The Daily COVID-19 Literature Surveillance Summary

January 04, 2021

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COVID-19 Daily Literature Surveillance

COVID19LST

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

LEVEL OF EVIDENCE

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

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

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

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

How to cite the Levels of Evidence Table

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

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

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

EXECUTIVE SUMMARY

Climate

- A systematic review by an international team of researchers highlights the significant underrepresentation of geriatric patients in published COVID-19 randomized control trials (RCTs). In the 12 RCTs included in the review, patients had mean age of 56.3 years, and were on average 20 years younger than patients from large observational trials. One explanation for this discrepancy is the strict exclusion criteria used for RCTs, which commonly exclude patients with cognitive impairment and multiple comorbidities frequently seen in the elderly population. The authors strongly advocate for future RCTs to include this vulnerable population that has been disproportionately affected by the COVID-19 pandemic.

Epidemiology

- Pediatric ischemic stroke is an infrequent complication of SARS-CoV-2. Physician members of the International Pediatric Stroke Study Group surveyed 61 international sites to assess the prevalence of SARS-CoV-2 infection in pediatric stroke patients. They found 3.6% (6/166) of pediatric arterial ischemic stroke, 0.9% (1/108) of neonatal arterial ischemic stroke, 1.9% (1/54) of pediatric cerebral sinovenous thrombosis, and zero (0/33) neonatal cerebral sinovenous thrombosis patients were positive for SARS-CoV-2. Authors suggest these results indicate that SARS-CoV-2 does not appear to increase the risk of stroke in neonatal and pediatric populations but acknowledge that more robust testing is needed to determine any role the virus has in pediatric stroke.

Transmission & Prevention

- Dry heat incubation and ambient temperature fail to consistently inactivate SARS-CoV-2 on N95 respirators. Internists and microbiologists from University of New Mexico assessed whether dry heat incubation could decontaminate N95 respirators and found SARS-CoV-2 was not inactivated when N95 coupons inoculated with the virus were heated to 60-75 degrees Celsius for either 30 or 60 minutes when placed on parchment paper but was inactivated when placed on tissue culture plates. When intact 3M 1860 N95 respirators were incubated at 70-75 degrees Celsius for 60 minutes, SARS-CoV-2 was not inactivated. Authors suggests that dry heat incubation is not a consistently effective method for deactivating SARS-CoV-2 on N95 respirators.

- SARS-CoV-2 appears to persist on personal protective equipment (PPE) for up to several days post exposure. Virologists from the United States Army Medical Research Institute of Infectious Diseases in Detrick, Maryland compared the stability of SARS-CoV-2 on multiple models of personal protective equipment used during airway procedures following 4.3 log10 plaque-forming units (PFUs) of SARS-CoV-2 exposure. They found that even 72 hours after exposure, between 1.1 and 2.3 log10 PFU/mL of SARS-CoV-2 was detectable, depending on material. Authors suggest that the persistence of SARS-CoV-2 on personal protective equipment highlights the importance of appropriate doffing, disposal, and disinfection in order to prevent fomite transmission.

- Decontamination of SARS-CoV-2 contaminated N95 filtering facepiece respirators (FFRs) can be achieved with moist heat generated by a multicooker. A multidisciplinary team of scientists from Battelle Memorial Institute in Ohio inoculated patches/coupons from N95 respirators with SARS-CoV-2 virus suspended in simulated saliva or lung fluids and subjected the samples to a temperature of 65°C for 30 minutes in a multicooker (i.e. crockpot) filled partially with water. They found that SARS-CoV-2 virus was undetectable by 20 minutes regardless of the respirator's model. All masks met performance criteria for collection efficiency (>95%) and inhalation resistance (<35 mmH2O) after 10 cycles if placed in a paper bag to absorb moisture during decontamination and allowed 30 minutes to dry. The authors conclude that moist heat treatment (65°C for 30 minutes) with a multicooker can successfully decontaminate N95 respirators which could allow for re-use during times of limited supply.

R&D: Diagnosis & Treatments

- Efficacy of lopinavir/ritonavir in the treatment of COVID-19 was not found to be considerable according to a systematic review. An international research team from Nested Knowledge, Inc conducted a systematic review of 16 studies assessing the effectiveness and safety of lopinavir/ritonavir (LPV/r) in the treatment of COVID-19 and found the majority of included studies showed no significant improvement in clinical outcomes (RT-PCR negativity, chest-CT findings, mortality, adverse events) following LPV/r treatment, though they could not perform meta-analysis due to the high heterogeneity of the comparison groups. Though their review suggests little survival or clinical benefit of LPV/r in COVID-19, authors recommend larger clinical trials are needed to more definitively explore its potential benefits due to the limitations of currently available data.

- What is the efficacy of COVID-19 vaccines and how good were the trials? Researchers at the Fred Hutch Institute in Seattle, WA collaborate with the University of North Carolina Department of Biostatistics to discuss limitations of current COVID-19 vaccination trials. The main critique of current study designs is the primary endpoint of "virologically confirmed symptomatic COVID-19 disease", which does not provide accurate data on mild or asymptomatic individuals. The authors propose an alternative model that includes 3 primary endpoints: 1) SARS-CoV-2 infection 2) Symptomatic COVID-19 disease 3) Severe COVID-19 disease. They assert that this strategy would provide important data on the vaccine's ability to protect against severe disease and also prevent mild and asymptomatic disease. Simulation studies are included to demonstrate these advantages.

Mental Health & Resilience Needs

- Experiences of New Zealand registered nurses of Chinese ethnicity during the COVID-19 pandemic are brought to light in one study. Nurses from the Waikato Institute of Technology in New Zealand conducted an anonymous online questionnaire of 51 Chinese nurses to assess their experiences at work during the COVID-19 pandemic. They found 47.06% experienced racial hostility due to being Chinese, 41.18% were concerned about catching SARS-CoV-2, and 57.14% felt supported in the workplace by their colleagues. Authors suggest that because New Zealand has a large ethnic-minority nursing base, health organizations must understand and support healthcare workers experiencing racial discrimination during the COVID-19 pandemic to adequately meet the demands on the healthcare system.

TABLE OF CONTENTS

A SYSTEMATIC REVIEW ASSESSING THE UNDER-REPRESENTATION OF ELDERLY ADULTS IN COVID-19 TRIALS

Prendki V, Tau N, Avni T, Falcone M, Huttner A, Kaiser L, Paul M, Leibovici-Weissmann Y, Yahav D; ESCMID Study Group for Infections in the Elderly (ESGIE).. BMC Geriatr. 2020 Dec 20;20(1):538. doi: 10.1186/s12877-020-01954-5.
Level of Evidence: 1 - Systematic review of randomized trials

