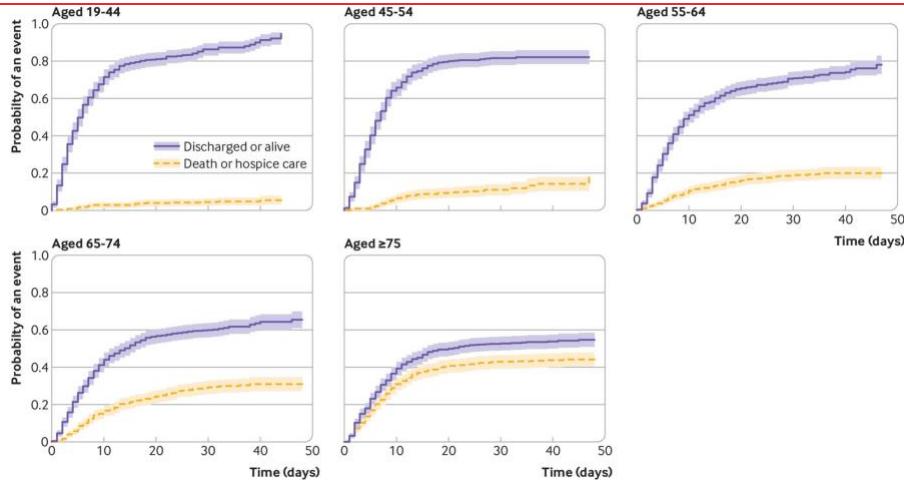


Fig 2: Cumulative incidence function for discharge alive or death, by age group. Shading represents 95% confidence intervals

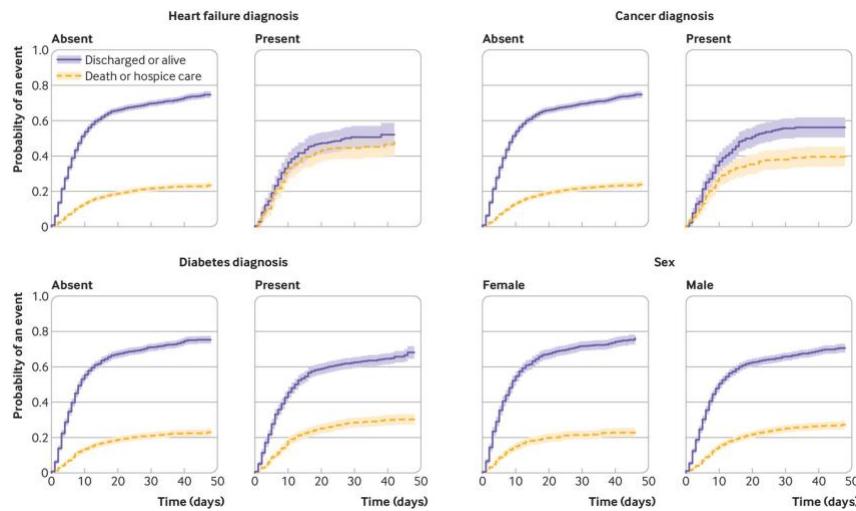


Fig 4: Cumulative incidence function for discharge alive or death, by admission oxygenation and D-dimer levels. Shading represents 95% confidence intervals

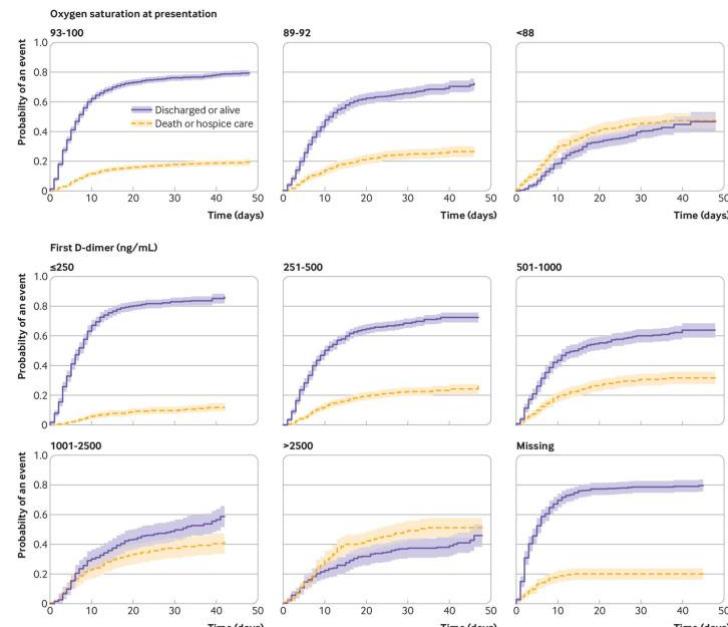


Fig 4: Cumulative incidence function for discharge alive or death, by admission oxygenation and D-dimer levels. Shading represents 95% confidence intervals

THE LANDSCAPE OF HUMAN CANCER PROTEINS TARGETED BY SARS-COV-2

Tutuncuoglu B, Cakir M, Batra J, Bouhaddou M, Eckhardt M, Gordon DE, Krogan NJ.. Cancer Discov. 2020 May 22;CD-20-0559. doi: 10.1158/2159-8290.CD-20-0559. Online ahead of print.

Level of Evidence: 5 -

BLUF

Researchers at University of California San Francisco discuss oncogenic pathways that are also targeted by SARS-CoV-2 (figure 1), suggesting that existing cancer therapeutics may be repurposed to treat COVID-19 (table 1).

ABSTRACT

Mapping SARS-CoV-2-human protein-protein interactions by Gordon et al. revealed druggable targets that are hijacked by the virus. Here, we highlight several oncogenic pathways identified at the host-virus interface of SARS-CoV-2 to enable cancer biologists apply their knowledge for rapid drug repurposing to treat COVID-19, and help inform the response to potential long-term complications of the disease.

FIGURES

Figure 1

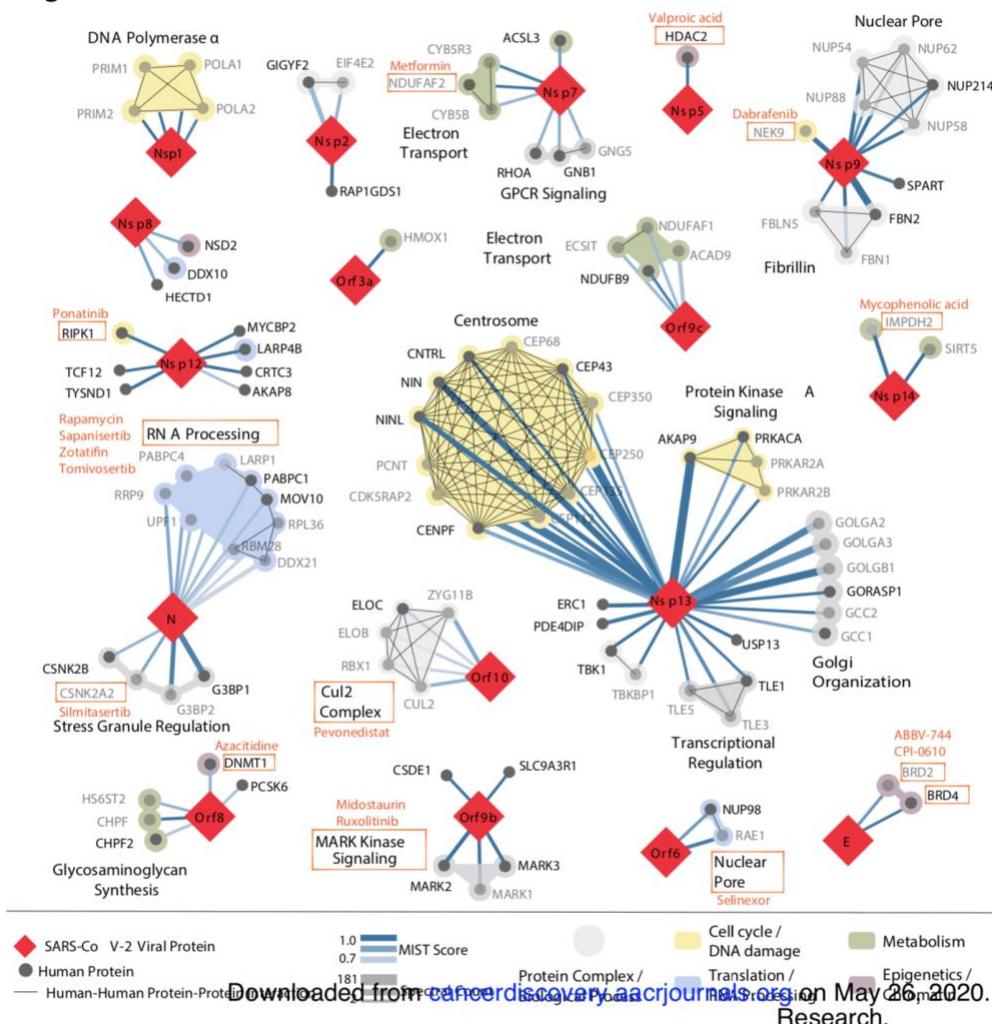


Figure 1. Cancer genes interacting with SARS-CoV-2. Known and candidate cancer genes are selected from the interactome of 26 SARS-CoV-2 proteins using Cancer Gene Census and Network of Cancer Genes databases (black), and literature review (gray). Proteins that are in the same protein complexes or processes with potential cancer genes are shaded. Currently cancer drugs that are currently used or in clinical trials Mist Score and Spectral Count of protein-protein interactions are based on the values obtained from the SARS-CoV-2-human protein-protein interaction map.

Supplementary Table 1.

Cancer drugs targeting the identified virus-host protein-protein interactions of SARS-CoV-2

Pathway	Target Gene	Drug	Status	Cancer Treatment Investigation	Effect on <i>in vitro</i> Viral Infection
Cell cycle / DNA damage	NEK9	Dabrafenib	Approved	BRAF-mutation related tumors	N/A
	RIPK1	Ponatinib	Approved	leukemia, lung	Neutral
	RIPK1	Pazopanib	Approved	solid tumors	Neutral
Metabolism	IMPDH2	Mycophenolic acid	Approved	leukemia	Neutral
	NDUFAF2	Metformin	Approved	oral, breast, prostate, colorectal, liver	Inhibitory
Epigenetics / Chromatin	HDAC2	Valproic acid	Approved	glioblastoma	Neutral
	DNMT1	Azacitidine	Approved	leukemia	N/A
	BRD2/4	ABBV-744	Clinical trials	leukemia	Neutral
	BRD2/4	CPI-0610	Clinical trials	solid tumors, leukemia	Neutral
Translation / RNA processing	mTOR	Rapamycin	Approved	solid tumors	Neutral
	mTOR	Sapanisertib	Clinical trials	solid tumors	Neutral
	eIF4A	Zotarifin	Clinical trials	solid tumors	Inhibitory
	MNK1/2	Tomivosertib	Clinical trials	breast, prostate, lymphoma	Neutral
	CRM1	Selinexor	Approved	myeloma, solid tumors	N/A
MARK-kinases	MARK2	Midostaurin	Approved	leukemia	Activating
	MARK2/3	Ruxolitinib	Approved	pancreatic, blood	Activating
Membrane transport	ABCC1	Daunorubicin	Approved	leukemia	Activating
	ABCC1	Verapamil	Approved	lung, colorectal, gastric, kidney	Neutral
Stress response	HSP90	Onalespib	Clinical trials	solid tumors	Inhibitory
Cul2 complex	NAE	Pevonedistat	Clinical trials	solid tumors, leukemia	N/A
Stress granule regulation	CSNKA2	Silmitasertib	Approved	medulloblastoma	Neutral
Autophagy	SIGMAR1	Hydroxychloroquine	Approved	solid tumors	Inhibitory
Replication	-	Brivudine	Clinical trials	colorectal	Activating

EFFECT OF ENVIRONMENTAL CONDITIONS ON SARS-COV-2 STABILITY IN HUMAN NASAL MUCUS AND SPUTUM

Matson MJ, Yinda CK, Seifert SN, Bushmaker T, Fischer RJ, van Doremalen N, Lloyd-Smith JO, Munster VJ.. Emerg Infect Dis. 2020 Jun 8;26(9). doi: 10.3201/eid2609.202267. Online ahead of print.

Level of Evidence: 5 - Mechanism-based reasoning

BLUF

In this study, authors analyzed human nasal mucus and sputum mixed with SARS-CoV-2 under three different environmental conditions in order to determine surface stability of the virus: 4 degrees C with 40% relative humidity, 21 degrees C with 40% relative humidity, and 27 degrees C with 85% relative humidity. The viral half-life (Table 1) and viral load (Figure 1) of SARS-CoV-2 were measured using reverse transcription polymerase chain reaction (RT-PCR) at each environmental condition for liquid nasal mucus, surface nasal mucus, liquid sputum, and surface sputum. They concluded the half-life and viral load of SARS-CoV-2 in both surface nasal mucus and surface sputum were decreased under conditions with warmer temperature and higher humidity, suggesting possible seasonal drive for future outbreaks peaking during cold and dry periods.

ABSTRACT

We found that environmental conditions affect the stability of severe acute respiratory syndrome coronavirus 2 in nasal mucus and sputum. The virus is more stable at low-temperature and low-humidity conditions, whereas warmer temperature and higher humidity shortened half-life. Although infectious virus was undetectable after 48 hours, viral RNA remained detectable for 7 days.

FIGURES

Figure

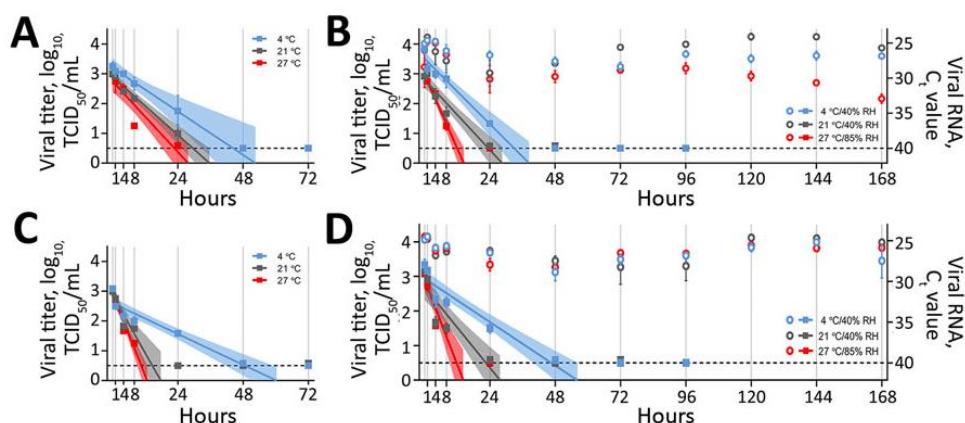


Figure Stability of severe acute respiratory syndrome coronavirus 2 over time in human nasal mucus and sputum under different environmental conditions: liquid nasal mucus (A), surface nasal mucus (B), liquid sputum (C), and surface sputum (D). For panels B and D, the squares correspond to viral titer on the left y-axis, and the circles correspond to viral RNA (C_t value) on the right y-axis. We collected samples in 1 mL media for each condition at 0, 1, 4, 8, and 24 hours, then daily for 7 days and performed end-point titrations in quadruplicate on Vero E6 cells and made calculations using the Spearman-Kärber method. We \log_{10} -transformed and fit titers with linear regression models, including 95% CIs (shaded area around lines of best fit), by using GraphPad Prism 8 (<https://www.graphpad.com>). We extracted aliquots of collected surface samples by using the QIAamp Viral RNA Mini Kit (QIAGEN, <https://www.qiagen.com>) and analyzed them for the presence of viral RNA by using quantitative reverse transcription PCR targeting the E gene. For both viral titers and C_t values, plots show means of 3 replicates with SE. The limit of detection for each experimental condition was $10^{3.5}$ TCID₅₀/mL for viral titer and 40 for C_t value and is indicated by the dashed line. Relative humidity is not applicable to liquid samples (panels A and C), which were in sealed tubes. C_t , cycle threshold; RH, relative humidity; TCID₅₀/mL, 50% tissue culture infective dose/mL.

Table

Half-life ($t_{1/2}$) for SARS-CoV-2 in human nasal mucus and sputum under different environmental conditions*

Sample and exposure type	Environment	Half-life, h (95% CI)
Nasal mucus		
Liquid	4°C	4.9 (3.5–8.7)
	21°C	3.7 (3.1–4.7)
	27°C	3.1 (2.3–4.4)
Surface	4°C/40% RH	3.3 (2.6–4.4)
	21°C/40% RH	3.1 (2.5–4.1)
	27°C/85% RH	1.5 (1.2–1.9)
Sputum		
Liquid	4°C	7.0 (5.8–8.9)
	21°C	1.9 (1.3–3.2)
	27°C	1.3 (1.1–1.7)
Surface	4°C/40% RH	5.8 (4.8–7.3)
	21°C/40% RH	3.1 (2.3–4.6)
	27°C/85% RH	1.5 (1.1–2.4)

*RH, relative humidity; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

FACIAL PROTECTION IN THE ERA OF COVID-19: A NARRATIVE REVIEW

Li DTS, Samaranayake LP, Leung YY, Neelakantan P.. Oral Dis. 2020 Jun 7. doi: 10.1111/odi.13460. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

Physicians in Hong Kong review literature on the efficacy of facial PPE (Table 1), methods of disinfection and reusability, and impacts on skin health (summarized below). While little conclusive evidence is available pertaining to SARS-CoV-2, the authors suggest that mask-wearing is likely to reduce transmission, and current best practices for disinfection should use moist heat instead of chemicals.