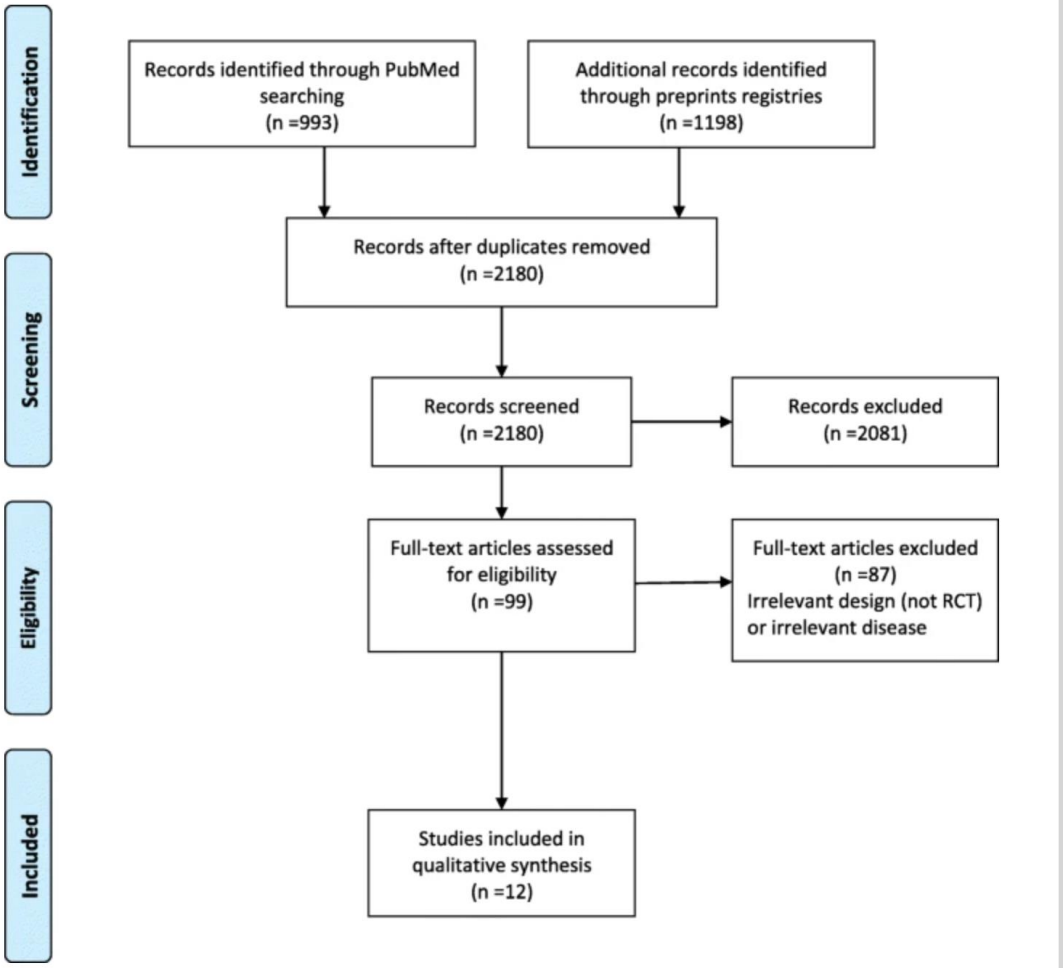
BLUF

A systematic review by an international team of researchers highlights the significant underrepresentation of geriatric patients in published COVID-19 randomized control trials (RCTs). In the 12 RCTs included in the review, patients had mean age of 56.3 years, and were on average 20 years younger than patients from large observational trials. One explanation for this discrepancy is the strict exclusion criteria used for RCTs, which commonly exclude patients with cognitive impairment and multiple comorbidities frequently seen in the elderly population. The authors strongly advocate for future RCTs to include this vulnerable population that has been disproportionately affected by the COVID-19 pandemic.

ABSTRACT

BACKGROUND: Coronavirus disease (COVID-19) has caused a pandemic threatening millions of people worldwide. Yet studies specifically assessing the geriatric population are scarce. We aimed to examine the participation of elderly patients in therapeutic or prophylactic trials on COVID-19. METHODS: In this review, randomized controlled trials (RCTs; n = 12) comparing therapeutic or prophylactic interventions registered on preprint repositories and/or published since December 2019 were analyzed. We searched in PubMed, leading journals websites, and preprint repositories for RCTs and large observational studies. We aimed to describe the age of included patients, the presence of an upper age limit and of adjusted analyses on age, any exclusion criteria that could limit participation of elderly adults such as comorbidities, cognitive impairment, limitation of life expectancy; and the assessment of long-term outcomes such as the need of rehabilitation or institutionalization. Mean participant ages were reported and compared with observational studies. RESULTS: Twelve RCTs assessing drug therapy for COVID-19 were included. Mean age of patients included in RCTs was 56.3 years. An upper age limit was applied in three published trials (25%) and in 200/650 (31%) trials registered at clinicaltrials.gov . One trial reported a subgroup analysis in patients >=65. Patients were excluded for liver-function abnormalities in eight trials, renal disease in six, cardiac disease or risk of torsade de pointes in five, and four for cognitive or mental criteria, which are frequent comorbidities in the oldest patients. Only three trials allowed a family member to provide consent. Patients enrolled in RCTs were on average 20 years younger than those included in large (n >= 1000) observational studies. Seven studies had as their primary outcome a clinical endpoint, but none reported cognitive, functional or quality of life outcomes or need for rehabilitation or long-term care facility placement. CONCLUSIONS: Elderly patients are clearly underrepresented in RCTs, although they comprise the population hardest hit by the COVID-19 pandemic. Long-term outcomes such as the need of rehabilitation or institutionalization were not reported. Future investigations should target specifically this vulnerable population.

Fig. 1



Flow of the Search Procedure for Randomized Controlled Trials

Figure 1. Flow of the Search Procedure for Randomized Controlled Trials

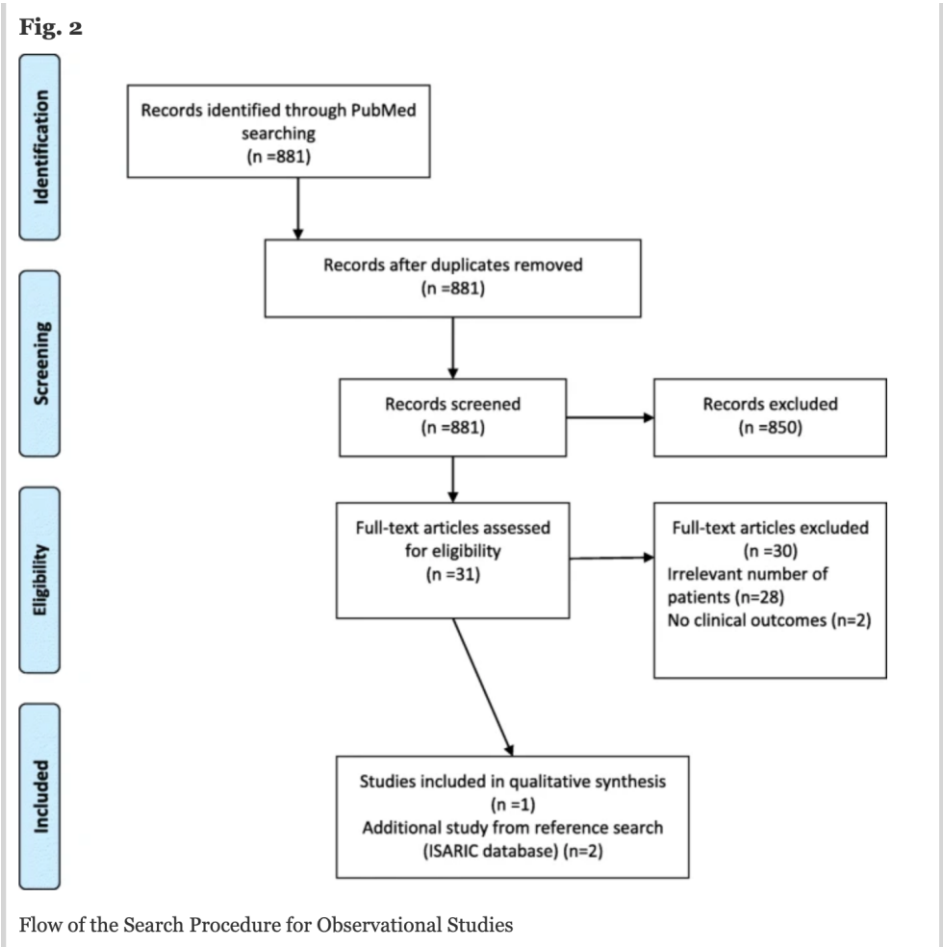
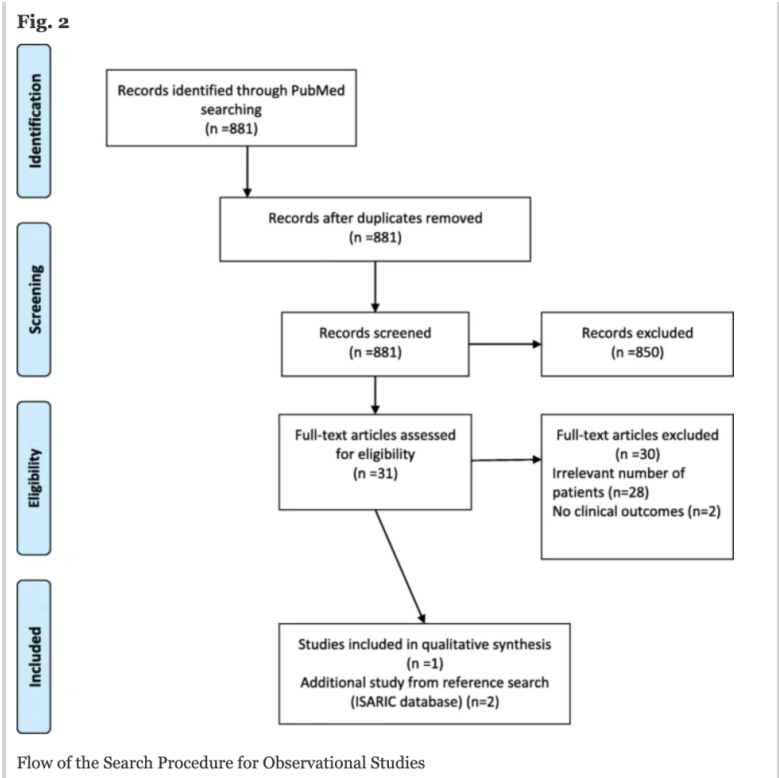


Figure 2. Flow of the Search Procedure for Observational Studies



PRAGMATIC RECOMMENDATIONS FOR SAFETY WHILE CARING FOR HOSPITALIZED PATIENTS WITH CORONAVIRUS DISEASE 2019 (COVID-19) IN LOW- AND MIDDLE-INCOME COUNTRIES

Inglis R, Barros L, Checkley W, Cizmeci EA, Lelei-Mailu F, Pattnaik R, Papali A, Schultz MJ, Ferreira JC, For The Covid-Lmic Task Force.. Am J Trop Med Hyg. 2020 Dec 22. doi: 10.4269/ajtmh.20-1128. Online ahead of print.
Level of Evidence: 5 - Guidelines and Recommendations

BLUF

An international team from the COVID-19 Low and Middle Income Country (LMIC) Task Force offer recommendations for implementing infection prevention and control measures in LMICs where it may be more difficult than in high income countries. They identified five primary questions and performed a literature review to develop best practices, addressing personal protective equipment policies, hand hygiene, and strategies for aerosolizing procedures (Table 1). The authors suggest these recommendations align with the best available evidence and are logistically and economically feasible to implement in LMICs.