SUMMARY

The authors' findings and recommendations included:

1. Respirator masks (N95/FFP2), while 95% efficient in filtering particles of 0.3 microns, are single use only. The tight fit and high filtering efficiency might induce shortness of breath and discomfort, and are thus recommended for healthcare providers only.
2. Surgical masks, classified by levels/types 1–3 corresponding to increasing filtration capacity, are looser fitting and not recommended for particulate filtration. Nonetheless, use is routine in healthcare settings, with type 3 filtration efficiency at 98% for particles greater than 0.3 microns.
3. In Hong Kong Special Administrative Region (HKSAR), a 96.6% compliance rate of mask-wearing correlated with a decreased SARS-CoV-2 transmission rate when compared to other cities in China over the study period.
4. Single use and cloth masks are not generally regarded as efficient filters of particulate matter; nonetheless, they are recommended in community settings.
5. Disinfection with heat in moist conditions reduced numbers of M2 bacteriophage and Methicillin Resistant Staph Aureus (MRSA) on deconstructed masks in test conditions without compromising the integrity of the filter; radiation and chemical means damaged filters and/or left potentially toxic residue.
6. Reusability has been poorly characterized for most masks, though N95 masks might be suitable for reuse up to 60 washes.
7. Face shields are still recommended for aerosol-generating procedures.

8. Powered air-purifying respirators (PAPR) are highly efficient filters, though the associated high cost and required training for proper use limit their use to healthcare settings when fit tests for other masks are failed.
9. The bridge of the nose is a particular area of damage with prolonged use of tight-fitting masks. Masks may also cause allergic reactions with prolonged use.

ABSTRACT

We live in extraordinary times, where COVID-19 pandemic has brought the whole world to a screeching halt. Tensions and contradictions that surround the pandemic ridden world include the availability, and the lack thereof, various facial protection measures to mitigate the viral spread. Here, we comprehensively explore the different type of facial protection measures, including masks, needed both for the public and the health care workers (HCW). We discuss the anatomy, the critical issues of disinfection and reusability of masks, the alternative equipment available for the protection of the facial region from airborne diseases, such as face shields and powered air purifying respirators (PAPR), and the skin-health impact of prolonged wearing of facial protection by HCW. Clearly, facial protection, either in the form of masks or alternates, appears to have mitigated the pandemic as seen from the minimal COVID-19 spread in countries where public mask wearing is strictly enforced. On the contrary, the healthcare systems, that appear to have been unprepared for emergencies of this nature, should be appropriately geared to handle the imbalance of supply and demand of personal protective equipment including face masks. These are two crucial lessons we can learn from this tragic experience.

FIGURES

	N95 respirator	Surgical mask	Cloth mask	PAPR
Required in Healthcare settings	✓	✓		✓
Recommended for community use by the CDC			✓	
Regulated by the NIOSH	✓			
Regulated by the ASTM		✓		
Requires fit testing	✓			
Loose fitting		✓	✓	✓
Custom fit (ideally)	✓			
Filters aerosols (particles <10μM)*	✓			✓
Filters droplets (particles <10um)*	✓	✓	✓	✓

Table 1. Advantages and disadvantages of currently used facial protection measures. CDC: U.S. Centres for Disease Control and Prevention; NIOSH: the National Institute for Occupational Safety and Health; ASTM: ASTM International-previously known as American Society for Testing and Materials; PAPR: Powered air purifying respirator; *(Samaranayake, 2018; dataform various sources).

PREVENTION IN THE COMMUNITY

UNIVERSAL AND SERIAL LABORATORY TESTING FOR SARS-COV-2 AT A LONG-TERM CARE SKILLED NURSING FACILITY FOR VETERANS - LOS ANGELES, CALIFORNIA, 2020

Dora AV, Winnett A, Jatt LP, Davar K, Watanabe M, Sohn L, Kern HS, Gruber CJ, Goetz MB.. MMWR Morb Mortal Wkly Rep. 2020 May 29;69(21):651-655. doi: 10.15585/mmwr.mm6921e1.

Level of Evidence: 4 - Case-series, case-control studies, or historically controlled studies

BLUF

A case series from a skilled nursing facility (SNF) in Los Angeles, California demonstrated a successful method that prevented further outbreak of COVID-19 during 3/29/20-4/23/20 after two residents tested positive for SARS-CoV-2 (Figure 1). The approach includes screening all residents (n=99) and staff members (n=136) with RT-PCR, serial testing for positive SARS-CoV-2 residents and cohort isolation for those who tested positive (see details below). The authors recommends all SNFs to adopt this approach to mitigate the transmission of SARS-CoV-2.

Positive COVID-19 cases:

- 8/136 presymptomatic staff members.
- 19/99 residents with majority being asymptomatic (Table).

RT-PCR Testing:

- Repeat serial RT-PCR testing weekly until all residents had negative results.
- Staff members did not receive serial testing due to limited supplies.

Cohorting:

- Isolation of residents and staff with COVID-19 into three cohorts (A, B, and C) based on shifts and exposure.
- Outbreaks decreased in Cohort A by 1 week, Cohort C by 2 weeks and no cases occurred in Cohort B.

SUMMARY

After the first two COVID-19 cases were identified there were no further cases. The authors attribute this success to a two-pronged approach. total positive COVID-19 cases included 8/136 presymptomatic staff members and 19/99 residents with majority being asymptomatic (Table). The authors believe the below two-pronged approach contributed to a relatively low number of total cases after the initial outbreak.

1. RT-PCR testing:

- All residents and staff members were tested after the identification of COVID-19 in two patients.
- The initial round of testing identified 27 additional cases {8/136 presymptomatic staff members and 19/99 residents with majority being asymptomatic (Table)}.
- Repeat serial RT-PCR testing weekly until all residents had negative results.
- Staff members did not receive serial testing due to limited supplies.

2. Cohorting:

- Isolation of residents and staff with COVID-19 into three cohorts (A, B, and C) based on shifts and exposure.
- Outbreaks decreased in Cohort A by 1 week, Cohort C by 2 weeks, and no cases occurred in Cohort B. Suppression of outbreaks was determined by a reduction in the number of new cases in each cohort.

ABSTRACT

On March 28, 2020, two residents of a long-term care skilled nursing facility (SNF) at the Veterans Affairs Greater Los Angeles Healthcare System (VAGLAHS) had positive test results for SARS-CoV-2, the cause of coronavirus disease 2019 (COVID-19), by reverse transcription-polymerase chain reaction (RT-PCR) testing of nasopharyngeal specimens collected on March 26 and March 27. During March 29-April 23, all SNF residents, regardless of symptoms, underwent serial (approximately weekly) nasopharyngeal SARS-CoV-2 RT-PCR testing, and positive results were communicated to the county health department. All SNF clinical and nonclinical staff members were also screened for SARS-CoV-2 by RT-PCR during March 29-April 10. Nineteen of 99 (19%) residents and eight of 136 (6%) staff members had positive test results for SARS-CoV-2 during March 28-April 10; no further resident cases were identified on subsequent testing on April 13, April 22, and April 23. Fourteen of the 19 residents with COVID-19 were asymptomatic at the time of testing. Among these residents, eight developed symptoms 1-5 days after specimen collection and were later classified as presymptomatic; one of these patients died. This report describes an outbreak of COVID-19 in an SNF, with case identification accomplished by implementing several rounds of RT-PCR testing, permitting rapid isolation of both symptomatic and asymptomatic residents with COVID-19. The outbreak was successfully contained following implementation of this strategy.

FIGURES



Figure 1: An approach that stopped a COVID-19 outbreak in a skilled nursing facility (SNF)

Characteristic	Asymptomatic* (n = 6)	Presymptomatic* (n = 8)	Symptomatic* (n = 5)	No. (%)
				All (N = 19)
Demographic				
Age, yrs, median (IQR)	75 (72–75)	67 (66–84.5)	84 (70–85)	75 (66–85)
Male sex	6 (100)	8 (100)	5 (100)	19 (100)
Race/Ethnicity†				
Asian	—	—	—	—
Black or African American	2 (33)	4 (50)	2 (40)	8 (42)
Native Hawaiian or Pacific Islander	—	1 (13)	—	1 (5)
White	3 (50)	3 (38)	2 (40)	8 (42)
Unknown	1 (17)	—	1 (20)	2 (11)
Hispanic	—	—	—	—
Underlying medical condition§				
Hypertension	5 (83)	5 (63)	3 (60)	13 (68)
Cardiovascular disease	3 (50)	4 (50)	5 (100)	12 (63)
Diabetes	4 (67)	5 (63)	2 (40)	11 (58)
Body mass index >30 kg/m ²	3 (50)	2 (25)	2 (40)	7 (37)
Chronic kidney disease (stage 4 or above)	—	2 (25)	1 (20)	3 (16)
Chronic obstructive pulmonary disease	1 (17)	1 (13)	2 (40)	4 (21)
Symptoms at time of or after testing¶				
Constitutional symptom	—	6 (75)	5 (100)	11 (58)
Fever	—	6 (75)	5 (100)	11 (58)
Myalgia	—	—	1 (20)	1 (5)
Headache	—	1 (13)	1 (20)	2 (11)
Respiratory symptom	—	4 (38)	5 (100)	9 (47)
Cough	—	2 (25)	5 (100)	7 (37)
Dyspnea	—	2 (25)	1 (20)	3 (16)
Gastrointestinal symptom	—	5 (63)	1 (20)	6 (32)
Nausea	—	1 (13)	—	1 (5)
Emesis	—	1 (13)	—	1 (5)
Diarrhea	—	2 (25)	—	2 (11)
Poor appetite	—	3 (38)	1 (20)	4 (21)
Laboratory findings on admission,**,†† median (IQR) [No.]				
WBC ($\times 1,000/\mu\text{L}$)	4.32 (3.67–5.91) [5]	4.35 (3.93–6.10) [8]	6.24 (6.09–7.08) [5]	5.32 (3.94–6.20) [18]
Lymphocytes (%)	31.5 (26.4–32.7) [5]	22.0 (17.5–25.9) [8]	16.7 (11.4–16.9) [5]	22.0 (17.0–30.3) [18]
Lymphocytes ($\times 1,000/\mu\text{L}$)	1,200 (1,140–1,200) [5]	960 (775–1,105) [8]	880 (770–1,200) [5]	1,025 (835–1,200) [18]
Creatinine (mg/dL)	1.00 (0.89–1.05) [4]	1.01 (0.82–1.07) [8]	2.84 (1.99–3.23) [5]	1.04 (0.88–1.41) [17]
AST (U/L)	19 (17–21) [3]	24 (20–29) [5]	31 (NA) [1]	22 (19–29) [9]
ALT (U/L)	16 (13–21) [4]	17 (14–44) [6]	28 (21–28) [3]	16 (14–28) [13]
D-Dimer ($\mu\text{g/mL}$ FEU)	0.54 (0.42–0.83) [4]	0.66 (0.55–1.42) [7]	0.94 (0.59–1.17) [3]	0.63 (0.50–1.29) [14]
Ferritin (ng/mL)	60.8 (51.2–99.7) [5]	343.0 (162.5–540.6) [8]	184.6 (NA) [2]	179.1 (59.0–354.2) [15]
CRP (mg/dL)	0.605 (0.420–1.190) [4]	1.070 (0.900–2.565) [7]	6.765 (NA) [2]	1.03 (0.71–2.63) [13]
Outcomes				
Supplemental oxygen required	—	4 (50)	4 (80)	8 (42)
Death	—	—	1 (20)	1 (5)
Length of hospital stay, days, median (IQR)	6 (1–6)	9 (7–10)	10 (5–13)	6 (5–10)

Table: Characteristics of long-term care skilled nursing facility residents with positive test results for SARS-CoV-2 (N = 19) — Veterans Affairs Greater Los Angeles Healthcare System, Los Angeles, California, 2020

COVID-19 INFECTION AT NIGHTTIME

Fujimura A, Ushijima K, Smolensky MH.. Chronobiol Int. 2020 Jun 8:1-2. doi: 10.1080/07420528.2020.1767642. Online ahead of print.

Level of Evidence: 5 - Review / Literature Review

BLUF

Chronobiology researchers present evidence suggesting nighttime exposure to SARS-CoV-2 may increase risk for severe COVID-19 disease. They cite research indicating sleep span exposure to influenza A in rodents was associated with increased mortality, likely due to suppression of the inflammatory myeloid cell response by brain and muscle ARNT-like1 (Bmal1) gene, which has increased expression during sleep span of the normal circadian rhythm. They advocate for reduced nighttime activities (e.g. bars, cinemas) in order to minimize risk of severe SARS-CoV-2 infections.

MANAGEMENT

ACUTE CARE

A NOVEL RISK SCORE TO PREDICT DIAGNOSIS WITH CORONAVIRUS DISEASE 2019 (COVID-19) IN SUSPECTED PATIENTS: A RETROSPECTIVE, MULTI-CENTER, OBSERVATIONAL STUDY

Huang D, Wang T, Chen Z, Yang H, Yao R, Liang Z.. J Med Virol. 2020 Jun 8. doi: 10.1002/jmv.26143. Online ahead of print.
Level of Evidence: 3 - Guidelines and Recommendations

BLUF

A retrospective observational study conducted in Sichuan, China, by the West China Hospital developed a novel risk score to predict diagnosis of COVID-19 ($n=475$, confirmed COVID-19 = 336). The patients were given a risk score based on independent risk factors such as epidemiological exposure history, vitals, imaging results, and laboratory testing (Table 3) and a score of 20 was determined to help predict the diagnosis of COVID-19 (specificity: 0.866, sensitivity: 0.813) (AUC 0.921; 95% CI: 0.896-0.945, p less than 0.01)(Figure 1). The authors believe this novel approach will assist with early management and be a suitable supplement to RT-PCR screening.

SUMMARY

The independent risk factors and point values included in this risk score included:

- Epidemiological exposure histories (OR:13.32, 95%CI 6.39-27.75) -13 points
- Weakness/fatigue (OR:4.51, 95%CI 1.70-11.96) - 5 points
- Heart rate <100 beat/min (OR:3.80, 95%CI 2.00-7.22) - 4 points
- Bilateral pneumonia (OR:3.60, 95%CI 1.83-7.10) -4 points
- Neutrophil count $\leq 6.3 \times 10^9 /L$ (OR: 6.77, 95%CI 2.52-18.19) - 7 points
- Eosinophil count $\leq 0.02 \times 10^9 /L$ (OR:3.14, 95%CI 1.58-6.22) - 3 points
- Glucose ≥ 6 mmol/L (OR:2.43, 95%CI 1.04-5.66) - 2 points
- D-dimer ≥ 0.5 mg/L (OR:3.49, 95%CI 1.22-9.96) - 3 points
- C- reactive protein < 5 mg/L (OR:3.83, 95%CI 1.86-7.92) - 4 points

Authors determined that a score of 20 was the cutoff to predict COVID-19 (specificity: 0.866, sensitivity: 0.813). This gives a clinical method for diagnosis of COVID-19 (see table 4 for performance of risk scores)

ABSTRACT

BACKGROUND: The aim of the study was to explore a novel risk score to predict diagnosis with COVID-19 among all suspected patients at admission.

METHODS: This was a retrospective, multi-center, observational study. The clinical data of all suspected patients were analyzed. Independent risk factors were identified via multivariate logistic regression analysis.

RESULTS: Finally, 336 confirmed COVID-19 patients and 139 control patients were included. We found nine independent risk factors for diagnosis with COVID-19 at admission to hospital: epidemiological exposure histories (OR:13.32, 95%CI 6.39-27.75), weakness/fatigue (OR:4.51, 95%CI 1.70-11.96), heart rate <100 beat/min (OR:3.80, 95%CI 2.00-7.22), bilateral pneumonia (OR:3.60, 95%CI 1.83-7.10), neutrophil count $\leq 6.3 \times 10^9 /L$ (OR: 6.77, 95%CI 2.52-18.19), eosinophil count $\leq 0.02 \times 10^9 /L$ (OR:3.14, 95%CI 1.58-6.22), glucose ≥ 6 mmol/L (OR:2.43, 95%CI 1.04-5.66), D-dimer ≥ 0.5 mg/L (OR:3.49, 95%CI 1.22-9.96), and C-reactive protein < 5 mg/L (OR:3.83, 95%CI 1.86-7.92). As for the performance of this risk score, a cut-off value of 20 (specificity: 0.866, sensitivity: 0.813) was identified to predict COVID-19 according to ROC curve and the area under the curve (AUC) was 0.921 (95%CI: 0.896-0.945, p <0.01).

CONCLUSIONS: We designed a novel risk score which might have a promising predictive capacity for diagnosis with COVID-19 among suspected patients.

FIGURES

Independent Risk factors	Score
Epidemiological exposure histories	13
Neutrophil count, $\times 10^9/\text{L}$ (≤ 6.3)	7
Weakness/Fatigue	5
Bilateral pneumonia	4
Heart rate (beat/min) (<100)	4
C-reactive protein, mg/L (<5)	4
Eosinophil count, $\times 10^9/\text{L}$ (≤ 0.02)	3
D-dimer, mg/L (≥ 0.5)	3
Glucose, mmol/L (≥ 6)	2

Table 3: The risk score for diagnosis with COVID-19 among suspected patients.

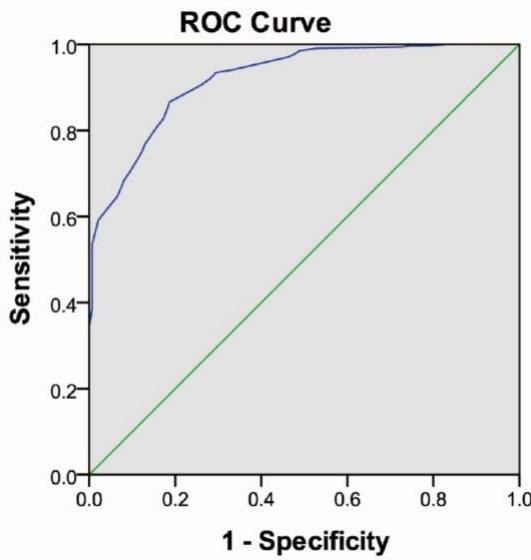


Table 3: The risk score for diagnosis with COVID-19 among suspected patients.