ABSTRACT

Infection prevention and control measures to control the spread of COVID-19 are challenging to implement in many low- and middle-income countries (LMICs). This is compounded by the fact that most recommendations are based on evidence that mainly originates in high-income countries. There are often availability, affordability, and feasibility barriers to applying such recommendations in LMICs, and therefore, there is a need for developing recommendations that are achievable in LMICs. We used a modified version of the GRADE method to select important questions, searched the literature for relevant evidence, and formulated pragmatic recommendations for safety while caring for patients with COVID-19 in LMICs. We selected five questions related to safety, covering minimal requirements for personal protective equipment (PPE), recommendations for extended use and reuse of PPE, restriction on the number of times healthcare workers enter patients' rooms, hand hygiene, and environmental ventilation. We formulated 21 recommendations that are feasible and affordable in LMICs.

TABLE 1

Recommendations and suggestions for safety while caring for patients with COVID-19 in low- and middle- income countries

Which items of PPE are mandatory when caring for a patient with COVID-19?

- We *recommend* that healthcare workers providing direct care to suspected or confirmed COVID-19 patients should wear a surgical mask, a single pair of gloves, eye protection (goggles and face shield), and a long-sleeved gown, provided no aerosol generating procedures are being performed (strong recommendation, low quality of evidence).
- We *recommend* that healthcare workers providing direct care to suspected or confirmed COVID-19 patients should wear an N95 respirator when aerosol generating procedures are being carried out, in addition to a single pair of gloves, eye protection, and a long-sleeved gown (strong recommendation, low quality of evidence).
- We *suggest* that institutions provide practical training on how to don and doff PPE safely and establish a policy on what PPE to wear in different scenarios (ungraded best practice statement).
- We *recommend* that all items of PPE for use in a healthcare setting meet the minimum manufacturing standards recommended by the WHO (ungraded best practice statement).
- We *recommend* that all healthcare workers be alert to the risks posed by substandard and counterfeit PPE and be familiar with how to spot suspect items (best practice statement).

Is reuse, extended use, or the substitution of alternative items of PPE a safe alternative to standard PPE when providing care for COVID-19 patients in LMICs?

- We *suggest* the extended use of surgical masks and N95 respirators in preference to reuse as long as the item does not become wet, damaged or difficult to breathe through, in which case it should be discarded (weak recommendation, low quality of evidence).
- If a reuse strategy is adopted for N95 respirators, we *suggest* that one of the three approved methods for decontamination should be used (hydrogen peroxide vapor, moist heat or UV-C radiation). If none are possible, then storing the mask for seven days before reuse by the original wearer is preferable to immediate reuse as a last resort measure (weak recommendation, low quality of evidence).
- If a reuse strategy is adopted for N95 respirators, we *suggest* that face shields be used in conjunction in order to reduce surface contamination of the respirator (weak recommendation, low quality of evidence).
- We *suggest* that surgical masks and disposable gloves are not reused (weak recommendation, very low quality of evidence).
- We *suggest* that cloth masks be used as a last resort by staff as these are better than no protection at all, preferably used alongside face shields (ungraded best practice statement).

In LMICs, is there evidence to guide the number of times that a healthcare worker should enter a COVID-19 patient's room to reduce the risk of infection and preserve PPE while maintaining patient safety?

- We *suggest* that healthcare workers should enter the patient's room as many times as needed to provide essential patient care but minimize the exposure time in the room once activities are completed (ungraded best practice statement).
- We *suggest* minimizing the number of times that a healthcare provider needs to enter the room of a patient with COVID-19 by:
  a. Rationalizing medication dosing and administration times
  b. Timing a patient's turns to coincide with medication administration and bundling other essential activities
  c. Establishing a means of monitoring the patient remotely, e.g. checking on the patient and the monitor through the window, setting the monitor and ventilator alarms to maximum volume
  d. Perform suctioning of the endotracheal tube as needed rather than routinely
  e. Providing awake patients with a means to attract the attention of staff when required, whether mobile phone, bell or improvised rattle
- (ungraded best practice statement)

What methods of hand hygiene are effective for COVID-19 in LMICs?

- When caring for patients with COVID-19, we *recommend* the use of WHO-approved alcohol-based hand sanitiser for a full 30 seconds, with a sufficient volume to ensure complete hand coverage, before and after each patient contact (strong recommendation, moderate quality of evidence).
- If WHO-approved alcohol-based hand sanitiser is not available, or when hands are visibly dirty, we *recommend* washing hands with soap & water for 40 – 60 seconds, followed by drying with a paper towel, before and after each patient contact (strong recommendation, moderate quality of evidence).
- We *suggest* that alcohol-based hand sanitiser is locally produced following the WHO specifications where commercial formulations are not available (ungraded best practice statement).

Can natural ventilation be used in lieu of mechanical environmental ventilation to carry out care involving aerosol-generating procedures for patients with COVID-19 in LMICs?

- Where mechanical air ventilation is not available, we *recommend* that natural ventilation can be an acceptable alternative when carrying out aerosol generating procedures for patients with COVID-19, provided flow rates of at least 160 L/second/patient or 12 air changes per hour are achieved. Where aerosol generating procedures are not performed, 60 L/second/patient or 6 air changes per hour is sufficient (strong recommendation, moderate quality of evidence).
- Where it is not possible to formally measure air flow, we *recommend* the use of a CO_2 analyzer to measure indoor CO_2 as a proxy indicator of ventilation (strong recommendation, moderate quality of evidence).
- We *suggest* that the room where aerosol-generating procedures are performed should be selected or modified to include some or all of the following design features, using the design principles from the WHO Natural Ventilation guidelines:
  a. Large, open windows
  b. Windows on more than one wall; opposite walls if possible
  c. High ceilings
  d. Additional air vents; open skylights or whirligig roof ventilator

  (strong recommendation, moderate quality of evidence)
- In a facility with natural ventilation, we recommend that the windows and other ventilation vents should be left open at all times to allow airflow. The door to the rest of the hospital should be left shut (strong recommendation, moderate quality of evidence).
- In a setting with insufficient natural ventilation, we *recommend* that a hybrid or mixed-mode system of air ventilation be created by installing exhaust fans in conjunction with the natural ventilation measures (strong recommendation, moderate quality of evidence).
- We *recommend* measures to improve natural ventilation should be taken in all areas where COVID-19 patients are being cared for, whether aerosol-generating procedures are being carried out or not (strong recommendation, low quality of evidence).

LMICs = Low- and middle- income countries; PPE = Personal protective equipment.
Grading: see Supplement for explanations.

ASHP PRINCIPLES FOR COVID-19 VACCINE DISTRIBUTION, ALLOCATION, AND MASS IMMUNIZATION

. Am J Health Syst Pharm. 2020 Dec 4;77(24):2112-2113. doi: 10.1093/ajhp/zxaa311.
Level of Evidence: 5 - Guidelines and Recommendations

BLUF

The American Society of Health-System Pharmacists (ASHP) board of directors has released 10 core principles surrounding the release of COVID-19 vaccines to serve as guidelines to support equal and fair vaccine distribution while maximizing effectiveness and percentage of the population vaccinated.

SUMMARY

Some core principles include:
1. Allowing vaccine development and surveillance to be rigorous and transparent.
2. Collaborate with other nations to include a fair and reasonable global vaccine distribution plan.
3. Minimize vaccine misinformation to decrease vaccine hesitance, thereby increasing vaccine uptake by the general population.

ABSTRACT

In an effort to expedite the publication of articles related to the COVID-19 pandemic, AJHP is posting these manuscripts online as soon as possible after acceptance. Accepted manuscripts have been peer-reviewed and copyedited, but are posted online before technical formatting and author proofing. These manuscripts are not the final version of record and will be replaced with the final article (formatted per AJHP style and proofed by the authors) at a later time.

ADULTS

POST-COVID-19 FATIGUE AND ANHEDONIA: A CROSS-SECTIONAL STUDY AND THEIR CORRELATION TO POST-RECOVERY PERIOD

El Sayed S, Shokry D, Gomaa SM.. Neuropsychopharmacol Rep. 2020 Dec 17. doi: 10.1002/npr2.12154. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

Psychiatrists from Hayat National Hospital in Riyadh, Kingdom of Saudi Arabia surveyed 200 recovered COVID-19 patients between July 10 and July 28, 2020 to assess frequency of fatigue and anhedonia. They found high scores across the self-assessment anhedonia and fatigue scales (Table 2), with a statistically significant positive correlation between fatigue and anhedonia (Figure 1) and negative correlation between time after recovery with the anhedonia and fatigue scales (Table 5). Authors suggest that post-COVID-19 sequelae and psychological distress are common after recovery and warrant further monitoring and research.

ABSTRACT

BACKGROUND: Individuals infected by the novel coronavirus (SARS-CoV-2) have experienced different psychiatric manifestations during the period of infectivity and post-COVID-19 infection. Fatigue and anhedonia are among the frequently reported manifestations after recovery from this novel viral pandemic, leading to early evaluation of those patients and proper management of their complaints which have a drastic burden on different domains of life. Also, the period after recovery might have an effect on the severity of these two psychiatric presentations. AIM OF THE WORK: This cross-sectional observational study aimed to investigate the occurrence of post-COVID-19 fatigue and anhedonia and whether the duration after 2 consecutive PCR-negative tests has an implication on the severity of the above-mentioned psychiatric manifestations. METHODS: Socio-demographic characteristics of 200 post-COVID-19 patients were collected, and also, the self-assessment anhedonia scale was used to evaluate the degree of anhedonia. Fatigue assessment scale used to investigate this domain. The study targeted to find a possible correlation between the period after recovery and the other variables including anhedonia and fatigue. RESULTS: The study revealed high scores of different subtypes of self-assessment anhedonia scale (including total intensity, total frequency, and total changes scores) in the studied group, also high score of fatigue assessment scale in those patients. Positive statistically significant correlation between anhedonia and fatigue in post-COVID-19 group, also negative statistically significant correlation between duration after recovery and the other 2 variables(anhedonia and fatigue) in the examined patients. CONCLUSION: Post-COVID-19 fatigue and anhedonia were prevalent and commonly reported in the post-COVID-19 period, also the duration after 2 consecutive negative PCR tests has an implication on the severity rating scale of both anhedonia and fatigue. These findings directed our attention to those reported manifestations which affected the socio-occupational functioning of the individuals during this whole world pandemic.

FIGURES

	Days after recovery from COVID-19		Fatigue assessment scale	
	r	*P*	*r*	*P*
Mean total intensity score	−.760	≤.001*	.728	≤.001*
Mean total frequency score	−.631	≤.001*	.601	≤.001*
Mean total change score	−.559	≤.001*	.515	≤.001*
Mean total anhedonia score	−.711	≤.001*	.670	≤.001*
Mean fatigue assessment scale score	−.900	≤.001*	-	-

The use of * means that this variable is statistically significant.

TABLE 5. Association between days after recovery from COVID-19, fatigue assessment scale, and self-assessment anhedonia scale

TABLE 2 Distribution of self-assessment anhedonia scale and fatigue assessment scale

	The studied group (n = 200)
Mean total intensity score	224.02 ± 20.72
Mean total frequency score	229.89 ± 18.80
Mean total change score	234.87 ± 16.58
Mean total anhedonia score	688.41 ± 52.98
Mean Fatigue assessment scale score	40.81 ± 5.75

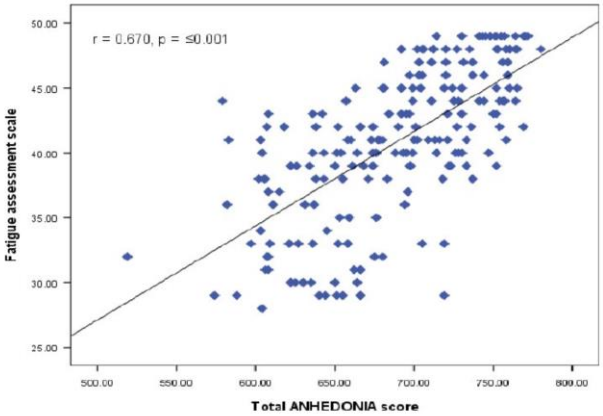


FIGURE 1 illustrated the association between mean fatigue score and mean anhedonia score

VITAMIN D DEFICIENCY AMONG PATIENTS WITH COVID-19: CASE SERIES AND RECENT LITERATURE REVIEW

Pinzon RT, Angela, Pradana AW.. Trop Med Health. 2020 Dec 20;48(1):102. doi: 10.1186/s41182-020-00277-w.
Level of Evidence: 4 - Case-series

BLUF

Researchers affiliated with multiple Universities in Indonesia conducted a case series (n=10) investigating Vitamin D levels in COVID-19 patients. The results (Table 1) revealed that all 10 patients had levels of Vitamin D below what is considered "sufficient", with 9/10 meeting criteria for vitamin D "deficiency" (defined as 25(OH)D levels < 10ng/mL). The authors interpret this data to support use of supplemental vitamin D in the prevention and treatment of COVID-19 and call for larger scale studies to further support the theory that Vitamin D deficiency may play a role in the pathogenesis of SARS-CoV-2. While Vitamin D is known to have an important role in immune function, there are currently no randomized controlled trials to show repletion has any improvement in COVID-19 mortality, however too much Vitamin D is known to cause significant toxicity (know as hypervitaminosis D).

ABSTRACT

BACKGROUND: The world is now challenging the pandemic of COVID-19 infection. This is the third and most extensive pandemic. Previous studies showed the plausibility of vitamin D prophylaxis and therapy for COVID-19, particularly in settings where hypovitaminosis D is frequent. Recent study from Indonesian showed that the prevalence of vitamin D deficiency was

23.0%. The examination of vitamin D status is not a routine in the Indonesian clinical setting. METHODS: This study is a case series from confirmed cases of COVID-19 in Bethesda Hospital Yogyakarta Indonesia. The data of clinical symptoms, signs and laboratory examinations were obtained from the electronic medical records. The vitamin D status was measured by Enzyme-Linked Fluorescent Assay (ELFA) method. We searched PubMed and Google Scholar for studies that included terms for Vitamin D and COVID-19. RESULTS: The data were obtained from 10 participants consisting of 50% male and 50% female. The mean age was 49.6 years. The prevalence of vitamin D deficiency in this study was 90% (vitamin D levels < 20 ng/mL) and 10% of insufficiency (vitamin D levels < 30 ng/mL). Patients in this study had various symptoms such as fatigue (60%), fever (50%), dry cough (40%), non-specific headache (10%), and diarrhea (10%); have no symptoms (20%); and also had the various chronic diseases as comorbidity such as hypertension (40%), diabetes (10%), COPD (10%), and post stroke (10%). CONCLUSIONS: All of the COVID-19 patients in this study had hypovitaminosis D. The prevalence of vitamin D deficiency in this case series is 90% and only 1 patient (10%) had vitamin D insufficiency. There are many health benefits of vitamin D and very few adverse effects. Randomized controlled trials need to determine and evaluate this recommendation in preventing or treating COVID-19. Clinicians should continue to treat people with vitamin D deficiency especially in managing COVID-19 patients.

FIGURES

Table 1 Demographics, clinical characteristics on admission, and laboratory results of 10 patients cases with COVID-19 infection

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9	Patient 10
Demographics										
Age (years)	49	51	17	40	65	73	14	54	69	64
Mean of age = 49.6 years										
Gender	Female	Male	Male	Male	Female	Male	Female	Female	Female	Male
Clinical findings on admission										
Symptom	Fatigue(close contact)	Fever, diarrhea	No symptoms (close contact)	Fever, fatigue, dry cough	Fever, fatigue, headache	Fever, fatigue, dry cough,	No symptoms, (close contact)	Fatigue, non-specific headache	Fatigue, dry cough	Fever, dry cough
Comorbidity	-	Diabetes	-	-	Hypertension	Hypertension, COPD	-	-	Hypertension	Post stroke, hypertension
SARS-CoV IgG	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Negative
SARS-CoV IgM	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive
Laboratory results										
Vitamin D levels (ng/mL)	<8.1	10.6	20.5	11.9	11.6	12.4	8.3	10.1	<8.1	<8.1
Vitamin D status	**Deficiency**	**Deficiency**	**Insufficiency**	**Deficiency**	**Deficiency**	**Deficiency**	**Deficiency**	**Deficiency**	**Deficiency**	**Deficiency**
Hemoglobin (g/dL)	12.4	16	17.6	14.3	12.6	13.5	14.6	12.2	10.7	12.4
White blood cell (10^3/µl)	6.80	7.14	6.81	6.94	7.62	5.62	5.64	7.07	5.97	9.84
Red blood cell (10^6/µl)	3.94	5.14	6.21	5.11	4.21	4.38	5.01	4.31	3.34	4.18
Platelets (10^3/µl)	451	174	289	384	542	184	290	190	312	327
Lymphocyte (%)	24.0	16.8 **(low)**	29.7	30.1	25.9	24.2 **(low)**	20.7	16.5	19.9	17.4
Monocyte (%)	5.6	7.4	6.6	8.1 **(high)**	10.0 **(high)**	11.4 **(high)**	12.4 **(high)**	5.0	11.6 **(high)**	5.5
Neutrophil (%)	67.5	75.7 **(high)**	56.1	57.6	61.6	63.8	66.4	77.9 **(high)**	63.3	76.6 **(high)**

Table 1. Demographics, clinical characteristics on admission, and laboratory results of 10 patients cases with COVID-19 infection.