DIAGNOSTIC RADIOLOGY

CHEST IMAGING IN PATIENTS WITH SUSPECTED COVID-19

Adams SJ, Dennie C.. CMAJ. 2020 May 22:cmaj.200626. doi: 10.1503/cmaj.200626. Online ahead of print.
Level of Evidence: Other -

BLUF

The authors from the Universities of Saskatchewan and Ottawa summarize practice recommendations and argue that chest imaging (radiograph and CT imaging) has poor sensitivity and specificity for diagnosing mild to moderate COVID19, but can be helpful in determining potential complications that would affect clinical decisions in patient care. Specific conclusions include:

- Recommend against repeat imaging (unless there is a change in a patient's clinical status).
- Radiography: between 25%-69% sensitivity, limited data on specificity CT: 44-98% sensitivity and 25-53% specificity

CRITICAL CARE

STANDARDS AND STEREOTYPES IN COVID-19

Epelbaum O.. Am J Respir Crit Care Med. 2020 Jun 8. doi: 10.1164/rccm.202005-1592LE. Online ahead of print.

Level of Evidence: Other - Expert Opinion

BLUF

This letter to the editor critiques a study by Ziehr et al. (2020); with the reporting of a surprisingly low mortality rate in 66 mechanically ventilated COVID-19 patients, Ziehr et al. advocate for the use of standard established acute respiratory distress syndrome (ARDS) therapies in COVID-19 patients. The author of this letter points out several skeptical features of this study, including the significant increase in statin usage among study participants, relatively low percentage of prone positioning intervention, and the uncharacteristically high tracheostomy (n=14/66, 21.2%) and intensive care unit (ICU) discharge rates (n=50/66, 75.8%) when compared to previous studies of ARDS patients. These findings caution against claiming that COVID-19 disease follows the ARDS pattern, and the author shares their belief that ICU outcomes may be more bleak than the optimistic results reported in the study by Ziehr et al. (2020).

MANAGEMENT OF A PATIENT PRESENTING WITH ANTERIOR STEMI WITH CONCOMITANT COVID-19 INFECTION EARLY IN THE COURSE OF THE U.S. PANDEMIC

Rothstein ES, Welch TD, Andrus BW, Jayne JE.. Catheter Cardiovasc Interv. 2020 May 29. doi: 10.1002/ccd.28967. Online ahead of print.

Level of Evidence: Other - Case Report

BLUF

The Dartmouth-Hitchcock Medical Center presents a case of a 79 year-old-female with an acute anterior ST elevation myocardial infarction (STEMI) and COVID-19 who received percutaneous coronary treatment but eventually died from multi-organ failure. The authors speculate that inflammation and the cytokine storm from COVID-19 potentially contributed to coagulopathy or coronary artery plaque rupture that resulted in downstream coronary vessel occlusion. Further research in this area is needed to understand the relationship between the inflammatory properties of COVID-19 and acute coronary syndrome (ACS) to further optimize management protocols for ACS in COVID-19 infection.

SUMMARY

A 79-year-old female with past medical history significant for dyslipidemia and diabetes mellitus presented in early March, 2020 with substernal chest pressure and fever to her local critical access hospital in New Hampshire, USA. Her ECG revealed anterior STEMI, and the ensuing coronary angiography (Figure 3) revealed 100% obstruction in the mid left anterior descending artery (LAD) and 80% obstruction in the left circumflex artery (LCX). After percutaneous coronary intervention (PCI) was performed on the LCX lesion, the patient remained hemodynamically stable and was transferred to the cardiac critical care unit where transthoracic echocardiogram (LV ejection fraction 38%) and labs (Table 1) were performed. The first three days following admission, the patient began to have intermittent fevers, which were initially thought to be from an inflammatory post-myocardial infarction syndrome. On day 3, she developed a cough and chest X-ray revealed patchy airspace opacities in the left lung, suggesting pneumonia (Figure 6). She began having myalgias and hypoxemia (O₂ sat. 72%) on day 4 and 5, requiring nasal cannula oxygen delivery. Progressive hypotension during day 5 led to IV fluid administration, discontinuation of ACE inhibitor and beta-blocker agents, and eventual use of low-dose phenylephrine. Worsening hypoxemia led to intubation and mechanical ventilation following the acute respiratory distress (ARDS) protocol. COVID-19 infection was confirmed in the evening of day 5, and hydroxychloroquine therapy was subsequently initiated. On Day 6, she developed distributive shock and renal failure and was treated with high dose norepinephrine, vasopressin, and empiric antibiotics. As her renal failure progressed, the decision was made to focus on comfort measures, and she eventually expired.

ABSTRACT

The coronavirus disease-2019 (COVID-19) is a viral illness with heterogenous clinical manifestations, ranging from mild symptoms to severe acute respiratory distress syndrome and shock caused by the severe acute respiratory syndrome coronavirus-2. The global healthcare community is rapidly learning more about the effects of COVID-19 on the cardiovascular

system, as well as the strategies for management of infected patients with cardiovascular disease. There is minimal literature available surrounding the relationship between COVID-19 infection and acute coronary syndrome. We describe the case of a woman who presented with an acute anterior ST-elevation myocardial infarction managed by primary percutaneous coronary intervention, who subsequently developed severe COVID-19 infection and ultimately succumbed to multisystem organ failure.

FIGURES

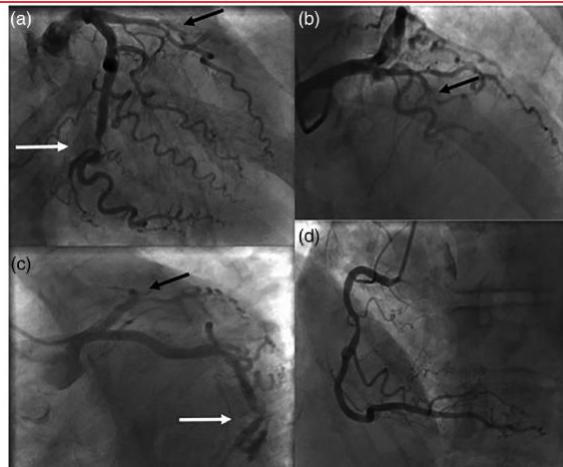


Figure 3. Initial angiography from multiple projections of the left coronary system (a-c) revealing the culprit 100% occlusion of the mid left anterior descending artery (black arrows), severe obstructive atherosclerotic disease of the mid left circumflex artery (white arrows), and mild diffuse atherosclerotic disease of the entire right coronary artery (d)

Admission laboratory values		
	Value	Normal ranges
White blood cells	9.2 ($\times 10^3/\text{mcl}$)	
Hemoglobin	12.9 (gm/dl)	
Platelets	213 ($\times 10^3/\text{mcl}$)	
Lymphocytes	0.7 ($\times 10^3/\text{mcl}$)	0.9–3.2 ($\times 10^3/\text{mcl}$)
Sodium	134 (mmol/L)	135–145 (mmol/L)
Potassium	4.3 (mmol/L)	
Creatinine	0.76 (mg/dl)	
Troponin-T	3.6 (ng/ml)	< 0.01 (ng/ml)
CK	2,540 (unit/L)	0–160 (unit/L)
AST	290 (unit/L)	0–30 (unit/L)
ALT	67 (unit/L)	0–30 (unit/L)

Note: Abnormal values are in bold.

Table 1. Admission laboratory values

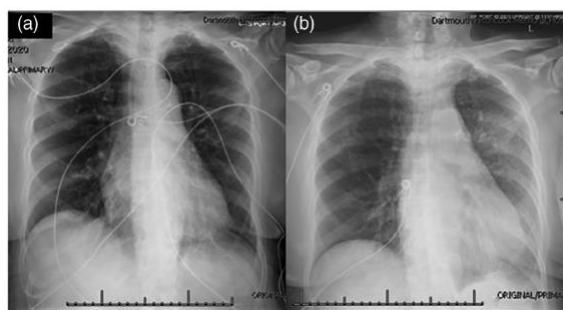


Table 1. Admission laboratory values

NEUROLOGY

CLINICAL CHARACTERISTICS AND OUTCOMES OF INPATIENTS WITH NEUROLOGIC DISEASE AND COVID-19 IN BRESCIA, LOMBARDY, ITALY

Benussi A, Pilotto A, Premi E, Libri I, Giunta M, Agosti C, Alberici A, Baldelli E, Benini M, Bonacina S, Brambilla L, Caratozzolo S, Cortinovis M, Costa A, Piccinelli SC, Cottini E, Cristillo V, Delrio I, Filosto M, Gamba M, Gazzina S, Gilberti N, Gipponi S, Imarisio A, Invernizzi P, Leggio U, Leonardi M, Liberini P, Locatelli M, Masciocchi S, Poli L, Rao R, Risi B, Rozzini L, Scalvini A, Schiano di Cola F, Spezi R, Vergani V, Volonghi I, Zoppi N, Borroni B, Magoni M, Pezzini A, Padovani A.. Neurology. 2020 May 22:10.1212/WNL.0000000000009848. doi: 10.1212/WNL.0000000000009848. Online ahead of print.

Level of Evidence: Other

BLUF

A retrospective cohort study conducted at a hospital in Brescia, Italy from February 21 to April 5, 2020 found that among 173 patients admitted to the general or vascular neurology unit with neurological diseases, those who had COVID-19 (n=56) diagnosed by RT-PCR were more likely to be older, have higher quick Sequential Organ Failure (qSOFA) score on admission, and more likely to be admitted with cerebrovascular disease (vs other neurological disease) compared to non-COVID-19 patients. They found that COVID-19 patients admitted with neurological disease had higher overall in hospital mortality than patients without COVID-19 admitted with neurological diseases. They recommend qSOFA exam as a quick risk stratification assessment tool on admission.

ABSTRACT

OBJECTIVE: To report clinical and laboratory characteristics, as well as treatment and clinical outcomes of patients admitted for neurologic diseases with and without COVID-19.

METHODS: In this retrospective, single center cohort study, we included all adult inpatients with confirmed COVID-19, admitted to a Neuro-COVID Unit from February 21, 2020, who had been discharged or died by April 5, 2020. Demographic, clinical, treatment, and laboratory data were extracted from medical records and compared (FDR-corrected) to those of neurologic patients without COVID-19 admitted in the same period.

RESULTS: One hundred seventy-three patients were included in this study, of whom 56 were positive for COVID-19 while 117 were negative for COVID-19. Patients with COVID-19 were older (77.0, IQR 67.0-83.8 vs 70.1, IQR 52.9-78.6, p = 0.006), had a different distribution regarding admission diagnoses, including cerebrovascular disorders (n = 43, 76.8% vs n = 68, 58.1%), and had a higher quick Sequential Organ Failure Assessment (qSOFA) score on admission (0.5, IQR 0.4-0.6 vs 0.9, IQR 0.7-1.1, p = 0.006). In-hospital mortality rates (n = 21, 37.5% vs n = 5, 4.3%, p < 0.001) and incident delirium (n = 15, 26.8% vs n = 9, 7.7%, p = 0.003) were significantly higher in the COVID-19 group. COVID-19 and non-COVID patients with stroke had similar baseline characteristics but patients with COVID-19 had higher modified Rankin scale scores at discharge (5.0, IQR 2.0-6.0 vs 2.0, IQR 1.0-3.0, p < 0.001), with a significantly lower number of patients with a good outcome (n = 11, 25.6% vs n = 48, 70.6%, p < 0.001). In patients with COVID-19, multivariable regressions showed increasing odds of in-hospital death associated with higher qSOFA scores (OR 4.47, 95% CI 1.21-16.5; p = 0.025), lower platelet count (0.98, 0.97-0.99; p = 0.005) and higher lactate dehydrogenase (1.01, 1.00-1.03; p = 0.009) on admission.

CONCLUSIONS: COVID-19 patients admitted with neurologic disease, including stroke, have a significantly higher in-hospital mortality, incident delirium and higher disability than patients without COVID-19.

MEDICAL SUBSPECIALTIES

NEPHROLOGY

CLINICAL FEATURES OF MAINTENANCE HEMODIALYSIS PATIENTS WITH 2019 NOVEL CORONAVIRUS-INFECTED PNEUMONIA IN WUHAN, CHINA

Wu J, Li J, Zhu G, Zhang Y, Bi Z, Yu Y, Huang B, Fu S, Tan Y, Sun J, Li X.. Clin J Am Soc Nephrol. 2020 May 22:CJN.04160320. doi: 10.2215/CJN.04160320. Online ahead of print.

Level of Evidence: 4

BLUF

This retrospective case-control study of 101 patients hospitalized with COVID-19 in Wuhan, China between January 30 and March 10, 2020 found that patients on maintenance hemodialysis were more likely to present with less severe symptoms such as fatigue and anorexia, lymphopenia, and prominent chest CT manifestations compared to controls without chronic kidney disease. Conversely, hemodialysis patients with COVID-19 were more likely to develop complications such as shock, acute respiratory distress syndrome, arrhythmia, and acute cardiac injury and had poorer clinical outcomes than controls (see Table 2). The authors emphasized the need for early diagnosis, isolation, and treatment of hemodialysis patients who may present atypically.

ABSTRACT

BACKGROUND AND OBJECTIVES: Previous reports on the outbreak of coronavirus disease 2019 were on the basis of data from the general population. Our study aimed to investigate the clinical features of patients on maintenance hemodialysis.

DESIGN, SETTING, PARTICIPANTS, & MEASUREMENTS: In this retrospective, single-center study, we included 49 hospitalized patients on maintenance hemodialysis and 52 hospitalized patients without kidney failure (controls) with confirmed coronavirus disease 2019 at Tongren Hospital of Wuhan University from January 30, 2020 to March 10, 2020. Demographic, clinical, laboratory, and radiologic characteristics and treatment and outcomes data were analyzed. The final date of follow-up was March 19, 2020.

RESULTS: The median age of 101 patients was 62 years (interquartile range, 49-72). All patients were local residents of Wuhan. In terms of common symptoms, there were differences between patients on hemodialysis and controls (fatigue [59% versus 83%], dry cough [49% versus 71%], and fever [47% versus 90%]). Lymphocyte counts were decreased ($0.8 \times 10^9/L$ [patients on hemodialysis] versus $0.9 \times 10^9/L$ [controls], $P=0.02$). Comparing patients on hemodialysis with controls, creatine kinase-muscle and brain type, myoglobin, hypersensitive troponin I, B-type natriuretic peptide, and procalcitonin were increased, and the percentage of abnormalities in bilateral lung was higher in computed tomographic scan (82% versus 69%, $P=0.15$) and unilateral lung was lower (10% versus 27%, $P=0.03$). Common complications including shock, acute respiratory distress syndrome, arrhythmia, and acute cardiac injury in patients on hemodialysis were significantly higher. Compared with controls, more patients on hemodialysis received noninvasive ventilation (25% versus 6%, $P=0.008$). As of March 19, 2020, three patients on hemodialysis (6%) were transferred to the intensive care unit and received invasive ventilation. Seven patients on hemodialysis (14%) had died.

CONCLUSIONS: The main symptoms of coronavirus disease 2019 pneumonia, including fever and cough, were less common in patients on hemodialysis. Patients on hemodialysis with coronavirus disease 2019 were at higher risk of death.

FIGURES

Complications and Treatments	No. (%)	
	Hemodialysis, <i>n</i> =49	Control, <i>n</i> =52
Complications		
Shock	8 (16)	2 (4)
ARDS	10 (20)	3 (6)
Arrhythmia	9 (18)	1 (2)
Acute cardiac injury	14 (29)	4 (8)
Treatments		
Oxygen inhalation	41 (84)	43 (83)
Antiviral therapy	47 (96)	51 (98)
Antibiotic therapy	29 (59)	35 (67)
Glucocorticoid therapy	8 (16)	14 (27)
Intermittent hemodialysis	49 (100)	0 (0)
Continuous KRT	17 (35)	0 (0)
Noninvasive ventilation	12 (25)	3 (6)
Invasive mechanical ventilation	3 (6)	1 (2)
ARDS, acute respiratory distress syndrome.		

Table 2: Complications and treatments of patients infected with severe acute respiratory syndrome coronavirus 2

PERCEPTIONS OF OBSTETRICIANS AND PEDIATRICIANS ABOUT THE RISK OF COVID-19 FOR PREGNANT WOMEN AND NEWBORNS

Obeidat N, Saadeh R, Obeidat M, Khasawneh W, Khader Y, Alfaqih M.. Int J Gynaecol Obstet. 2020 Jun 8. doi: 10.1002/ijgo.13264. Online ahead of print.

Level of Evidence: 3 - Local non-random sample

BLUF

This cross sectional study conducted in Jordan between March 23, 2020 and March 30, 2020 surveyed 147 obstetric and pediatric physicians to better gauge their level of understanding of COVID-19 and its associated risks. They found that most participants were well-versed on the transmission of SARS-CoV-2, its clinical presentation, and the necessary protective measures required during infection, but there was variability in knowledge of the safety of perinatal care, delivery, and breastfeeding with concurrent COVID-19 infection, highlighting the importance for physicians to stay updated on such guidelines.

ABSTRACT

OBJECTIVE: To assess the perception of obstetricians and pediatricians about risks of COVID-19 on pregnant women and possible complications in newborns.

METHODS: A structured 27-item online survey was sent via social media messaging to obstetricians and pediatricians from public, academic, and private sectors in Jordan between March 23-30, 2020. Descriptive statistics were used to represent numbers and percentages of participants' responses to survey items.