ACUTE DIGITAL NECROSIS IN A PATIENT WITH RAYNAUD'S PHENOMENON AND COVID-19 INFECTION

Shih L, Ferry AM, Gravina PR, Wang ED, Reece EM, Maricevich M, Winocour SJ.. Am Surg. 2020 Dec 19:3134820979788. doi: 10.1177/0003134820979788. Online ahead of print.
Level of Evidence: 5 - Case report

BLUF

An interdisciplinary group of researchers from the Baylor College of Medicine as well as Texas Children's Hospital describe a case of a patient with a history of hypertension, pre-diabetes, systemic sclerosis, and Raynaud's phenomenon who experienced an episode of digital ischemia while actively infected with SARS-CoV-2 (hospital course in summary). This study describes the first reported case of digital necrosis requiring amputation in a patient infected with SARS-CoV-2 with a preexisting history of digital ischemia. The study supports the necessity for early hand consultation to manage patients with a pre-existing vaso-occlusive disease and increased risk of digital ischemia. The authors do remark on the possibility that the patient could have suffered from a drug induced hyper-coagulable state after having been placed in the "Adaptive COVID-10 Treatment Trial 2" due to previous evidence of baricitinib (the administered drug in the trial) being associated with unexplainable venous thromboembolism.

SUMMARY

Hospital Course:
After presenting to the emergency department with a 1-week history of finger pain and shortness of breath, the patient was admitted for acute respiratory distress and tested positive for COVID-19 during her admission. The patient was placed on low molecular weight heparin while admitted and also was enrolled in the "Adaptive COVID-19 Treatment Trial 2". After experiencing an acute worsening of her respiratory condition, the patient was transferred to the ICU with a subsequent improvement in her condition without the necessity of mechanical ventilatory support. The patient's digital ischemia continued to deteriorate throughout her admission despite treatment with calcium channel blockers and phosphodiesterase inhibitors. In an attempt to manage the patient's pain, botulinum toxin was administered which resulted in an improvement both in the pain that the patient was experiencing as well as perfusion of her finger. However, three weeks after the patient's discharge the patient's finger continued to worsen, necessitating a future surgical amputation.

FIGURES

Figure 1. Prebotulinum toxin injection. Left index finger with early signs of digital necrosis of the distal phalanx and nail bed and threatened necrosis of the proximal phalanx.

Figure 2. Three weeks after botulinum toxin injection. Extension of soft tissue necrosis to the proximal left index finger.

PEDIATRICS

PEDIATRIC ISCHEMIC STROKE: AN INFREQUENT COMPLICATION OF SARS-COV-2

Beslow LA, Linds AB, Fox CK, Kossorotoff M, Zuñiga Zambrano YC, Hernández-Chávez M, Hassanein SMA, Byrne S, Lim M, Maduaka N, Zafeiriou D, Dowling MM, Felling RJ, Rafay MF, Lehman LL, Noetzel MJ, Bernard TJ, Dlamini N; International Pediatric Stroke Study Group.. Ann Neurol. 2020 Dec 17. doi: 10.1002/ana.25991. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

Physician members of the International Pediatric Stroke Study Group surveyed 61 international sites between March and May 2020 to assess the prevalence of SARS-CoV-2 infection in pediatric stroke patients. They found 3.6% (6/166) of pediatric arterial ischemic stroke, 0.9% (1/108) of neonatal arterial ischemic stroke, 1.9% (1/54) of pediatric cerebral sinovenous thrombosis, and zero (0/33) neonatal cerebral sinovenous thrombosis patients were positive for SARS-CoV-2. Authors suggest these results indicate that SARS-CoV-2 does not appear to increase the risk of stroke in neonatal and pediatric populations but acknowledge that more robust testing is needed to determine any role the virus has in pediatric stroke.

ABSTRACT

OBJECTIVE: Severe complications of SARS-CoV-2 include arterial ischemic stroke (AIS) in adults and pediatric multisystem inflammatory syndrome. Whether stroke is a frequent complication of pediatric SARS-CoV-2 is unknown. This study aimed to determine the proportion of pediatric SARS-CoV-2 cases with ischemic stroke and the proportion of pediatric strokes with SARS-CoV-2 in the first three months of the pandemic in an international cohort. METHODS: We surveyed 61 international sites with pediatric stroke expertise. Survey questions included: numbers of hospitalized pediatric (<=18 years) SARS-CoV-2 patients; numbers of incident neonatal and childhood ischemic strokes; frequency of SARS-CoV-2 testing for pediatric stroke patients; and numbers of stroke cases positive for SARS-CoV-2 March 1-May 31, 2020. RESULTS: Of 42 centers with SAR-CoV-2 hospitalization numbers, 8/971 (0.82%) with SARS-CoV-2 had ischemic strokes. Proportions of stroke cases positive for SARS-CoV-2 from March-May 2020 were: 1/108 neonatal AIS (0.9%), 0/33 neonatal cerebral sinovenous thrombosis (CSVT; 0%), 6/166 childhood AIS (3.6%), and 1/54 childhood CSVT (1.9%) cases. However, only 30.5% of neonates and 60% of children with strokes were tested for SARS-CoV-2. Therefore, these proportions represent 2.9%, 0%, 6.1%, and 3.0% of stroke cases

tested for SARS-CoV-2. Seven of eight with SARS-CoV-2 had additional established stroke risk factors. INTERPRETATION: As in adults, pediatric stroke is an infrequent complication of SARS-CoV-2, and SARS-CoV-2 was detected in only 4.7% of pediatric ischemic stroke patients tested. However, <50% of strokes were tested. SARS-CoV-2 testing should be considered in pediatric stroke patients as the pandemic continues to determine SARS-CoV-2's role in pediatric stroke.

HEALING AFTER COVID-19: ARE SURVIVORS AT RISK FOR DEVELOPMENT OF PULMONARY FIBROSIS?

McDonald LT.. Am J Physiol Lung Cell Mol Physiol. 2020 Dec 23. doi: 10.1152/ajplung.00238.2020. Online ahead of print.
Level of Evidence: 5 - Review / Literature Review

BLUF

A post-doctoral researcher from the Department of Pathology and Lab Medicine at the Ralph H. Johnson VA Medical Center in South Carolina reviews potential mechanisms of SARS-CoV-2 induced pulmonary fibrosis, including viral activation of pro-fibrotic pathways, cellular injury from direct viral infection, host inflammatory response, and mechanical injury from ventilation (Figure 1, Table 1). Because previous studies have shown that 27-62% of SARS-CoV patients had increased fibrosis and decreased lung function, the author suggests more research to better understand this pathophysiology is needed to better understand long term impacts of SARS-CoV-2 infection.

ABSTRACT

The novel SARS-CoV-2 coronavirus, responsible for Covid-19 disease, was first reported in Wuhan, China in December of 2019. The virus rapidly spread, and the World Health Organization declared a pandemic by March 2020. With millions of confirmed cases world-wide, there is growing concern and considerable debate regarding the potential for coronavirus infection to contribute to an appreciable burden of chronic respiratory symptoms or fibrotic disease among recovered individuals. As the first case of Covid-19 was documented less than one year ago, data regarding long-term clinical outcomes are not yet available and predictions for long-term outcome are speculative at best. However, due to the staggering number of cases and the severity of disease in many individuals, there is a critical need to consider the potential long-term implications of Covid-19. This review examines current basic and clinical data regarding fibrogenic mechanisms of viral injury in the context of SARS-CoV-2. Several intersecting mechanisms between coronavirus infection and fibrotic pathways are discussed to highlight factors and processes that may be targetable to improve patient outcome. Reports of post-infection sequelae from previous coronavirus outbreaks are presented toward the goal of improved recognition of potential contributing risk factors for fibrotic disease.

FIGURES

Viral Activation of Profibrotic Pathways	Altered Renin-Angiotensin System balance
	Inhibition of host translation and altered cell cycle
	Activation of growth factors (eg. FGF, EGF, TGFβ)
	Cytoskeletal rearrangement
Direct Cellular Injury	Type II Alveolar Epithelial Cells
	Macrophages
	Endothelial Cells
Cytokine-induced injury	Acute Respiratory Distress Syndrome
	Immune Recruitment
	-Neutrophil Reactive Oxygen Species
	-Macrophage Exosomes
	Aberrant Wound Healing Response
Mechanical Injury	Volutrauma/Atelectrauma
	Barotrauma
	Biotrauma
Age	Altered Cellular Communication
	Stem Cell Exhaustion
	Extracellular Matrix Dysregulation

Table 1. Summary of fibrogenic mechanisms associated with viral infection.

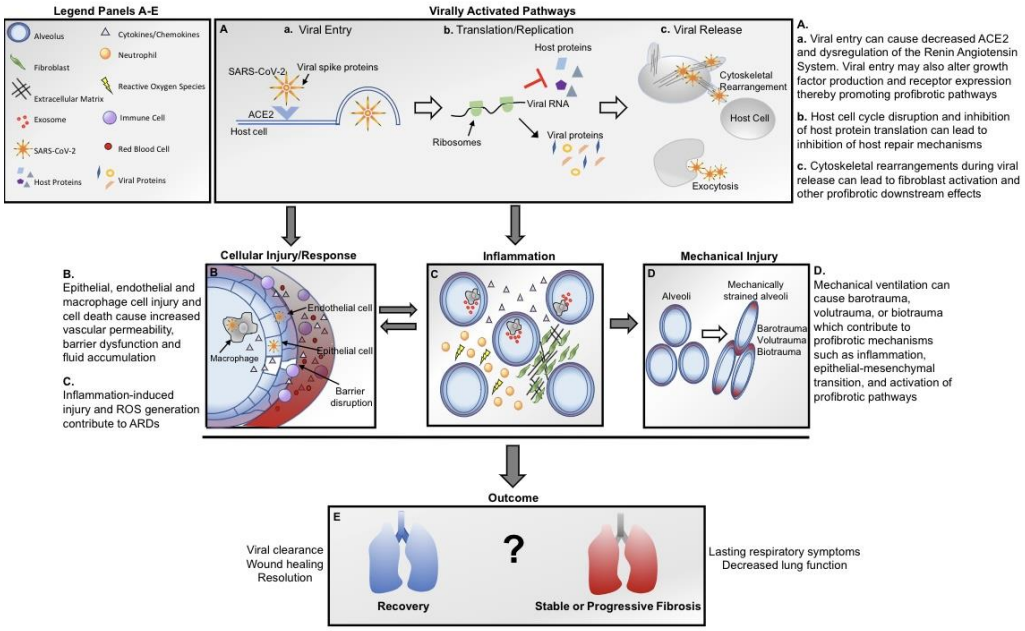


Figure 1. Summary of cellular and molecular mechanisms of viral injury

PREDICTION OF POTENTIAL RESPIRATORY TRACT INFECTION FROM SARS-COV-2 THROUGH HAND-TO-FACE CONTACT TRANSMISSION

Furuya H.. Tokai J Exp Clin Med. 2020 Dec 20;45(4):170-175.
Level of Evidence: 5 - Modeling

BLUF

A public health expert affiliated with the Tokai University School of Medicine in Japan utilizes a mathematical modeling approach to estimate the risk of SARS-CoV-2 infection from various types of "face touching" behavior (hand to nose, eyes, and mouth) and in different environments (porous vs non-porous). The results (Figures 1-3) demonstrate that risk of infection from a non-porous environment was higher than that from a porous environment, and the probability of hand-to-eye transmission was higher than ocular tropism (direct infection), reinforcing the importance of handwashing in preventing SARS-CoV-2 transmission.

ABSTRACT

OBJECTIVE: The Ministry of Health of China reported a cluster of severe pneumonia cases of unknown etiology in Wuhan city, the cause of which was later identified as a novel coronavirus. However, the risk of infection through indirect transmission routes remains unclear. METHODS: A mathematical modeling approach was used to estimate the risk of infection through hand-to-face contact. The probability of infection for various routes of transmission through face-touching behavior was then calculated. RESULTS: The probabilities of infection through hand-to-mouth transmission from nonporous and porous environments had log-normal (LN) distributions with geometric means (GMs) of 0.0116 and 0.0002, geometric deviations (GDs) of 2.9822 and 3.5560, and medians of 0.0127 and 0.0002, respectively, while those through hand-to-nose transmission from nonporous and porous environments had LN distributions with GMs of 0.0006 and 0.0000, GDs of 43.2310 and 47.3372, and medians of 0.0009 and 0.0000, respectively. The probability of infection through hand-to-eye transmission from a nonporous environment had a beta distribution with alpha = 2.38803, beta = 13.60457, a minimum of 0.0045, a maximum of 0.9021, and a median of 0.1179, while that from a porous environment had a Weibull distribution with a scale parameter of 0.0030, a shape parameter of 1.323, and a median of 0.0023. CONCLUSION: SARS-CoV-2 infection will occur through hand-to-face contact via contaminated environment.

FIGURES

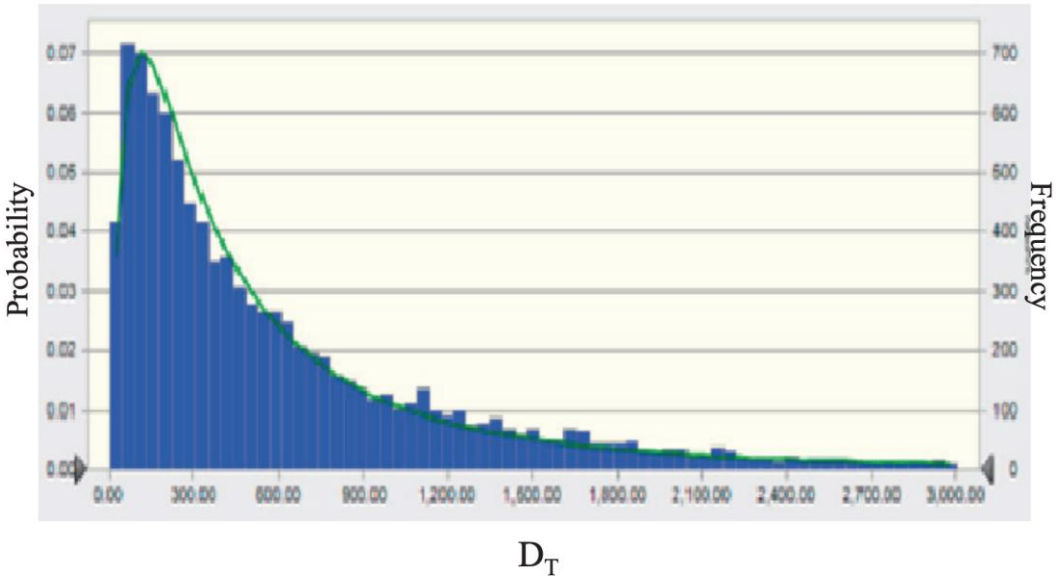


Fig. 1 The distribution of expected dose DT for hand-to-mouth transmission from non-purus environment. (The line showed an lognormal distribution)

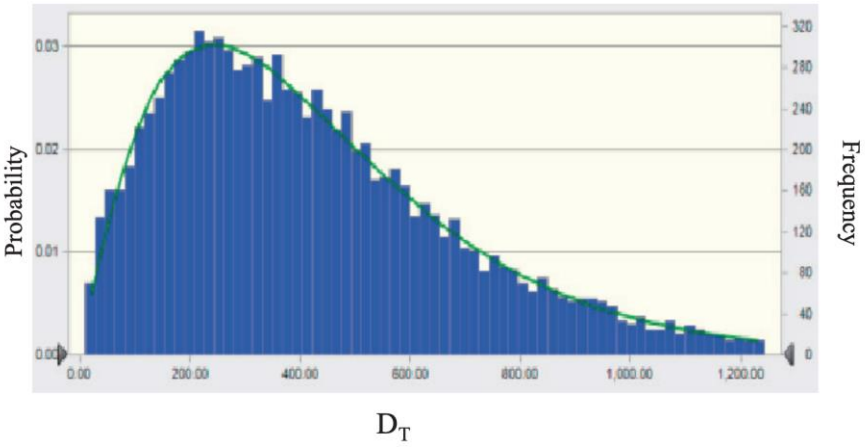


Fig. 2 The distribution of DT for hand-to-eye transmission from non-porous environment. (The line showed a beta distribution)

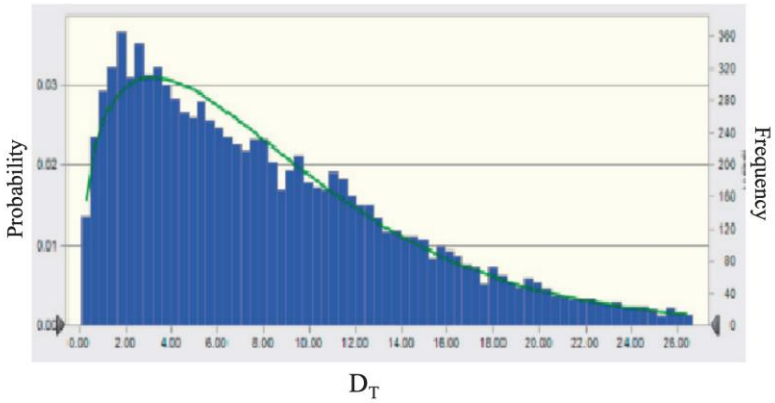


Fig. 3 The distribution of DT for hand-to-eye transmission from porous environment. (The line showed a Weibull distribution)

DEVELOPMENTS IN TRANSMISSION & PREVENTION

COVID-19 GLOBAL PANDEMIC PLANNING: DRY HEAT INCUBATION AND AMBIENT TEMPERATURE FAIL TO CONSISTENTLY INACTIVATE SARS-COV-2 ON N95 RESPIRATORS

Perkins DJ, Nofchissey RA, Ye C, Donart N, Kell A, Foo-Hurwitz I, Muller T, Bradfute SB.. Exp Biol Med (Maywood). 2020 Dec 20:1535370220977819. doi: 10.1177/1535370220977819. Online ahead of print.
Level of Evidence: 5 - Mechanism-based reasoning

BLUF

Internists and microbiologists from University of New Mexico assessed whether dry heat incubation could decontaminate N95 respirators (Figure 1). They found SARS-CoV-2 was not inactivated when N95 coupons inoculated with the virus were heated to 60-75 degrees Celsius for either 30 or 60 minutes when placed on parchment paper but was inactivated when placed on tissue culture plates (Table 3). When intact 3M 1860 N95 respirators were incubated at 70-75 degrees Celsius for 60 minutes, SARS-CoV-2 was not inactivated (Table 4). Authors suggests that dry heat incubation is not a consistently effective method for deactivating SARS-CoV-2 on N95 respirators.