RESULTS: A total of 147 physicians participated (107 obstetricians, 40 pediatricians). Participants were well informed about the symptoms, diagnosis, modes of transmission, and methods of prevention. Participants had variable perceptions about COVID-19 risk during pregnancy, including potential vertical transmission, preferred route of delivery, and safety of breastfeeding. Most participants felt that pregnant women should be prioritized for testing and medical care provision.

CONCLUSION: While evidence-based strategies to reduce the risks of COVID-19 in pregnant women and newborns are evolving, healthcare providers showed excellent knowledge of the infection and were vigilant regarding its complications for mothers and newborns. To ensure safe pregnancy, physicians must keep informed of developing guidance on best and safest prenatal and perinatal health services. Implementing local hospital policies and adequate training in infection control measures is strongly encouraged.

CLINICAL CHARACTERISTICS AND LABORATORY RESULTS OF PREGNANT WOMEN WITH COVID-19 IN WUHAN, CHINA

Wang Z, Wang Z, Xiong G.. Int J Gynaecol Obstet. 2020 Jun 8. doi: 10.1002/ijgo.13265. Online ahead of print.

Level of Evidence: 4 - Case-series or casecontrol studies, or poor quality prognostic cohort study

BLUF

A retrospective study conducted in Wuhan, China by obstetrics/gynecology and cardiothoracic surgeons from December 2019 until April 2020 found that 30 pregnant women with COVID-19 (13 diagnosed by SARS-CoV-2 testing, 17 by typical CT findings) had distinct serologic profiles from their 42 non-pregnant counterparts with the disease (all 42 diagnosed by both SARS-CoV-2 testing and typical CT findings - see Tables 1 and 2). These differences, including increases in inflammatory markers and in white blood cell count, suggest that several immune factors may have acted protectively and may be associated with pregnant women having less severe cases of COVID-19 and shorter hospital stays.

ABSTRACT

OBJECTIVE: To evaluate the clinical characteristics and laboratory test results in pregnant women with coronavirus disease 2019 (COVID-19).

METHODS: A retrospective study to review and compare clinical data including electronic medical records and laboratory tests from pregnant and nonpregnant patients admitted the Central Hospital of Wuhan, China from December 8, 2019 to April 1, 2020.

RESULTS: A total of 72 women (30 pregnant and 42 nonpregnant) with COVID-19 were included. No patients developed severe pneumonia during the study. Compared with the nonpregnant group, pregnant patients were admitted to hospital earlier (0.25 vs 11.00 days; $P<0.001$), presented milder symptoms, had a higher rate of asymptomatic infection (26.7% vs 0%), and shorter length of hospital stay (14.5 vs 17.0 days; $P<0.01$). Laboratory test results showed that levels of inflammation

markers such as white blood cell count, neutrophil count and percentage, C-reactive protein, procalcitonin, and D-dimer were significantly higher in pregnant women, whereas mean lymphocyte percentage was significantly lower compared with nonpregnant women.

CONCLUSION: In some respects, the clinical characteristics and laboratory test results of COVID-19 in pregnant patients seems to be distinctive from their nonpregnant counterparts. Appropriate advice and positive treatment might be critical to the prognosis when dealing with these pregnant patients. Pregnant patients with COVID-19 had their own positive clinical characteristics and special laboratory test results. Responsive medical advice and active treatment for those patients are critical to recovery.

FIGURES

TABLE 1 Clinical characteristics of the study population (n=72).^a

Clinical characteristics	Pregnant women (n=30)	Nonpregnant women (n=42)	P value
Positive for SARS-CoV-2	13 (43.3)	42 (100.0)	-
Manifestations on chest CT	17 (56.7)	42 (100.0)	-
Age, y	29.9 (26.8–33.3)	30.0 (27.0–34.0)	0.50
Onset of symptoms to admission, d	0.25 (0–1.0)	11.0 (5.0–15.0)	<0.001
Hospitalization, d	14.5 (12.8–17.5)	17.0 (14.0–24.0)	0.01
Gestational age, wk	37.8 (30–40.9)	-	-
Delivery mode			-
Cesarean	23 (76.7)	-	-
Vaginal	7 (23.3)	-	-
Hospitalization to delivery, d	1.1 (0–1.0)	-	-
Initial symptoms			-
No clinical symptoms	8 (26.7)	0	-
Fever	11 (36.7)	28 (66.7)	-
Cough	5 (16.7)	21 (50.0)	-
Abdominal pain	4 (13.3)	-	-
Blood-tinged mucus	4 (13.3)	-	-
Ruptured membranes at term	5 (16.7)	-	-
Chest tightness	1 (3.3)	4 (9.5)	-
Asthma	0	5 (11.9)	-
Fatigue	3 (10.0)	3 (7.1)	-
Poor appetite	6 (20.0)	3 (7.1)	-
Headache	0	1 (2.4)	-
Nausea or vomiting	0	1 (2.4)	-
Complications			-
Pneumonia	30 (100.0)	42 (100.0)	-
Hypertension	5 (16.7)	1 (4.8)	-
Diabetes	2 (6.6)	1 (2.4)	-
Twin pregnancy	1 (3.3)	-	-
Hypothyroidism	1 (3.3)	-	-
Intrahepatic cholestasis of pregnancy	1 (3.3)	-	-
Premature rupture of membranes	6 (20.0)	-	-
Obesity	1 (3.3)	-	-

^a Values are given as number (percentage) or median (interquartile range) unless otherwise indicated.

TABLE 2 Laboratory test results of patients with COVID-19 (n=72).

Test	Normal range	Median (IQR)		<i>P</i> value
		Pregnant women (n=30)	Nonpregnant women (n=42)	
White blood cell count, $\times 10^9/\text{L}$	3.5–9.5	7.5 (6.4–10.3)	5.6 (4.1–7.3)	0.01
Neutrophil %	40–75	77.5 (67.5–82.6)	58.9 (50.6–68.0)	<0.001
Lymphocyte %	20–50	16.1 (11.5–23.6)	31.5 (21.5–37.5)	<0.001
Neutrophil count, $\times 10^9/\text{L}$	1.8–6.3	5.9 (4.5–9.2)	3.1 (2.2–4.7)	<0.001
Lymphocyte count, $\times 10^9/\text{L}$	1.1–3.2	1.4 (1.1–2.0)	1.6 (1.3–2.0)	0.130
Hemoglobin, g/L	130–175	117 (108–129)	132.0 (121.8–141.3)	0.002
Platelet count, $\times 10^9/\text{L}$	125–350	189 (159–262)	214.0 (170.8–255.5)	0.238
Total bile acid, $\mu\text{mol}/\text{L}$	2–20.4	8.7 (7.2–10.3)	11.4 (7.8–15.9)	0.10
Alanine transaminase, U/L	7–40	9.4 (7.1–14.0)	21.5 (12.5–43.0)	<0.001
Aspartate aminotransferase, U/L	13–35	15.6 (12.6–21.4)	16.8 (14.6–23.0)	0.717
Albumin, g/L	40–55	35.9 (34.0–39.8)	42.7 (40.4–45.6)	<0.001
Globulin, g/L	20–40	28.0 (24.9–30.7)	28.6 (22.5–33.8)	0.393
Blood urea nitrogen, mmol/L	2.9–8.2	2.7 (2.2–3.0)	3.9 (3.2–5.0)	<0.001
Creatinine, $\mu\text{mol}/\text{L}$	41–73	43.4 (35.9–55.9)	58.8 (48.7–69.1)	<0.001
D-dimer, $\mu\text{g}/\text{mL}$	0–1	2.5 (1.4–4.6)	0.3 (0.1–0.85)	<0.001
C-reactive protein, mg/dL	0–0.6	1.0 (0.28–2.84)	0.1 (0.04–0.91)	0.022
Procalcitonin, ng/mL	<0.046	0.06 (0.04–0.16)	0.04 (0.03–0.06)	0.025
Lactate dehydrogenase, U/L	80–285	148.0 (127.0–182.0)	162.0 (129.5–190.0)	0.801
Interleukin-6, pg/mL	<7	5.9 (2.9–8.7)	1.5 (1.5–2.4)	0.115

ADJUSTING PRACTICE DURING COVID-19

COVID-19 AND INEQUITIES IN ORAL HEALTH CARE FOR OLDER PEOPLE: AN OPPORTUNITY FOR EMERGING PARADIGMS

León S, Giacaman RA.. JDR Clin Trans Res. 2020 Jun 8:2380084420934742. doi: 10.1177/2380084420934742. Online ahead of print.

Level of Evidence: Other - Expert Opinion

BLUF

The authors emphasized the negative effects of COVID-19 on oral healthcare in Latin America particularly within the older population due to unequal access to dental care. They report older individuals have an increased risk of developing systemic infections from poor oral care and observed a decrease in the people seeking dental services during the COVID-19 pandemic. As a preventative intervention, the authors proposed the use of teledentistry and minimal intervention dentistry (for long-term care) to provide adequate preventative care for these susceptible populations.

ABSTRACT

Severe restrictions have been imposed in most countries for oral health care to the general population, allowing treatment only for emergencies, because of the generation of aerosols during clinical procedures and to ration personal protective equipment (PPE) during the pandemic. This article stresses the critical situation that affects oral health for older persons in the complex times of the COVID-19 pandemic. Older adults are at high risk for the viral infection, but neglected dental conditions may worsen their health, triggering infections that can lead to local and systemic complications, compromising general health. We propose that under current and possibly future scenarios, teledentistry and the minimal intervention dentistry approach may play a pivotal role in reshaping the profession. The already existent inequities in oral health care may be exacerbated due to the pandemic, especially in the developing world. More research along with a strong educational component in the dental curriculum must be emphasized. COVID-19 may be an opportunity to change canonical paradigms. The dental profession must reflect and take action to face future challenges. Knowledge Transfer Statement: This article provides an overview of the oral health situation imposed by COVID-19 and the minimal intervention alternatives to provide care to older people who are at risk and have reduced access to care.

FOR HEALTHCARE PROFESSIONALS

WEARABLE TECHNOLOGY AND HOW THIS CAN BE IMPLEMENTED INTO CLINICAL PRACTICE

Greiwe J, Nyenhuis SM.. Curr Allergy Asthma Rep. 2020 Jun 6;20(8):36. doi: 10.1007/s11882-020-00927-3.

Level of Evidence: Other - Expert Opinion

BLUF

US allergy and immunology physicians advocate for wearable technology and its potential for advancing telemedicine. They note the recent surge in telemedicine use and advances in personal health technology provide an ideal opportunity for this intervention and they recommend several personal health and fitness apps that patients can utilize to monitor their health (Table 1 and 2).

ABSTRACT

PURPOSE OF REVIEW: Our day-to-day life is saturated with health data that was previously out of reach. Over the last decade, new devices and fitness technology companies are attempting to tap into this data, uncovering a treasure trove of useful information that, when applied correctly, has the potential to revolutionize the way we approach healthcare and chronic conditions like asthma, especially in the wake of the COVID-19 pandemic.

RECENT FINDINGS: By harnessing exciting developments in personalization, digitization, wellness, and patient engagement, care providers can improve health outcomes for our patients in a way we have never been able to do in the past. While new technologies to capture individual health metrics are everywhere, how can we use this information to make a real difference in our patients' lives? Navigating the complicated landscape of personal wearable devices, asthma inhaler sensors, and exercise apps can be daunting to even the most tech savvy physician. This manuscript will give you the tools necessary to make lasting changes in your patients' lives by exposing them to a world of usable, affordable, and relatable health technology that

resonates with their personal fitness and wellness goals. These tools will be even more important post-COVID-19, as the landscape of clinical outpatient care changes from mainly in-person visits to a greater reliance on telemedicine and remote monitoring.

FIGURES

Table 1 Top rated fitness and nutrition apps

App	Supporting devices	Cost structure	Details
For all-around healthy lifestyle			
8fit	iOS, Android	Free; \$59.99 per year; \$44.99 per half-year; \$19.99 per month for meal plans and more workouts	On-demand workouts and meal planning for people who like a lot of guidance, suggestions, reminders, and instructions. Provides realistic assessment of how hard or easy it will be to reach your health and fitness goals.
Yoga			
Asana Rebel	iOS, Android	\$39.99 for 3 months; \$58.99 for 12 months	Yoga-inspired fitness that has guided yoga flows alongside regular workouts. Input goals, track progress, and choose classes based on experience level.
Yoga Wake Up	iOS, Android	\$10 per month	Offers different audio yoga and meditation sequences that are designed to start in bed and end with you on your feet.
Alo Moves	iOS, Android	\$20 per month	Has over 2000 videos organized into 200 plans and over 500 single classes taught by the top names in yoga.
YogaGlo	iOS, Android	\$18 per month	Offers more than 3800 yoga workouts and guided mediation classes.
On-demand workouts			
Peloton Digital	iOS, Android	\$20 per month	Access live-streamed classes to use on any bike or treadmill or try one of their boot camp, strength, or outdoor classes.
Fitbit Coach	iOS, Android	Free; \$9.99 per month or \$79.99 per year for Premium	Takes users daily Fitbit activity data to recommend exercises and personalized fitness feedback. Large database of workout videos with step-by-step directions and tips. Compatible with Fitbit Radio.
Nike Training Club	iOS, Android	Free; \$14.99 per month or \$119.99 per year for Premium	Has classic short sessions but includes workout routines that are 30, 45, or even 60 min long. A Premium account also comes with programs led by trainers and nutrition and wellness guidance.
Sworkit	iOS, Android	\$10 per month	Custom no-equipment training plans, complete with guided videos for each workout ranging from 5 to 60 min. Users can also connect with personal trainers to ask questions and get expert advice.
Aaptiv	iOS, Android	\$15 per month	Audio classes taught by trainers guiding users through a fitness studio-style session. Over 2500 workouts in cycling, yoga, strength training, stretching, elliptical workouts, and more. Also comes with full marathon, half marathon, 10K, and 5K training programs.
Fitness tracking			
Strava	iOS, Android, Web	Free; \$7.99 per month or \$59.99 per year	Users can compete against themselves or others who have run, biked, or swam the same routes. The app uses phone/watches GPS to track where users go and how fast then compares with other users creating a leaderboard.
Map My Fitness	iOS, Android	Free; \$5.99 per month or \$29.99 per year for MVP	Recommended for those just getting started on a fitness journey. Has hundreds of activities you can track, everything from vacuuming to rock climbing motivating user to keep a more active lifestyle. Consolidates data from various fitness trackers or apps such Fitbit.

Table 1 (continued)

App	Supporting devices	Cost structure	Details
Charity Miles	iOS, Android	Free	Motivates by donating money to charity for every mile users run, walk, or bicycle. Supports a variety of nonprofit organizations, such as ASPCA, Habitat for Humanity, St. Jude Children's Hospital, UNICEF, Save the Children, and the Wounded Warrior Project.
Nutrition-Tracking			
MyFitnessPal	iOS, Android	Free; \$9.99 per month or \$49.99 per year for Premium	Calorie counting app that also figures out how many calories users should eat to gain, lose, or maintain weight. Consolidates everything users eat and drink, plus all their activities to calculate calories consumed against calories burned. It also has tools for tracking weight and other body changes over time. It has the largest database of foods and is the best food logging app on the market.
Noom	iOS, Android	\$59 per month, \$199 per year (additional pricing options available)	Complete weight loss program with daily interactive content, a personal goal coach, and plenty of content to help users master the psychology involved with changing their relationships to food.
MyPlate	iOS, Android, Web	Free; \$9.99 per month, \$30 for six months, or \$44.99 per year for Gold	All-in-one fitness app, combining calorie counting, weight management, recipes, and workouts. Users look up and record everything they eat and can see a nutritional analysis of macronutrient intake for free (requires paid subscription in MyFitnessPal).
WW Digital (formally WeightWatchers)	iOS, Android, Web	\$23.99 per month or \$219.99 per year	Highly supportive community and app that focuses more on personalization and overall health rather than weight loss alone. Users do not have to attend meetings or meet with a counselor (although this is an option for an added fee). Monitors food intake with SmartPoints rather than counting calories or fat.
Mindfulness and meditation			
Calm	iOS, Android	\$14.99 per month or \$69.99 per year	Guided mindfulness meditation that initially offers a "7 Days of Calm" course which introduces users to mindfulness meditation, as well as some guided and unguided meditation sessions. Paid users have access to more multi-day courses, a "Daily Calm" course, and many, many more guided meditations.
Headspace	iOS, Android	\$12.99 per month or \$69.99 per year	Guided meditation for health issues, emotions, challenges, and productivity. There are even "SOS" sessions for some of the more stressful times in life. Recently added free content called Weathering the Storm for those struggling with the emotional effects of COVID-19.
The Mindfulness App	iOS, Android	\$9.99 per month or \$59.99 per year	Starts with a 5-day introduction to mindfulness along with guided meditations to get you familiar with meditating. With subscription choose guided or silent meditation sessions for challenges, travel, sleep, relationships, stress relief, emotions, body awareness, focus, and relationships.