ABSTRACT

The ongoing pandemic of the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has placed a substantial strain on the supply of personal protective equipment, particularly the availability of N95 respirators for frontline healthcare personnel. These shortages have led to the creation of protocols to disinfect and reuse potentially contaminated personal protective equipment. A simple and inexpensive decontamination procedure that does not rely on the use of consumable

supplies is dry heat incubation. Although reprocessing with this method has been shown to maintain the integrity of N95 respirators after multiple decontamination procedures, information on the ability of dry heat incubation to inactivate SARS-CoV-2 is largely unreported. Here, we show that dry heat incubation does not consistently inactivate SARS-CoV-2-contaminated N95 respirators, and that variation in experimental conditions can dramatically affect viability of the virus. Furthermore, we show that SARS-CoV-2 can survive on N95 respirators that remain at room temperature for at least five days. Collectively, our findings demonstrate that dry heat incubation procedures and ambient temperature for five days are not viable methods for inactivating SARS-CoV-2 on N95 respirators for potential reuse. We recommend that decontamination procedures being considered for the reuse of N95 respirators be validated at each individual site and that validation of the process must be thoroughly conducted using a defined protocol.

FIGURES

Table 4. Dry heat incubation of high (1×10^5 pfu) or low (3×10^3 pfu) doses of SARS-CoV-2 on intact 3M™ 1860 N95 respirators.

Amount of virus	Temperature	Duration of incubation	Sample placement	# samples positive for CPE/total # samples
1×10^5 pfu	70°C	60 min	Hanging	6/6
1×10^5 pfu	75°C	60 min	Hanging	6/6
3×10^3 pfu	70°C	60 min	Hanging	6/6
3×10^3 pfu	75°C	60 min	Hanging	4/6
Controls				
1×10^5 pfu	RT	60 min	Hanging	3/3
3×10^3 pfu	RT	60 min	Hanging	3/3
No virus	RT	60 min	Hanging	0/6
No virus	70°C	60 min	Hanging	0/6
No virus	75°C	60 min	Hanging	0/6

Table 3. Dry heat incubation of (1×10^5 pfu) or low (3×10^3 pfu) doses of SARS-CoV-2 on N95 coupons (3M™ 1860S) placed on either parchment paper or tissue culture plate wells.

Amount of virus	Temperature	Duration of incubation	Sample placement	# samples positive for CPE/total # samples
1×10^5 pfu	70°C	60 min	Parchment paper	3/3
1×10^5 pfu	75°C	60 min	Parchment paper	3/3
3×10^3 pfu	70°C	60 min	Parchment paper	3/3
3×10^3 pfu	75°C	60 min	Parchment paper	3/3
1×10^5 pfu	70°C	60 min	Tissue culture plate	0/3
1×10^5 pfu	75°C	60 min	Tissue culture plate	0/3
3×10^3 pfu	70°C	60 min	Tissue culture plate	0/3
3×10^3 pfu	75°C	60 min	Tissue culture plate	0/3
Controls				
1×10^5 pfu	RT	60 min	Parchment paper	3/3
1×10^5 pfu	RT	60 min	Tissue culture plate	3/3
3×10^3 pfu	RT	60 min	Parchment paper	3/3
3×10^3 pfu	RT	60 min	Tissue culture plate	3/3
No virus	RT	60 min	Parchment paper	0/3
No virus	RT	60 min	Tissue culture plate	0/3

Note: Placement of the N95 coupons on parchment paper or in tissue culture plate wells was run concomitantly in the same heat chamber.

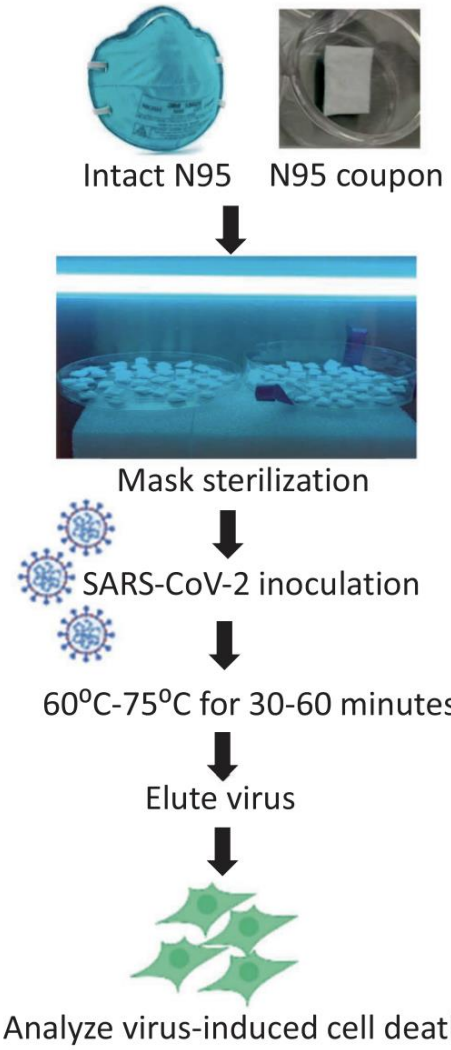


Figure 1. Experimental design. N95 coupons or whole (intact) respirators were UV-inactivated to ensure sterility and then inoculated with 1×10^5 pfu or 1×10^3 pfu of SARS-CoV-2. Samples were then placed in a dry heat chamber for various times at different temperatures. Virus was eluted from the mask material and incubated on Vero E6 cells for six days, at which time cells were analyzed for cytopathic effect (CPE). (A color version of this figure is available in the online journal.)

PREVENTION IN THE HOSPITAL

MODELING THE STABILITY OF SARS-COV-2 ON PERSONAL PROTECTIVE EQUIPMENT (PPE)

Haddow AD, Watt TR, Bloomfield HA, Fetterer DP, Harbourt DE.. Am J Trop Med Hyg. 2020 Dec 22. doi: 10.4269/ajtmh.20-1508. Online ahead of print.
Level of Evidence: 5 - Modeling

BLUF

Virologists from the United States Army Medical Research Institute of Infectious Diseases in Detrick, Maryland compared the stability of SARS-CoV-2 on multiple models of personal protective equipment (PPE) used during airway procedures following 4.3 log10 plaque-forming units (PFUs) of SARS-CoV-2 exposure (Table 1). They found that even 72 hours after exposure, between 1.1 and 2.3 log10 PFU/mL of SARS-CoV-2 was detectable depending on material (Figure 1). Authors suggest that the persistence of SARS-CoV-2 on personal protective equipment highlights the importance of appropriate doffing, disposal, and disinfection in order to prevent fomite transmission.

ABSTRACT

We modeled the stability of SARS-CoV-2 on personal protective equipment (PPE) commonly worn in hospitals when carrying out high-risk airway procedures. Evaluated PPE included the visors and hoods of two brands of commercially available powered air purifying respirators, a disposable face shield, and Tyvek coveralls. Following an exposure to 4.3 log10 plaque-forming units (PFUs) of SARS-CoV-2, all materials displayed a reduction in titer of > 4.2 log10 by 72 hours postexposure, with detectable titers at 72 hours varying by material (1.1-2.3 log10 PFU/mL). Our results highlight the need for proper doffing and disinfection of PPE, or disposal, to reduce the risk of SARS-CoV-2 contact or fomite transmission.