*The authors are aware of the transient nature of fitness, nutrition, and lifestyle apps and understand that the recommendations provided at the time of this publication might not be available in the future

Table 2 Current and emerging technologies in asthma

Technology	Measures	Outcomes in asthma studies	Comments
Wearable technology – Fitbit™ – Apple™ Watch	Fitbit: heart rate (available on most but not all models), steps/day, physical activity (light, moderate and vigorous), sedentary time, sleep efficiency, wake counts Apple Watch: heart rate, EKG, steps/day, physical activity (light, moderate and vigorous), sedentary time	– Fitbit overestimated sleep efficiency and underestimated wake counts compared with actigraphy. ¹⁸ – Fitbit-derived sleep quality correlated with PROMIS pediatric asthma impact score. ²¹	Corresponding Apps: Apple Watch App on iPhone, Fitbit App on iPhone and Android Pros: portable; commercially available; may be useful when used with other measures such as air quality, lung function and asthma symptoms to digitally phenotype asthma patients Cons: No sleep data available on Apple Watch without 3rd party App Data sharing: Data does not sync to EMR directly but patient can access file and send to provider via mail, secure email, or patient portal.
Electronic monitoring devices (e.g., inhaler sensors ± digital health platform)	Digitaler™: – Inhaler time of inhaler use, peak inspiratory flow rate (PIFR), time to PIFR, inhalation volume and duration. Propeller Health System: – Inhaler sensor: date, time and number of doses taken – Asthma Health Platform App: Location of inhaler use using phone GPS, current weather/pollen counts/air pollution and self-report asthma symptoms/triggers Hailie™ solution: – Inhaler sensor: date, time, number of inhaler actuations and missed doses – Hailie™ App: medication adherence, daily medication reminders Inhaler compliance assessment device: Time of dose, inhaler technique errors Self-monitoring of: – Asthma symptoms – Triggers – Medication use	– Greater asthma control ^{31,38-39} and symptom-free days ³³ – Reduction in daily symptoms ³¹ , rescue medication use ^{29,32-33} , and exacerbations ^{34,38-39} – Improved medication adherence ³⁶⁻⁴⁰ – High patient acceptability of device and digital health platform ³⁶⁻³⁷ .	Corresponding Apps: Digitaler™, Propeller Health, Hailie™. Web-based platform also available for Propeller Health, Hailie™ solution. Pros: portable, high acceptability among patients, improvements in asthma control in those with a digital health platform (e.g., Propeller Health, Hailie™ solution). Cons: Additional efficacy studies of the devices are needed, cost of devices are not always covered by insurance reimbursement Data sharing: Provider platform available to share results (e.g. Digitaler™, Propeller Health, Hailie™ solution), patients may share data from Digitaler™ also via file share.
Mobile-based applications	Time of dose, inhaler technique errors Self-monitoring of: – Asthma symptoms – Triggers – Medication use	– Improvements in asthma control through low-quality evidence ⁴⁵ – Improvements in asthma control in five studies, lung function in two studies and quality of life in three studies ⁴⁶	Pros: Acceptable and feasible to use Cons: Vary in quality; data are self-reported, most apps have not been validated; risk of loss of privacy of health information Data sharing: Vary in ability to share with provider, most are up to user to share with provider

ACUTE CARE

COVID-19 AND PULMONARY EMBOLISM: DIAGNOSTIC IMAGING TRENDS

Karimzadeh S, Raut A, Nguyen Tien H. J Nucl Med. 2020 May 22:jnumed.120.248518. doi: 10.2967/jnumed.120.248518.

Online ahead of print.

Level of Evidence: Other -

BLUF

Authors respond to a previous publication suggesting non-ventilation approaches for pulmonary embolism (PE) evaluation (Zuckier et al., 2020) with concerns that pretest risk screenings may not be a sufficient predictor of PE in COVID-19 patients and that ventilation/perfusion (V/Q) scans cannot exclude PE entirely in COVID-19 patients due to higher probabilities of PE in COVID-19 patients. Authors note that additional considerations are needed to improve diagnostic efficacy, specifically for those with confirmed or suspected SARS-CoV-2 infection.

SUMMARY

In the previously published article, "Diagnostic Evaluation of Pulmonary Embolism During the COVID-19 Pandemic" (Zuckier et al., 2020), a novel algorithm for the evaluation of pulmonary embolism (PE) was proposed to minimize aerosolized secretions in the nuclear medicine suite during the COVID-19 pandemic. The authors of this article raise additional issues to be considered when using this approach. First, the previous publication suggests reducing the number of patients evaluated for PE during this time by using pretest risk screenings such as the Wells' criteria, Pulmonary Embolism Ruleout Criteria (PERC) and the Geneva scoring system. However, these tests may not be a sufficient predictor of PE in COVID-19 patients, given severity of illness and greater hemodynamic instability. Therefore, these pretest screenings should be limited to an outpatient setting and only to patients where COVID-19 is not suspected. Second, the previous publication also suggests that for patients with low probability for PE, a combined ventilation/perfusion (V/Q) scan is sufficient for evaluation. However, in COVID-19 patients, as probability for PE is higher, a negative perfusion scan alone cannot exclude PE entirely, and additional studies must be considered to definitively rule out PE.

CARDIOLOGY

CHALLENGES IN THE MANAGEMENT OF OLDER PATIENTS WITH ACUTE CORONARY SYNDROMES IN THE COVID-19 PANDEMIC

Rowland B, Kunadian V.. Heart. 2020 May 22:heartjnl-2020-317011. doi: 10.1136/heartjnl-2020-317011. Online ahead of print.

Level of Evidence: Other - Literature Review

BLUF

This review conducted in the UK found that it is necessary to adjust critical care management for older patients with acute coronary syndrome (ACS) as these patients have higher rates of morbidity and mortality related to COVID-19. The possible pathogenesis of this is outlined in Figure 1. The authors advocate for protocols for the management of older patients with ACS to be created by weighing the risks and benefits of treatments (Figure 2).

ABSTRACT

Ischaemic heart disease (IHD), in particular acute coronary syndrome (ACS), comprising ST-elevation myocardial infarction, non-ST-elevation myocardial infarction and unstable angina, is the leading cause of death worldwide. Age is a major predictor of adverse outcome following ACS. COVID-19 infection seems to escalate the risk in older patients with heart disease.

Increasing odds of in-hospital death is associated with older age following COVID-19 infection. Importantly, it seems older patients with comorbidities such as cardiovascular disease (CVD), in particular IHD, diabetes and hypertension, are at the highest risk of mortality following COVID-19 infection. The evidence is sparse on the optimal care of older patients with ACS with lack of robust randomised controlled trials. In this setting, with the serious threat imposed by the COVID-19 pandemic in the context of rapidly evolving knowledge with much unknown, it is important to weigh the risks and benefits of treatment strategies offered to older patients. In cases where risks outweigh the benefits, it might not be an unreasonable option to treat such patients with a conservative or a palliative approach. Further evidence to elucidate whether invasive management is beneficial in older patients with ACS is required out-with the COVID-19 pandemic. Though it is hoped that the actual acute phase of COVID-19 infection will be short lived, it is vital that important clinical research is continued, given the long-term benefits of ongoing clinical research for patients with long-term conditions, including CVD. This review aimed to evaluate the challenges and the management strategies in the care of older patients presenting with ACS in the context of the COVID-19 pandemic.

FIGURES

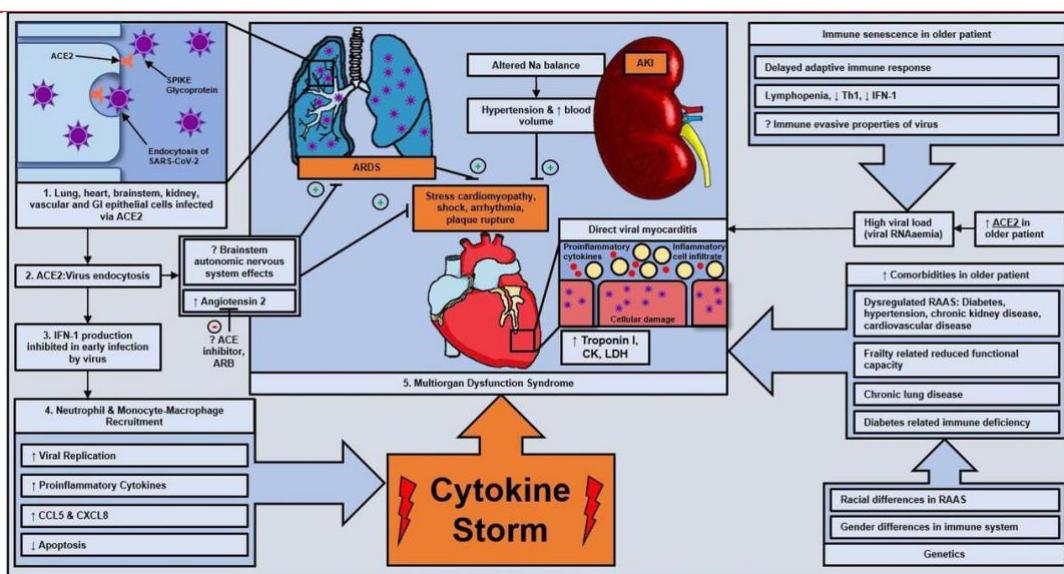
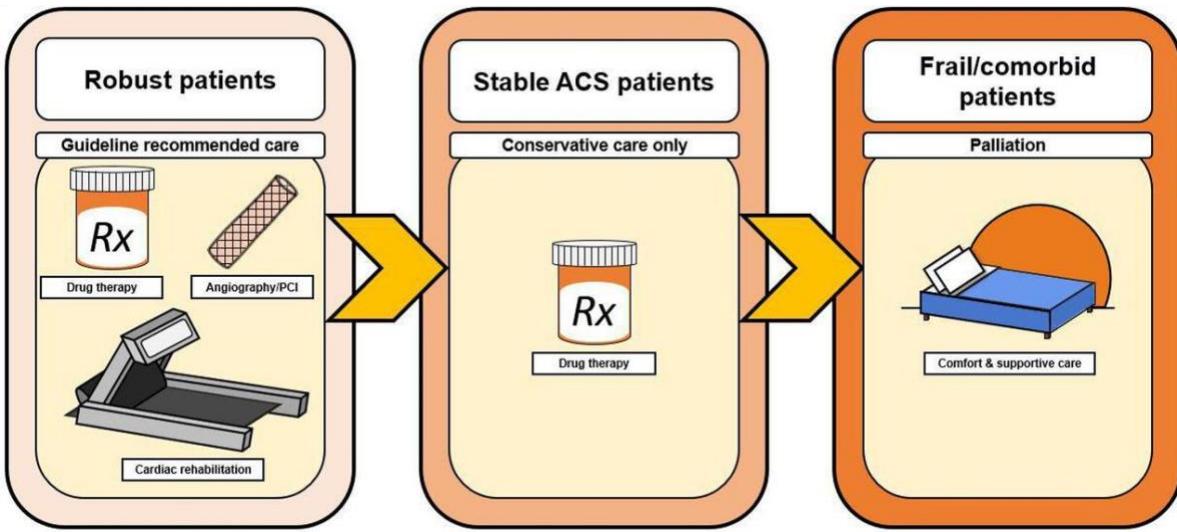


Figure 1: Hypothesised pathogenesis of acute cardiac injury in older patients. AKI, acute kidney injury; ARDS, acute respiratory distress syndrome; CCL5, chemokine ligand 5; CK, creatine kinase; CXCL8, C-X-C motif chemokine ligand 8; GI, gastrointestinal; IFN-1, interferon type 1; LDH, lactate dehydrogenase; Na, sodium; RAAS, renin–angiotensin–aldosterone system; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; Th1, type 1 T-helper cell.



HEMATOLOGY AND ONCOLOGY

ROUTINE ANTIEMETIC PROPHYLAXIS WITH DEXAMETHASONE DURING COVID-19: SHOULD ONCOLOGISTS RECONSIDER?

Marinella MA.. J Oncol Pharm Pract. 2020 Jun 6:1078155220931921. doi: 10.1177/1078155220931921. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

Previous studies have demonstrated that dexamethasone often causes lymphopenia, and recent evidence that lymphopenia is associated with worse outcomes in COVID-19 patients. An oncologist with Wright State University School of Medicine thus argues that physicians should reconsider routine use of prophylactic dexamethasone as an anti-emetic in cancer patients during the current COVID-19 pandemic, particularly if other treatments are available.

ABSTRACT

The ongoing pandemic caused by severe acute respiratory syndrome (SARS) coronavirus type 2 (SARS-CoV-2, also known as COVID-19) has caused unprecedented strain on the global healthcare system, causing thousands of deaths worldwide. Patients with underlying conditions such as cancer are at substantial risk of acquiring and dying from this novel coronavirus. Numerous reports have shown that infection with SARS-CoV-2 causes depletion of B- and T-lymphocytes, including CD4 and CD8 T-cells, and is associated with severe illness and death and that patients with higher lymphocyte levels may have better outcomes. Dexamethasone, a widely prescribed antiemetic for acute and delayed nausea and vomiting from a variety of cancer drugs, causes B and T cell depletion, which may augment immunosuppression. Since it seems that lymphocytes are vital in the immune response to novel coronavirus, oncologists should reconsider the routine use of prophylactic dexamethasone in uninfected patients, to avoid inducing lymphopenia, which may increase risk of infection or lead to inferior outcomes if a cancer patient subsequently becomes infected. Since many cancer drugs and malignant diseases inherently cause lymphopenia, further reduction of lymphocytes with dexamethasone should be avoided if possible and if safe and effective alternative antiemetics are available during the COVID-19 crisis.

MANAGEMENT OF PATIENTS WITH MULTIPLE MYELOMA IN THE ERA OF COVID-19 PANDEMIC: A CONSENSUS PAPER FROM THE EUROPEAN MYELOMA NETWORK (EMN)

Terpos E, Engelhardt M, Cook G, Gay F, Mateos MV, Ntanasis-Stathopoulos I, van de Donk NWCJ, Avet-Loiseau H, Hajek R, Vangsted AJ, Ludwig H, Zweegman S, Moreau P, Einsele H, Boccadoro M, San Miguel J, Dimopoulos MA, Sonneveld P.. Leukemia. 2020 May 22. doi: 10.1038/s41375-020-0876-z. Online ahead of print.

Level of Evidence: Other - Guidelines

BLUF

The European Myeloma Network (EMN) released a consensus statement to guide treatment decisions during the COVID-19 pandemic, summarized in Figure 1. The EMN also urges participation in international registries to record data on multiple myeloma patients and COVID-19 to help further guide management.

ABSTRACT

Patients with multiple myeloma (MM) seem to be at increased risk for more severe COVID-19 infection and associated complications due to their immunocompromised state, the older age and comorbidities. The European Myeloma Network has provided an expert consensus statement in order to guide therapeutic decisions in the era of the COVID-19 pandemic. Patient education for personal hygiene and social distancing measures, along with treatment individualization, telemedicine and continuous surveillance for early diagnosis of COVID-19 are essential. In countries or local communities where COVID-19 infection is widely spread, MM patients should have a PCR test of nasopharyngeal swab for SARS-CoV-2 before hospital admission, starting a new treatment line, cell apheresis or ASCT in order to avoid ward or community spread and infections. Oral agent-based regimens should be considered, especially for the elderly and frail patients with standard risk disease, whereas de-intensified regimens for dexamethasone, bortezomib, carfilzomib and daratumumab should be used based on patient risk and response. Treatment initiation should not be postponed for patients with end organ damage, myeloma emergencies and aggressive relapses. Autologous (and especially allogeneic) transplantation should be delayed and extended induction should be administered, especially in standard risk patients and those with adequate MM response to induction. Watchful waiting should be considered for standard risk relapsed patients with low tumor burden, and slow biochemical relapses. The conduction of clinical trials should continue with appropriate adaptations to the current circumstances. Patients with MM and symptomatic COVID-19 disease should interrupt anti-myeloma treatment until recovery. For patients with positive PCR test for SARS-CoV-2, but with no symptoms for COVID-19, a 14-day quarantine should be considered if myeloma-related events allow the delay of treatment. The need for surveillance for drug interactions due to polypharmacy is highlighted. The participation in international COVID-19 cancer registries is greatly encouraged.

FIGURES

Fig. 1: Decision-making algorithm for the management of patients with MM in the era of the COVID-19 pandemic.

From: [Management of patients with multiple myeloma in the era of COVID-19 pandemic: a consensus paper from the European Myeloma Network \(EMN\)](#)

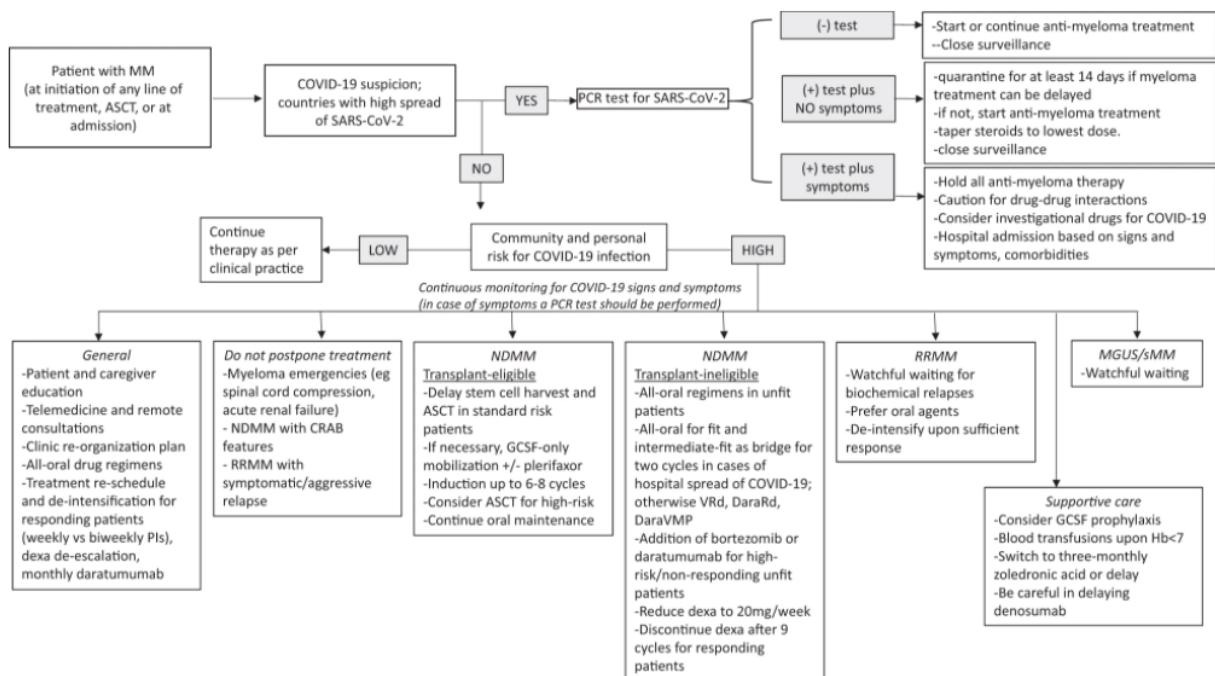


Figure 1. Decision-making algorithm for the management of patients with multiple myeloma (MM) in the era of the COVID-19 pandemic. NDMM: newly diagnosed MM, RRMM: relapsed/refractory MM, MGUS: monoclonal gammopathy of undetermined significance, sMM: smoldering MM.

NEPHROLOGY

RAAS INHIBITORS DO NOT INCREASE THE RISK OF COVID-19

Fernández-Ruiz I.. Nat Rev Cardiol. 2020 May 22. doi: 10.1038/s41569-020-0401-0. Online ahead of print.
Level of Evidence: Other -

BLUF

A review conducted by Nature editor Irene Fernandez-Ruiz in May of 2020 focusing on five large observational studies involving a variety of populations and methods found that the use of renin-angiotensin-aldosterone system inhibiting medication does not increase a patient's chance of contracting COVID-19 and does not increase disease severity if the patient does contract the disease.

SLEEP MEDICINE

THE COVID-19 PANDEMIC PRESENTS AN OPPORTUNITY TO REASSESS THE VALUE OF POLYSOMNOGRAPHY

Patel SR, Donovan LM.. Am J Respir Crit Care Med. 2020 Jun 8. doi: 10.1164/rccm.202005-1546ED. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

Sleep specialists at the Puget Sound Veteran's Association question the necessity of polysomnography (PSG) for clinical diagnosis of sleep disorders, highlighting that the COVID-19 pandemic has diminished the capacity of sleep labs, and therefore reduced use of PSG. The authors further note that centering PSG as key for diagnosis of sleep disorders 1) hinders the use of home technologies and clinical judgment for diagnosis, 2) allows insurance companies to center billing metrics around semi-objective PSG values, and 3) restricts access to proper care to those who actually can visit clinics. Thus, they argue that COVID-19 offers a chance to advance sleep medicine beyond PSG.

SURGICAL SUBSPECIALTIES

RAPID IN-VITRO INACTIVATION OF SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2 (SARS-COV-2) USING POVIDONE-IODINE ORAL ANTISEPTIC RINSE

Bidra AS, Pelletier JS, Westover JB, Frank S, Brown SM, Tessema B.. J Prosthodont. 2020 Jun 8. doi: 10.1111/jopr.13209.
Online ahead of print.
Level of Evidence: 5 - Mechanism-based reasoning

BLUF

An in vitro study conducted by the University of Connecticut Health Center in Farmington, Connecticut in May 2020 investigated povidone-iodine (aka PVP-I or Betadine) for use as oral antiseptic against SARS-CoV-2. They found that PVP-I in concentrations of 0.5% can completely inactivate SARS-CoV-2 in 15 seconds compared with 70% ethanol which took 30 seconds to inactivate the virus (Tables 1 and 2 for results of PVP-I, ethanol, water viral titers). This study suggests that using PVP-I oral rinse prior to dental or prosthodontic procedures will decrease the risk of transmission in dental practice.

ABSTRACT

PURPOSE: To investigate the optimal contact time and concentration for viricidal activity of oral preparation of povidone-iodine (PVP-I) against SARS-CoV-2 ('corona virus') to mitigate the risk and transmission of the virus in the dental practice.

MATERIALS AND METHODS: The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) USA-WA1/2020 strain, virus stock was tested against oral antiseptic solutions consisting of aqueous povidone-iodine (PVP-I) as the sole active ingredient. The PVP-I was tested at diluted concentrations of 0.5%, 1% and 1.5%. Test media without any virus was added to 2 tubes of the compounds to serve as toxicity and neutralization controls. Ethanol (70%) was tested in parallel as a positive control, and water only as a negative control. The test solutions and virus were incubated at room temperature (22 ± 2 °C) for time periods of 15 and 30 seconds. The solution was then neutralized by a 1/10 dilution in minimum essential medium (MEM)

2% fetal bovine serum (FBS), 50 mug/mL gentamicin. Surviving virus from each sample was quantified by standard end-point dilution assay and the log reduction value (LRV) of each compound compared to the negative (water) control was calculated.

RESULTS: PVP-I oral antiseptics at all tested concentrations of 0.5%, 1% and 1.5%, completely inactivated SARS-CoV-2 within 15 seconds of contact. The 70% ethanol control group was unable to completely inactivate SARS-CoV-2 after 15 seconds of contact, but was able to inactivate the virus at 30 seconds of contact.

CONCLUSIONS: PVP-I oral antiseptic preparations rapidly inactivated SARS-CoV-2 virus in vitro. The viricidal activity was present at the lowest concentration of 0.5 % PVP-I and at the lowest contact time of 15 seconds. This important finding can justify the use of preprocedural oral rinsing with PVP-I (for patients and health care providers) may be useful as an adjunct to personal protective equipment, for dental and surgical specialties during the COVID-19 pandemic.

FIGURES

Test Product	PVP-I Concentration (%) After 1:1 Dilution	Incubation Time (in seconds)	Virus Titer ^a	LRV ^b
PVP-I 3.0% Oral Rinse Antiseptic	1.5	15	<0.67	3.0
PVP-I 1.5% Oral Rinse Antiseptic	0.75	15	<0.67	3.0
PVP-I 1.0% Oral Rinse Antiseptic	0.5	15	<0.67	3.0
Ethanol 70%	N/A	15	1.5	2.17
Water	N/A	15	3.67	N/A

^a Log₁₀ CCID₅₀ of virus per 0.1 mL. The assay lower limit of detection is 0.67 Log₁₀ CCID₅₀/0.1 mL.

^b LRV (log reduction value) is the reduction of virus compared to the virus control.

Table 1. Virus titers and log reduction value of SARS-CoV-2 when incubated with various concentrations of PVP-I and the controls for 15 seconds. Each experimental sample was tested 3 times and average virus titers are reported.

Test Product	PVP-I Concentration (%) After 1:1 Dilution	Incubation Time (in seconds)	Virus Titer ^a	LRV ^b
PVP-I (3.0%) Oral Rinse Antiseptic	1.5	30	<0.67	3.33
PVP-I (1.5%) Oral Rinse Antiseptic	0.75	30	<0.67	3.33
PVP-I (1.0%) Oral Rinse Antiseptic	0.5	30	<0.67	3.33
Ethanol 70%	N/A	30	<0.67	3.33
Water	N/A	30	4.0	N/A

^a Log₁₀ CCID₅₀ of virus per 0.1 mL. The assay lower limit of detection is 0.67 Log₁₀ CCID₅₀/0.1 mL.

^b LRV (log reduction value) is the reduction of virus compared to the virus control.

Table 2. Virus titers and log reduction value of SARS-CoV-2 when incubated with various concentrations of PVP-I and the controls for 30 seconds. Each experimental sample was tested 3 times and average virus titers are reported.

REDUCING TRANSMISSION OF COVID-19 USING A CONTINUOUS NEGATIVE PRESSURE OPERATIVE FIELD BARRIER DURING ORAL MAXILLOFACIAL SURGERY

Gonzalez-Ciccarelli LF, Nilson J, Oreadi D, Fakitsas D, Sekhar P, Quraishi SA.. Oral Maxillofac Surg Cases. 2020 Sep;6(3):100160. doi: 10.1016/j.omsc.2020.100160. Epub 2020 May 30.

Level of Evidence: Other - Case Report

BLUF

In a case report, authors affiliated with Tufts Medical Center recommend the use of continuous negative air pressure with standard, readily available equipment during oral and maxillofacial surgical procedures to reduce exposure to SARS-CoV-2 from aerosol droplets in the operating room during the COVID-19 pandemic. The authors describe a patient with a left maxillary sinus lesion, awaiting COVID-19 testing, who was operated on using continuous negative air pressure on the operative site. The authors believe that the use of continuous negative pressure during surgical procedures in patients with COVID-19 will "minimize exposure and decrease cross-contamination to the operating room personnel."

ABSTRACT

Oral and maxillofacial surgery in patients with suspected or confirmed COVID-19, presents a high risk of exposure and cross contamination to the operative room personnel. We designed, simulated and implemented a continue negative pressure operative field barrier to provide an additional layer of protection, using standard equipment readily available in most operative rooms during oral and maxillofacial procedures.

EFFICACY AND SAFETY OF CONVALESCENT PLASMA FOR SEVERE COVID-19 BASED ON EVIDENCE IN OTHER SEVERE RESPIRATORY VIRAL INFECTIONS: A SYSTEMATIC REVIEW AND META-ANALYSIS

Devasenapathy N, Ye Z, Loeb M, Fang F, Najafabadi BT, Xiao Y, Couban R, Bégin P, Guyatt G.. CMAJ. 2020 May 22:cmaj.200642. doi: 10.1503/cmaj.200642. Online ahead of print.

Level of Evidence: 1 -

BLUF

The authors present a GRADE-guided systematic review (Table 3) of six studies of therapeutic convalescent plasma (CP) using the results from four influenza randomized trials and one non-randomized study of both SARS-CoV and Ebola (Figure 2), while no studies including COVID-19 patients were included. Despite its demonstrated safety, they conclude that these trials do not demonstrate therapeutic efficacy across patient outcomes, length of hospital or ICU stay, or viral load reduction. Given the use of hemagglutination inhibition to nonspecifically categorize CP in some trials herein, the authors urge direct study of verified CP from recently recovered COVID-19 patients to gauge its efficacy.

ABSTRACT

BACKGROUND: The safety and efficacy of convalescent plasma in severe coronavirus disease 2019 (COVID-19) remain uncertain. To support a guideline on COVID-19 management, we conducted a systematic review and meta-analysis of convalescent plasma in COVID-19 and other severe respiratory viral infections.

METHODS: In March 2020, we searched international and Chinese biomedical literature databases, clinical trial registries and prepublication sources for randomized controlled trials (RCTs) and nonrandomized studies comparing patients receiving and not receiving convalescent plasma. We included patients with acute coronavirus, influenza and Ebola virus infections. We conducted a meta-analysis using random-effects models and assessed the quality of evidence using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach.

RESULTS: Of 1099 unique records, 6 studies were eligible, and none of these included patients with COVID-19. One nonrandomized study ($n = 40$) on convalescent plasma in severe acute respiratory syndrome coronavirus (SARS-CoV) provided uninformative results regarding mortality (relative risk [RR] 0.10, 95% confidence interval [CI] CI 0.01 to 1.70). Pooled estimates from 4 RCTs on influenza ($n = 572$) showed no convincing effects on deaths (4 RCTs, RR 0.94, 95% CI 0.49 to 1.81), complete recovery (2 RCTs, odds ratio 1.04, 95% CI 0.69 to 1.64) or length of stay (3 RCTs, mean difference -1.62, 95% CI -3.82 to 0.58, d). The quality of evidence was very low for all efficacy outcomes. Convalescent plasma caused few or no serious adverse events in influenza RCTs (RR 0.85, 95% CI 0.56 to 1.29, low-quality evidence).

INTERPRETATION: Studies of non- COVID-19 severe respiratory viral infections provide indirect, very low-quality evidence that raises the possibility that convalescent plasma has minimal or no benefit in the treatment of COVID-19 and low-quality evidence that it does not cause serious adverse events.

FIGURES

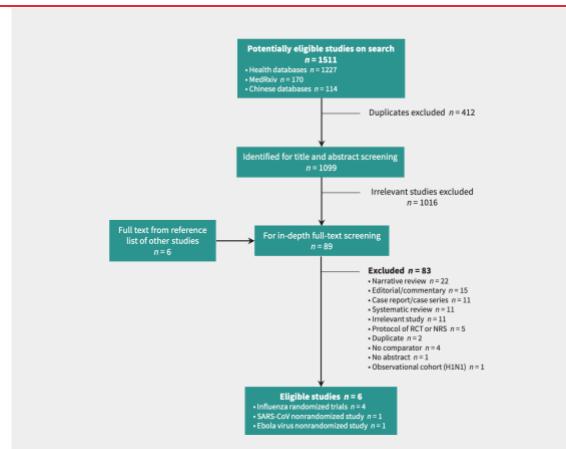


Figure 2. Study selection flow chart. Note: NRS = nonrandomized study, RCT = randomized controlled trial, SARS-CoV = severe acute respiratory syndrome coronavirus.

Table 3: GRADE summary of findings on use of convalescent plasma in COVID-19

Patient or population: Children or adults with severe COVID-19 infection
 Intervention: Convalescent or hyperimmune intravenous immunoglobulin
 Comparison: Usual care + placebo (saline or intravenous immunoglobulin)

Outcome	Relative effects, source of evidence	Absolute effects			Plain-language summary
		Baseline risk for control group (per 1000)	Difference (95% CI) (per 1000)	Certainty/quality of evidence	
Mortality (7–28 d)	RR 0.94 (95% CI 0.49 to 1.80) Based on 572 patients with influenza in 4 RCTs	104*	-6 (-53 to 84)	Very low ⊕⊕⊕⊕ (Very serious indirectness and serious imprecision)†	Convalescent plasma may have little to no effect on mortality, but the evidence is very uncertain.
Mortality (22 d)	RR 0.10 (95% CI 0.01 to 1.70) Based on 40 patients with SARS in 1 observational study	104*	-94 (-103 to 73)	Very low ⊕⊕⊕⊕ (Serious indirectness, very serious risk of bias and serious imprecision)‡	Convalescent plasma could have an important effect on decreasing or increasing mortality, but the evidence is very uncertain.
Recovery by 28 days as measured by a 6-point ordinal scale§	Proportional OR for recovery§ OR 1.05 (95% CI 0.67 to 1.64) Based on 438 patients with influenza from 2 RCTs	104*	5 (-30 to 56)	Very low ⊕⊕⊕⊕ (Very serious indirectness and serious imprecision)†	Convalescent plasma may have little to no effect on recovery, but the evidence is very uncertain.
Length of hospital stay, d	Based on 259 patients with influenza in 3 RCTs	Median 13¶	MD -1.62 (-3.82 to 0.58)	Very low ⊕⊕⊕⊕ (Very serious indirectness and serious imprecision)†	Convalescent plasma may confer a small reduction in hospital length of stay, but the evidence is very uncertain.
Length of ICU stay, d	Based on 149 patients with influenza in 2 RCTs	Median 7**	MD -0.32 (CI -3.20 to 2.56)	Very low ⊕⊕⊕⊕ (Very serious indirectness and serious imprecision)†	Convalescent plasma may have little to no effect in reducing duration of ICU stay, but the evidence is very uncertain.
Time on mechanical ventilation, d	Based on 83 patients with influenza in 2 RCTs	Median 9.25**	MD -3.67 (CI -7.70 to 0.36)	Very low ⊕⊕⊕⊕ (Very serious indirectness and serious imprecision)†	Convalescent plasma may reduce days of mechanical ventilation, but the evidence is very uncertain.
Serious adverse events	RR 0.85 (95% CI 0.56 to 1.29) Based on 576 patients with influenza in 3 RCTs	80††	-12 (-35 to 23)	Low ⊕⊕⊕⊕ (Serious indirectness and imprecision)‡‡	Convalescent plasma may result in little or no difference in the number of serious adverse events.

DEVELOPMENTS IN DIAGNOSTICS

A FULLY AUTOMATIC DEEP LEARNING SYSTEM FOR COVID-19 DIAGNOSTIC AND PROGNOSTIC ANALYSIS

Wang S, Zha Y, Li W, Wu Q, Li X, Niu M, Wang M, Qiu X, Li H, Yu H, Gong W, Bai Y, Li L, Zhu Y, Wang L, Tian J.. Eur Respir J. 2020 May 22:2000775. doi: 10.1183/13993003.00775-2020. Online ahead of print.

Level of Evidence: 4 -

BLUF

A retrospective cohort study conducted across 7 Chinese cities (Figure 1) used 4106 lung cancer patient CTs and EGFR sequences to "pre-train" their deep learning (DL) system (Figure 2), while the remaining 1266 patients were used in one of three ways: to further train the DL program to differentiate between COVID-19 vs other pneumonia, to validate the system's training against other pneumonia (Area Under the Curve = 0.87 and 0.88, Figure 3) and viral pneumonia (AUC = 0.86), and finally, to determine the DL's ability to provide an accurate prognosis, separating patients into high-risk ($p=0.013$) and low-risk ($p=0.014$) groups. The authors believe that utilization of the DL system can expedite COVID-19 diagnoses, as well as provide accurate identification of high-risk patients needing specialized care.

SUMMARY

The authors collected data from seven Chinese cities and provinces. Patients who had COVID-19 or other pneumonia and had CT imaging performed were included in the analysis (n=5372). The majority of these cases (n=4106) were patients with lung cancer who had both CT imaging and EGFR sequencing performed. Data from these patients was used to "pre-train" a deep learning (DL) artificial intelligence program. The remaining 1266 cases (n=924 COVID-19 positive, of these n=471 had 5+ days of follow-up; n=342 pneumonia positive/COVID-19 negative) were analyzed in a three step process.

- A 709 case training set from Wuhan and Henan was used to further train of the DL programming in identification of COVID-19 vs other pneumonia.
- Four additional data sets of known COVID-19 positive and negative cases were used for validation of this training.

- Patients with 5+ days of follow up from the Wuhan and Henan training set and the four validations sets were analyzed to determine the prognostic value of the system.
- See figure 1 for details.

Results from the investigation were as follows:

- The DL system is effectively able to differentiate COVID-19 from other pneumonia (AUC = 0.87 and 0.88) and viral pneumonia (AUC= 0.86). The DL score showed a significant difference between COVID-19 and other pneumonia groups ($p<0.0001$) (Figure 3).
- The DL system is able to designate patients from the COVID-19 dataset (n=471 patients with 5+ days follow-up) into high-risk ($p=0.013$) and low-risk ($p=0.014$) groups based on severity of the lung abnormalities on chest CT.

These findings demonstrate that the automated DL system for analyzing chest CT imaging is helpful in both diagnosis and prognosis of COVID-19. The authors believe this approach will be helpful in optimizing medical resources and early treatment of COVID-19 patients and may identify high-risk groups for special care and prioritization of resources.

ABSTRACT

Coronavirus disease 2019 (COVID-19) has spread globally, and medical resources become insufficient in many regions. Fast diagnosis of COVID-19, and finding high-risk patients with worse prognosis for early prevention and medical resources optimisation is important. Here, we proposed a fully automatic deep learning system for COVID-19 diagnostic and prognostic analysis by routinely used computed tomography. We retrospectively collected 5372 patients with computed tomography images from 7 cities or provinces. Firstly, 4106 patients with computed tomography images were used to pre-train the DL system, making it learn lung features. Afterwards, 1266 patients (924 with COVID-19, and 471 had follow-up for 5+ days; 342 with other pneumonia) from 6 cities or provinces were enrolled to train and externally validate the performance of the deep learning system. In the 4 external validation sets, the deep learning system achieved good performance in identifying COVID-19 from other pneumonia (AUC=0.87 and 0.88) and viral pneumonia (AUC=0.86). Moreover, the deep learning system succeeded to stratify patients into high-risk and low-risk groups whose hospital-stay time have significant difference ($p=0.013$ and 0.014). Without human-assistance, the deep learning system automatically focused on abnormal areas that showed consistent characteristics with reported radiological findings. Deep learning provides a convenient tool for fast screening COVID-19 and finding potential high-risk patients, which may be helpful for medical resource optimisation and early prevention before patients show severe symptoms.

FIGURES

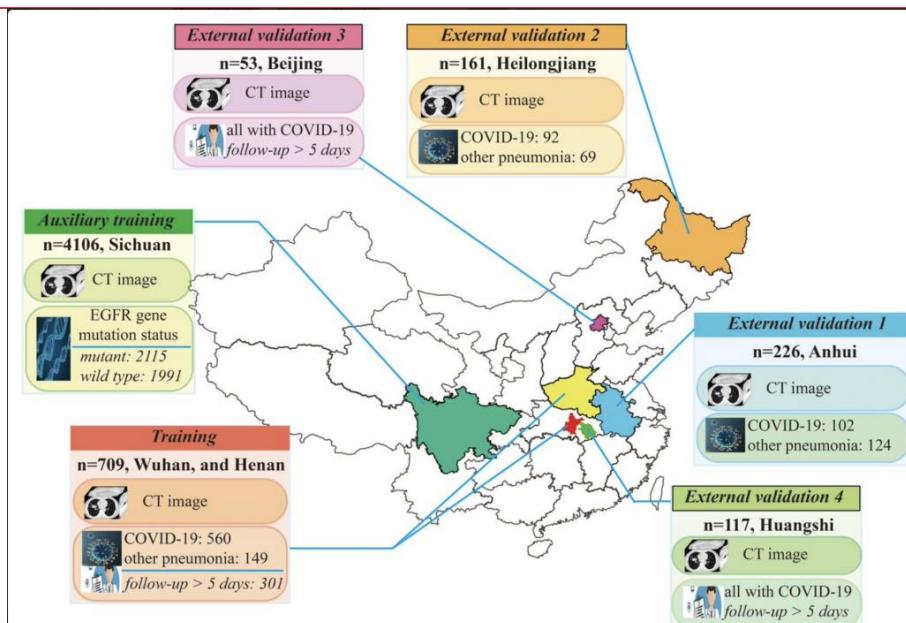


Figure 1. Datasets used in this study. A total of 5372 patients with CT images from 7 cities or provinces were enrolled in this study. The auxiliary training set includes 4106 patients with lung cancer and EGFR gene mutation status information, and is used to pre-train the COVID-19 Net to learn lung features from CT images. The training set includes 709 patients from Wuhan city and Henan province. The external validation set 1 (226 patients) from Anhui province, and the external validation set 2 (161 patients) from Heilongjiang province are used to test the diagnostic performance of the DL system. The external validation set 3 (53 patients with COVID-19) from Beijing, and the external validation set 4 (117 patients with COVID-19) from Huangshi city are used to evaluate the prognostic performance of the DL system.

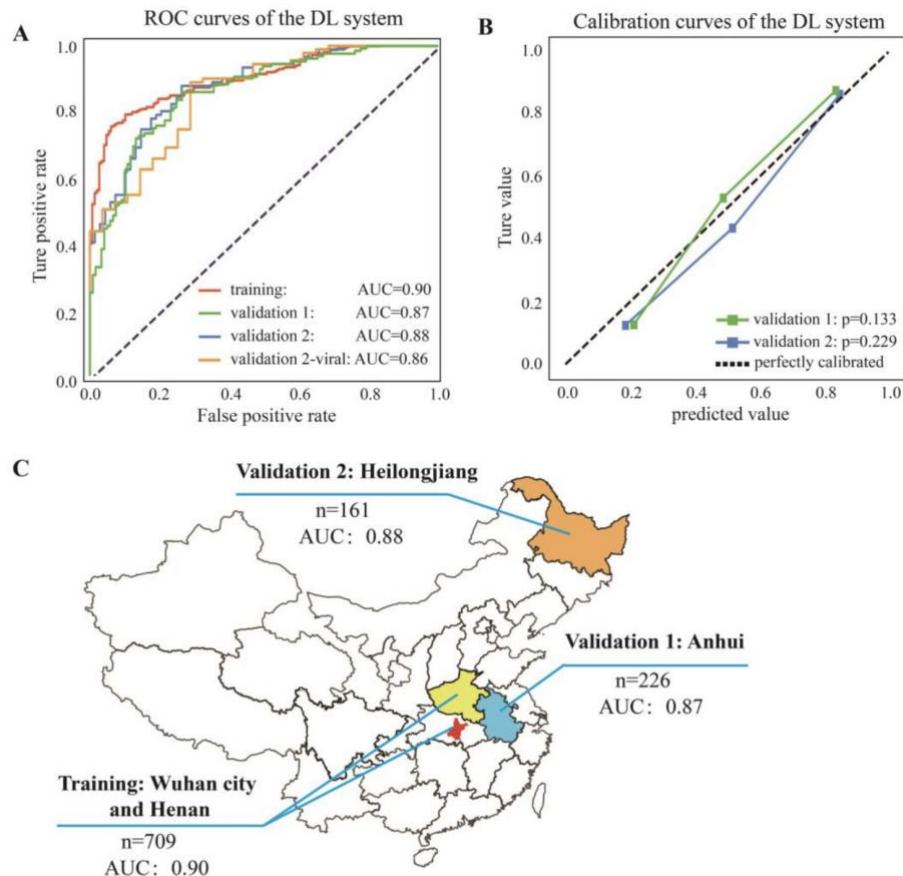


Figure 3. Diagnostic performance of the DL system. a). ROC curves of the DL system in the training set and the two independent external validation sets. Validation 2-viral is a stratified analysis using the patients with COVID-19 and viral pneumonia in the validation set 2. b). Calibration curves of the DL system in the two external validation sets. c). AUC and distribution of the training set and the two external validation sets.

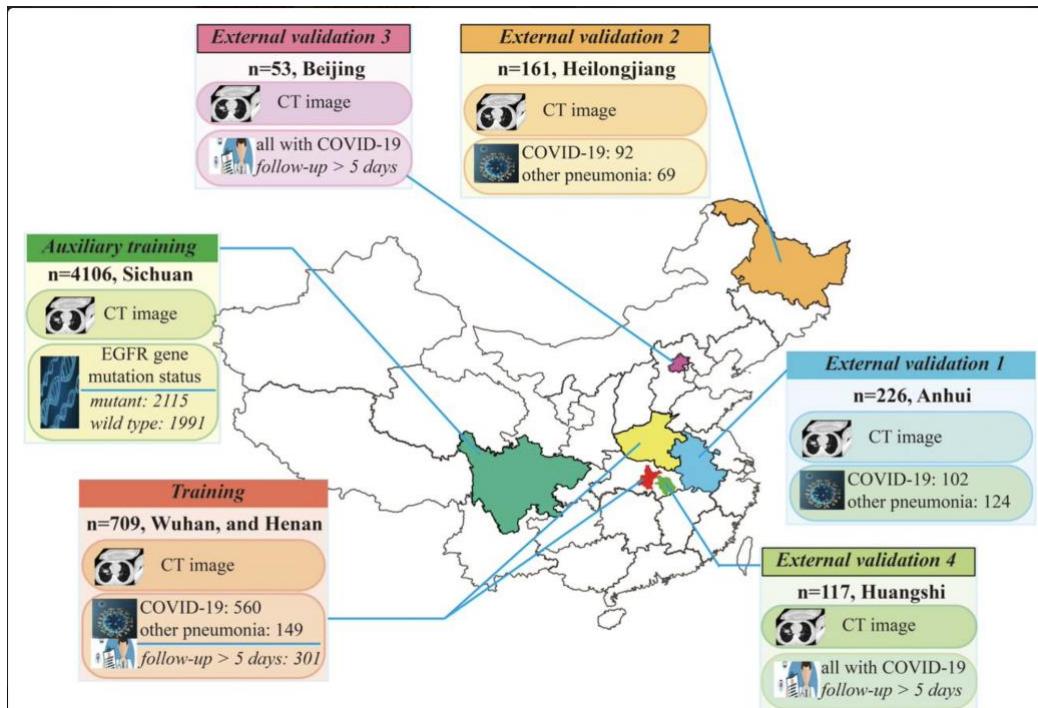


Figure 3. Diagnostic performance of the DL system. a). ROC curves of the DL system in the training set and the two independent external validation sets. Validation 2-viral is a stratified analysis using the patients with COVID-19 and viral pneumonia in the validation set 2. b). Calibration curves of the DL system in the two external validation sets. c). AUC and distribution of the training set and the two external validation sets.

A STUDY ON CLINICAL EFFECT OF ARBIDOL COMBINED WITH ADJUVANT THERAPY ON COVID-19

Chen W, Yao M, Fang Z, Lv X, Deng M, Wu Z.. J Med Virol. 2020 Jun 8. doi: 10.1002/jmv.26142. Online ahead of print.
Level of Evidence: 3 - Non-randomized controlled cohort/follow-up study

BLUF

A randomized control trial of 62 hospitalized COVID-19 patients conducted at First Hospital of Jiaxing (China) from January to March 2020 sought to compare outcomes of the control group receiving standard therapy (consisting of an antiviral agent (interferon) and as needed treatments for symptoms of respiratory inflammation (Asmeton, Eucalyptol, and Moxifloxacin), dyspnea (oxygen therapy), fever (physical cooling and ibuprofen), and cough/expectoration (Mucosolvan), n=20) versus those receiving the same standard treatment plus Arbidol (a hemagglutinin inhibitor, n=42). Results showed a shorter duration of cough and fever in the treatment group compared to control (table 2), suggesting that COVID-19 symptom duration may be shortened with the addition of Arbidol to standard treatment.

ABSTRACT

OBJECTIVES: This study aims to explore the clinical effect of Arbidol (ARB) combined with adjuvant therapy on patients with coronavirus disease 2019 (COVID-19).

METHODS: The study included 62 patients with COVID-19 admitted to the First Hospital of Jiaxing from January to March, 2020, and all patients were divided into the test group and the control group according to whether they received ARB during hospitalization. Various indexes in the two groups before and after treatment were observed and recorded, including fever, cough, hypodynamia, nasal obstruction, nasal discharge, diarrhea, C-reactive protein (CRP), procalcitonin (PCT), blood routine indexes, blood biochemical indexes, time to achieve negative virus nucleic acid and so on.

RESULTS: The fever and cough in the test group were relieved markedly faster than those in the control group ($p<0.05$); there was no obvious difference between the two groups concerning the percentage of patients with abnormal CRP, PCT, blood routine indexes, aspartate aminotransferase and alanine aminotransferase ($p>0.05$); the time for two consecutive negative nucleic acid tests in the test group were shorter than that in the control group; the hospitalization period of the patients in the test group and control group were (16.5 + 7.14) d and (18.55 + 7.52) d, respectively.

CONCLUSION: ARB combined with adjuvant therapy might be able to relieve the fever of COVID-19 sufferers faster and accelerate the cure time to some degree, hence it's recommended for further research clinically. This article is protected by copyright. All rights reserved.

FIGURES

Table 2: Table 2 Indexes recovery time of the two groups

Indexes	Time for recovery (day)	Test group (n=42)	Control group (n=20)	P values
Fever	4.98 ± 1.79	6.01 ± 1.80	0.021	

Dry cough	4.39 ± 1.30	5.08 ± 1.42	0.040
Nasal obstruction	3.42 ± 0.85	3.36 ± 1.09	0.800
Nasal discharge	3.95 ± 0.27	3.88 ± 0.36	0.366
Sore throat	3.47 ± 1.14	3.91 ± 1.28	0.139
Hypodynamia	2.25 ± 0.56	2.11 ± 0.48	0.340
Diarrhea	3.39 ± 0.62	3.57 ± 0.75	0.284

Table 2. Table 2 Indexes recovery time of the two groups

ANTIVIRAL EFFICACIES OF FDA-APPROVED DRUGS AGAINST SARS-COV-2 INFECTION IN FERRETS

Park SJ, Yu KM, Kim YI, Kim SM, Kim EH, Kim SG, Kim EJ, Casel MAB, Rollon R, Jang SG, Lee MH, Chang JH, Song MS, Jeong HW, Choi Y, Chen W, Shin WJ, Jung JU, Choi YK.. mBio. 2020 May 22;11(3):e01114-20. doi: 10.1128/mBio.01114-20.

Level of Evidence: 5 -

BLUF

An in vivo study performed in the Republic of Korea in collaboration with researchers in California, USA evaluate efficacies of antiviral treatments against COVID-19 in a ferret infection model. Only emtricitabine-tenofovir showed decreased in vivo viral titers compared to phosphate-buffered saline in nasal washes. Hydroxychloroquine sulfate and lopinavir-ritonavir showed no efficacy.

ABSTRACT

Due to the urgent need of a therapeutic treatment for coronavirus (CoV) disease 2019 (COVID-19) patients, a number of FDA-approved/repurposed drugs have been suggested as antiviral candidates at clinics, without sufficient information. Furthermore, there have been extensive debates over antiviral candidates for their effectiveness and safety against severe acute respiratory syndrome CoV 2 (SARS-CoV-2), suggesting that rapid preclinical animal studies are required to identify potential antiviral candidates for human trials. To this end, the antiviral efficacies of lopinavir-ritonavir, hydroxychloroquine sulfate, and emtricitabine-tenofovir for SARS-CoV-2 infection were assessed in the ferret infection model. While the lopinavir-ritonavir-, hydroxychloroquine sulfate-, or emtricitabine-tenofovir-treated group exhibited lower overall clinical scores than the phosphate-buffered saline (PBS)-treated control group, the virus titers in nasal washes, stool specimens, and respiratory tissues were similar between all three antiviral-candidate-treated groups and the PBS-treated control group. Only the emtricitabine-tenofovir-treated group showed lower virus titers in nasal washes at 8 days postinfection (dpi) than the PBS-treated control group. To further explore the effect of immune suppression on viral infection and clinical outcome, ferrets were treated with azathioprine, an immunosuppressive drug. Compared to the PBS-treated control group, azathioprine-immunosuppressed ferrets exhibited a longer period of clinical illness, higher virus titers in nasal turbinate, delayed virus clearance, and significantly lower serum neutralization (SN) antibody titers. Taken together, all antiviral drugs tested marginally reduced the overall clinical scores of infected ferrets but did not significantly affect in vivo virus titers. Despite the potential discrepancy of drug efficacies between animals and humans, these preclinical ferret data should be highly informative to future therapeutic treatment of COVID-19 patients.

IMPORTANCE The SARS-CoV-2 pandemic continues to spread worldwide, with rapidly increasing numbers of mortalities, placing increasing strain on health care systems. Despite serious public health concerns, no effective vaccines or therapeutics

have been approved by regulatory agencies. In this study, we tested the FDA-approved drugs lopinavir-ritonavir, hydroxychloroquine sulfate, and emtricitabine-tenofovir against SARS-CoV-2 infection in a highly susceptible ferret infection model. While most of the drug treatments marginally reduced clinical symptoms, they did not reduce virus titers, with the exception of emtricitabine-tenofovir treatment, which led to diminished virus titers in nasal washes at 8 dpi. Further, the azathioprine-treated immunosuppressed ferrets showed delayed virus clearance and low SN titers, resulting in a prolonged infection. As several FDA-approved or repurposed drugs are being tested as antiviral candidates at clinics without sufficient information, rapid preclinical animal studies should proceed to identify therapeutic drug candidates with strong antiviral potential and high safety prior to a human efficacy trial.

FIGURES

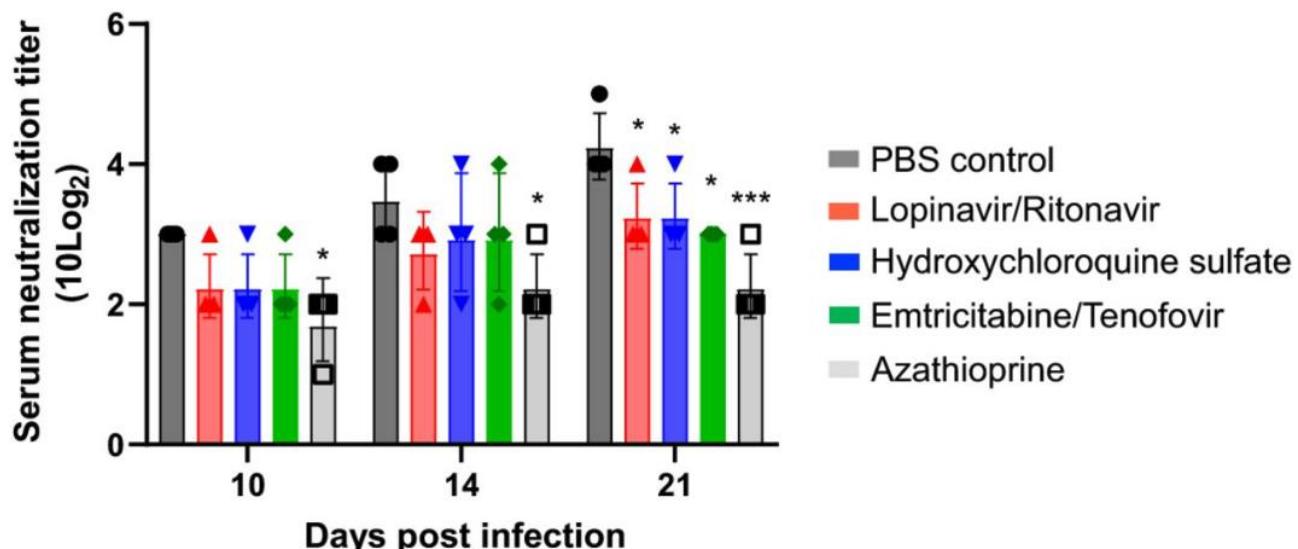


Figure 4. Comparison of serum neutralization antibody titers of drug-treated ferrets. Blood was collected at 10, 14, and 21 dpi from each group of ferrets ($n = 4$), and serum neutralization antibody titers were measured in Vero cells. The serum neutralization titer of each ferret is represented by an individual dot in each bar graph. Asterisks indicate statistical significance between the control and each group, as determined by two-way ANOVA and subsequent Dunnett's test (*, $P < 0.05$; ***, $P < 0.001$).

PREDICTIONS OF SYSTEMIC, INTRACELLULAR, AND LUNG CONCENTRATIONS OF AZITHROMYCIN WITH DIFFERENT DOSING REGIMENS USED IN COVID-19 CLINICAL TRIALS

Hughes JH, Sweeney K, Ahadieh S, Ouellet D.. CPT Pharmacometrics Syst Pharmacol. 2020 Jun 8. doi: 10.1002/psp4.12537. Online ahead of print.

Level of Evidence: Other - Modeling

BLUF

Authors affiliated with Pfizer Inc. developed a population pharmacokinetic model to predict azithromycin concentration in lung tissue, poly/mononuclear cells (PBL/PMN), and alveolar macrophages (AM) compared to in vitro 90% effective concentrations in order to optimize dosing in patients with SARS-CoV-2. They found azithromycin accumulated most in PBL/PMNs and AMs with exposure depending on total dose administered, not specific dosing regimens (Figure 4). They hope that this information can help support the use of azithromycin in the current management of COVID-19 and in future clinical trials.

ABSTRACT

Azithromycin, a broad-spectrum macrolide antibiotic, is being investigated in patients with COVID-19. A population pharmacokinetic model was implemented to predict lung, intracellular poly/mononuclear cell (PBM/PML), and alveolar macrophage (AM) concentrations using published data and compared against preclinical EC90 for SARS-CoV-2. The final model described the data reported in 8 publications adequately. Consistent with its known properties, concentrations were higher in AM and PBM/PML, followed by lung tissue, and lowest systemically. Simulated PBM/PML concentrations exceeded EC90 following the first dose and for approximately 14 days following 500 mg QD for 3 days or 500 mg QD for 1 day/250 mg QD on days 2-5, 10 days following a single 1000 mg dose, and for more than 20 days with 500 mg QD for 10 days. AM

concentrations exceeded the IC90 for more than 20 days for all regimens. These data will better inform optimization of dosing regimens for azithromycin clinical trials.

FIGURES

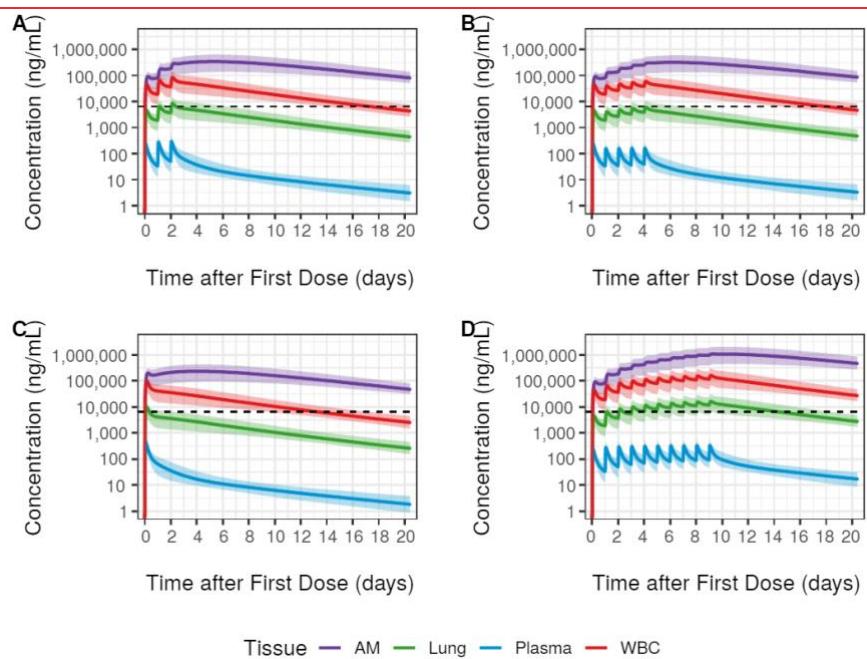


Figure 4. Final model simulation of azithromycin concentrations for different treatment regimens. Treatment regimens were: (A) 500 mg daily for 3 days; (B) 500 mg initial dose, followed by 250 mg daily for 4 days; (C) 1000 mg single dose; (D) 500 mg daily for 10 days. Solid lines represent the median concentration from 1000 simulated individuals (body weight 79kg), while shaded areas represent the 90% prediction intervals. Black dashed line represents in vitro IC90.

DRUGS BEING INVESTIGATED FOR CHILDREN WITH COVID-19

Deniz M, Tapisiz A, Tezer H.. Acta Paediatr. 2020 Jun 7. doi: 10.1111/apa.15399. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

This article written by authors from Gazi University in Turkey reviews two drugs (remdesivir and favipiravir) currently under investigation for the treatment of COVID-19 in pediatric populations, both of which drew interest based on their role in previous outbreaks; however, neither medication has yet been proven to be effective in treating children with COVID-19. Remdesivir has shown promise in vitro against SARS-CoV-2 and is currently in phase three trials in adults and in children above 12 years of age. Favipiravir demonstrated faster viral clearance and higher recovery rates than lopinavir and ritonavir in patients above the age of 16 and could be utilized in pediatric patients.

ABSTRACT

We were interested to read the review paper on COVID-19 by Ludvigsson in *Acta Paediatrica* (1). The author mentioned that COVID-19 appeared to be milder in children than in adults but said there was a knowledge gap about antiviral treatment in severely ill patients. We would like to provide some comments about the experimental drugs that are being considered to treat children with the disease.

INFLAMMASOMES AND PYROPTOSIS AS THERAPEUTIC TARGETS FOR COVID-19

Yap JKY, Moriyama M, Iwasaki A.. *J Immunol*. 2020 Jun 3:ji2000513. doi: 10.4049/jimmunol.2000513. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

This review article discusses the potential benefits of inhibiting inflammasomes, as a means of treating patients with severe COVID-19. In particular the NLRP3 inflammasome is highlighted as a potential target, but additional studies are recommended to determine the safety and efficacy of these immune modulators.

ABSTRACT

The inflammatory response to severe acute respiratory syndrome-related coronavirus 2 infection has a direct impact on the clinical outcomes of coronavirus disease 2019 patients. Of the many innate immune pathways that are engaged by severe acute respiratory syndrome-related coronavirus 2, we highlight the importance of the inflammasome pathway. We discuss available pharmaceutical agents that target a critical component of inflammasome activation, signaling leading to cellular pyroptosis, and the downstream cytokines as a promising target for the treatment of severe coronavirus disease 2019-associated diseases.

MENTAL HEALTH & RESILIENCE NEEDS

COVID-19'S IMPACT ON HEALTHCARE WORKFORCE

THE SOCIAL PSYCHOLOGICAL IMPACT OF THE COVID-19 EPIDEMIC ON MEDICAL STAFF IN CHINA: A CROSS-SECTIONAL STUDY

Dong ZQ, Ma J, Hao YN, Shen XL, Liu F, Gao Y, Zhang L.. Eur Psychiatry. 2020 Jun 1:1-22. doi: 10.1192/j.eurpsy.2020.59.

Online ahead of print.

Level of Evidence: 3 - Local non-random sample

BLUF

A cross sectional study of 4,618 health professionals in Sichuan and Yunnan done via anonymous questionnaires between March 2-13, 2020 found a higher Huaxi Emotional Distress Index (HEI) for those exposed to the COVID-19 outbreak. 24.2% of those surveyed experienced higher levels of anxiety and/or depressive symptoms since the start of the COVID-19 outbreak. While these concerns were related to exposure of family and friends, family relationships were also found to have a protective effect against higher HEI levels.

IMPACT ON PUBLIC MENTAL HEALTH

RESILIENCE IS SPREADING: MENTAL HEALTH WITHIN THE COVID-19 PANDEMIC

PeConga EK, Gauthier GM, Holloway A, Walker RSW, Rosencrans PL, Zoellner LA, Bedard-Gilligan M.. Psychol Trauma. 2020 Jun 4. doi: 10.1037/tra0000874. Online ahead of print.

Level of Evidence: Other - Opinion

BLUF

This article addresses four common misconceptions about resilience and shares how to promote individual and community resiliency through social support, adaptive meaning, and direct prosocial behaviors aimed at reaching those most vulnerable in the pandemic.

SUMMARY

Four misconceptions are challenged in this article.

1. Trauma exposure inevitably means mental illness: Our world collectively demonstrates a strong resolve to overcome traumatic, life-altering events, as has been shown in the recent past with the World Trade Center attacks and previous SARS outbreak. Few individuals (<10-15%) suffer from clinically significant post-traumatic stress disorder symptoms related to these events. Thus, history suggests we will develop a long-term resilience towards the COVID-19 pandemic.

2. Resilient people do not have bad days or weeks: Resilience may vary greatly depending on the stressor. Each individual responds differently while coping from a stressful event, but importantly, everyone continues adapting.

3. Resilience is something you either have or you do not have: Resilience is actively shaped by behavioral, cognitive, and environmental processes. Resilience is developed most strongly by engaging in prosocial acts.

4. The risk to mental health from COVID-19 is a hoax: Individuals' mental health has been affected in the short-term. However, the community can actively meet the needs of those facing adversity at the advent of the pandemic.

ABSTRACT

The COVID-19 global pandemic is in many ways uncharted mental health territory, but history would suggest that long-term resilience will be the most common outcome, even for those most directly impacted by the outbreak. We address 4 common myths about resilience and discuss ways to systematically build individual and community resiliency. Actively cultivating social support, adaptive meaning, and direct prosocial behaviors to reach the most vulnerable can have powerful resilience promoting effects.

RESOURCES

UNITED STATES DISTRIBUTION OF PATIENTS AT RISK FOR COMPLICATIONS RELATED TO COVID-19

Smith-Ray R, Roberts EE, Littleton DE, Singh T, Sandberg T, Taitel M.. JMIR Public Health Surveill. 2020 Jun 8. doi: 10.2196/19606. Online ahead of print.

Level of Evidence: 3 - Modeling

BLUF

A resource created by researchers affiliated with Walgreen's (a United States pharmacy chain) utilizes health data from prescription orders to identify a geographic distribution of U.S. patients most at risk for developing serious complications from COVID-19 inferred by diagnoses of comorbidities such as COPD, Hypertension and Diabetes (Figure 1). A non-random sample of approximately 10% of the U.S. population was included in this project (average age = 55, average number of comorbidities = 2-3) and the authors indicate that the interactive map could support planning of healthcare resource distribution.

ABSTRACT

BACKGROUND: The COVID-19 virus has spread exponentially across the United States. Older adults with underlying health conditions are at especially high risk of developing life-threatening complications if infected. Most ICU admissions and non-ICU hospitalizations have been among patients with at least one underlying health condition.

OBJECTIVE: This study developed a model to estimate the risk status of patients of a nationwide pharmacy chain in the US and to identify the geographic distribution of patients who are at the highest risk of severe COVID-19 complications.

METHODS: A risk model was developed using a training test split approach to identify patients who are at high-risk of developing serious complications from COVID-19. Adult patients (age 18+) were identified from the Walgreens pharmacy electronic data warehouse. Patients were considered eligible to contribute data to the model if they had at least one prescription filled at a Walgreens location between October 27, 2019 and March 25, 2020. Risk parameters included age, whether the patient is being treated for a serious or chronic condition, and urban density classification. Parameters were differentially weighted based on their association with severe complications reported in earlier cases. An at-risk rate per 1000 population was calculated at the county level, and ESRI ArcMap was used to depict rate of patients at high risk for severe complications from COVID-19. Real-time COVID-19 cases captured by the Johns Hopkins University Center for Systems Science and Engineering (CSSE) was layered in the risk map to show where cases exist relative to the high risk populations.

RESULTS: Of the 29,824,409 adults included in this study, the average age is 55 years old, 15% have at least one specialty medication, and the average patient has 2 to 3 comorbidities. Nearly 20% of patients have the greatest risk score, and an additional 26.58% of patients are considered high risk with a scores of 8 - 10. Age accounts for 53% of a patient's total risk, followed by the number of comorbidities (30%), inferred COPD, Hypertension, or Diabetes (14%), and urban density classification (4%).

CONCLUSIONS: This risk model utilizes data from approximately 10% of the US population. Currently, this is the most comprehensive US model to estimate and depict county-level prognosis of COVID-19 infection. This study shows that there are counties across the US whose residents are at high risk of developing severe complications from COVID-19. Our county-level risk estimates may be used alongside other data sets to improve the accuracy of anticipated healthcare resource needs. The interactive map can also aid in proactive planning and preparations among employers that are deemed critical, such as pharmacies and grocery stores to prevent the spread of COVID-19 within their facilities.

FIGURES

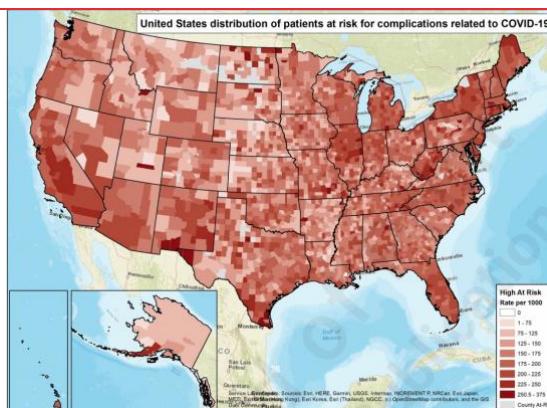


Figure 1. United States distribution of patients at risk for complications related to COVID-19.

A GUIDE TO COVID-19: A GLOBAL PANDEMIC CAUSED BY THE NOVEL CORONAVIRUS SARS-COV-2

Atzrodt CL, Maknojia I, McCarthy RDP, Oldfield TM, Po J, Ta KTL, Stepp HE, Clements TP.. FEBS J. 2020 May 23. doi: 10.1111/febs.15375. Online ahead of print.

Level of Evidence: Other -

BLUF

Scientists from Vanderbilt University in Nashville, Tennessee, present a scoping review of our knowledge on prior coronavirus epidemics, the current COVID-19 crisis, and endeavors underway to address this pandemic.

SUMMARY

This scoping review of COVID-19 and prior coronavirus pandemics highlights many features to provide a detailed overview of what is currently known:

- Coronaviridae are classified as single-stranded, positive-sense RNA genome-bearing viruses.
- Notable coronavirus strains include SARS-CoV (with 8000 cases and 774 deaths worldwide), MERS-CoV (considered the most lethal), and the current SARS-CoV-2 strain (which has affected 214 countries and territories as of April 2020).
- Although the symptoms of SARS-CoV-2 are similar to prior strains, it is significantly more infectious in transmission, with a high likelihood of asymptomatic transmission and an basic reproduction number (R_0) likely between 2.2 to 3.22.
- RT-PCR has arisen as the most common form of testing, but clinicians are still navigating potential false negative and false positive results.
- There is no current cure or vaccine for this infection, but the World Health Organization (WHO) has reported four drugs as potential candidates: remdesivir, lopinavir/ritonavir, interferon beta-1a, and hydroxychloroquine/chloroquine. Governments have also created more lenient regulations regarding possible vaccine candidates as well.

ABSTRACT

The emergence of the SARS-CoV-2 strain of the human coronavirus has thrown the world into the midst of a new pandemic. In the human body, the virus causes COVID-19, a disease characterized by shortness of breath, fever, and pneumonia, which can be fatal in vulnerable individuals. SARS-CoV-2 has characteristics of past human coronaviruses, with close genomic similarities to SARS-CoV, the virus that causes the disease SARS. Like these related coronaviruses, SARS-CoV-2 is transmitted through the inhalation of droplets and interaction with contaminated surfaces. Across the world, laboratories are developing candidate vaccines for the virus - with vaccine trials underway in the US and the United Kingdom - and considering various drugs for possible treatments and prophylaxis. Here, we provide an overview of SARS-CoV-2 by analyzing its virology, epidemiology, and modes of transmission while examining the current progress of testing procedures and possible treatments through drugs and vaccines.

ACKNOWLEDGEMENTS

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