FIGURES

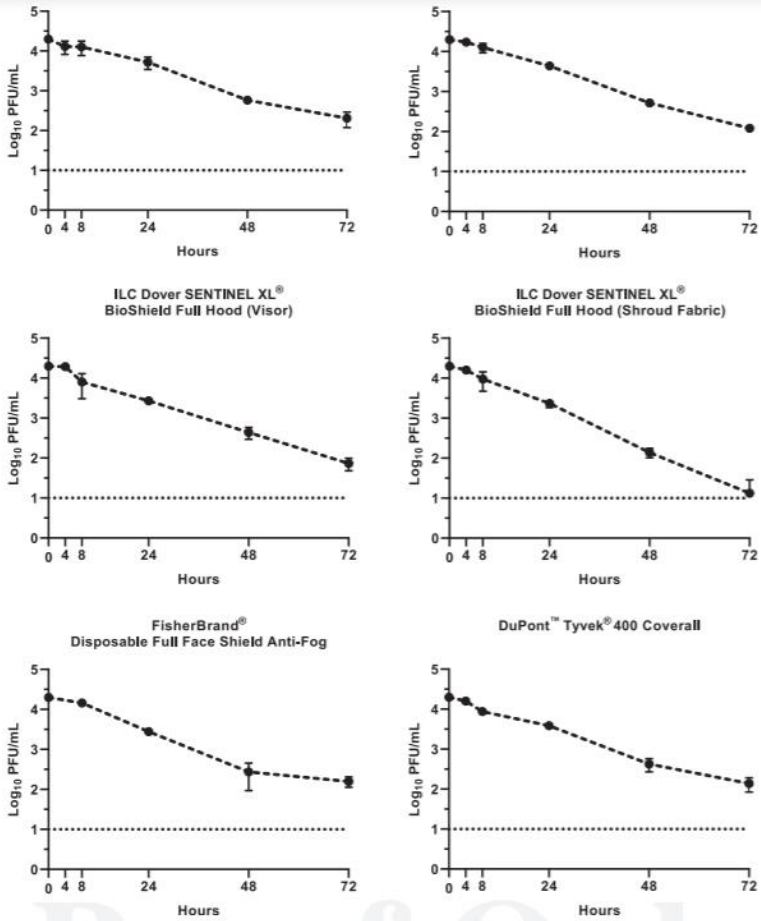


FIGURE 1. Detection of infectious virus on personal protection equipment following a SARS-CoV-2 exposure. No data are reported for the FisherBrand disposable full face shield antifog at 4 hours postexposure as all three samples were inadvertently flipped onto their exposed surface because of a static charge while transferring. The lower limit of detection was 1.0 $\log_{10}$ plaque-forming unit (PFU)/mL.

TABLE 1

Personnel protective equipment evaluated and associated geometric mean half-life in hours by material

Product	Manufacturer	Material	Material description	Geometric mean half-life* (95% CI)
3M Versaflo economy hood	3M (Cat No. S-403)	Visor	Polyethylene terephthalate glycol	10.05 (9.496–10.642)
		Shroud fabric	Polypropylene-coated nonwoven polypropylene	9.12 (8.444–9.858)
ILC Dover SENTINEL XL BioShield full hood	ILC Dover (Cat No. S-2028)	Visor	Optically clear polyester	8.72 (7.615–9.981)
		Shroud fabric	Spunbound polypropylene nonwoven with a polyethylene outer film	6.74 (5.639–8.051)
FisherBrand disposable full face shield antifog	ThermoFisher Scientific (Cat No. 19-460-102)	Visor	Polyester treated with an antifog and antistatic coating	8.83 (7.383–10.554)
DuPont Tyvek 400 coverall	DuPont (Cat No. TY127SWH)	Fabric	DuPont Tyvek 400	9.08 (7.635–10.802)

*Hours.

DECONTAMINATION OF SARS-COV-2 CONTAMINATED N95 FILTERING FACEPIECE RESPIRATORS (FFRS) WITH MOIST HEAT GENERATED BY A MULTICOOKER

Choi YW, Richardson AW, Sunderman M, Mladineo MJ, Keyes PH, Hofacre KC, Middleton JK.. Lett Appl Microbiol. 2020 Dec 21. doi: 10.1111/lam.13443. Online ahead of print.
Level of Evidence: 5 - Mechanism-based reasoning

BLUF

A multidisciplinary team of scientists from Battelle Memorial Institute in Ohio inoculated patches/coupons from N95 respirators with SARS-CoV-2 virus suspended in simulated saliva or lung fluids and subjected the samples to a temperature of 65°C for 30 minutes in a multicooker (i.e. crockpot) filled partially with water. They found that SARS-CoV-2 virus was undetectable by 20 minutes regardless of the respirator's model (Figure 3). All masks met performance criteria for collection efficiency (>95%) and inhalation resistance (<35 mmH2O) after 10 cycles if placed in a paper bag to absorb moisture during decontamination and allowed 30 minutes to dry. The authors conclude that moist heat treatment (65°C for 30 minutes) with a multicooker can successfully decontaminate N95 respirators which could allow for re-use during times of limited supply.

ABSTRACT

Decontamination of N95 filtering facepiece respirators (FFRs) is a crisis capacity strategy allowed when there are known shortages of FFRs. The application of moist heat is one decontamination method that has shown promise and is the approach approved in the Steris Steam Emergency Use Authorization (EUA). This effort examines the use of multicookers to apply moist heat, as they are available in retail stores and more affordable than methods requiring more sophisticated equipment. Four of five multicooker models examined met the acceptance criteria for the test and one model was selected for inactivation testing. Tests were performed on four different FFR models with SARS-CoV-2 suspended in culture media, simulated saliva, or simulated lung fluid. Moist heat treatment reduced recoverable titers of SARS-CoV-2 virus to levels below the limit of detection in all tests. Furthermore, these four FFR models showed no loss in collection efficiency, inhalation resistance, or visual damage after up to 10 decontamination cycles. Two (2) FFR models showed a slight change in strap elasticity (<9%). These data show that moist heat treatment using a multicooker is a viable option for FFR decontamination in a crisis capacity strategy.

FIGURES

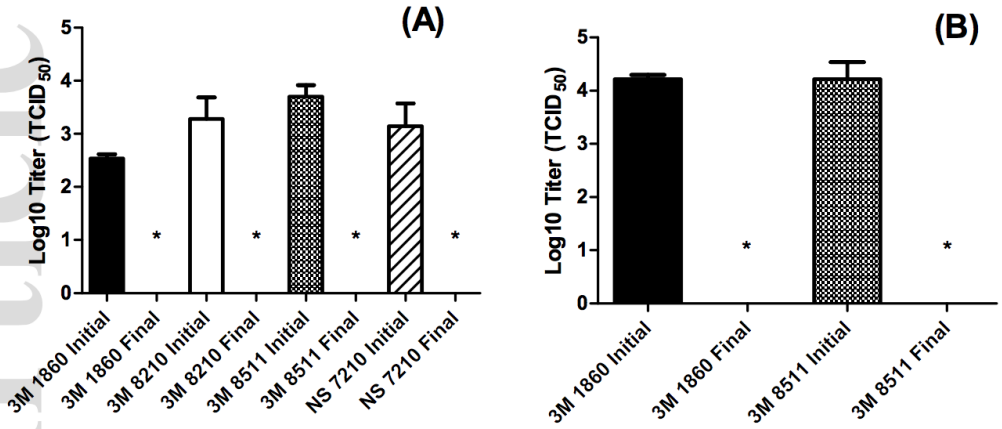


Fig. 3 Inactivation of SARS-CoV-2 in simulated saliva (A) and simulated lung fluid (B) when spiked onto FFR coupons and treated with moist heat in a multicooker. Inactivation below detection (1.12 Log_{10} $TCID_{50}$) indicated by an (*).

CRITICAL CARE

A PROSPECTIVE STUDY OF VOICE, SWALLOW AND AIRWAY OUTCOMES FOLLOWING TRACHEOSTOMY FOR COVID-19

Rouhani MJ, Clunie G, Thong G, Lovell L, Roe J, Ashcroft M, Holroyd A, Sandhu G, Al Yaghchi C.. Laryngoscope. 2020 Dec 20. doi: 10.1002/lary.29346. Online ahead of print.

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

BLUF

A prospective study from the National Center for Airway Reconstruction in London, UK, studied 41 patients who required tracheostomy for severe COVID-19 respiratory failure, finding that the average duration of endotracheal intubation was 24 days, with 63% of tracheostomies performed on day 21-35 of mechanical ventilation. The authors highlight how this timeline is delayed compared to the generally accepted principle that patients should be transitioned to tracheostomy on day 10-14 of mechanical ventilation, and speculate that this may explain the high incidence of laryngeal injury observed in this cohort on 2 month post-hospital follow up (Figure 1-3).

ABSTRACT

OBJECTIVE: The COVID-19 pandemic has led to unprecedented demands on healthcare with many requiring intubation. Tracheostomy insertion has often been delayed and the enduring effects of this on voice, swallow and airway outcomes in COVID-19 tracheostomy patients are unknown. The aim of this study was to prospectively assess these outcomes in this patient cohort following hospital discharge. METHODS: All COVID-19 patients who had undergone tracheostomy insertion, and were subsequently decannulated, were identified at our institution and followed up two months post-discharge. Patient-reported (PROMS) and clinician-reported outcome measures, endoscopic examination and spirometry were used to assess voice, swallow and airway outcomes. RESULTS: Forty-one patients were included in the study with a mean age of 56 years and male:female ratio of 28:13. Average duration of endotracheal intubation was 24 days and 63.4% of tracheostomies were performed at day 21-35 of intubation. 53.7% had an abnormal GRBAS score and 30% reported abnormal swallow on EAT-10 questionnaire. 81.1% had normal endoscopic examination of the larynx however positive endoscopic findings correlated with the patient self-reported VHI-10 ($p=0.036$) and EAT-10 scores ($p=0.027$). 22.5% had spirometric evidence of fixed upper airway obstruction using the Expiratory-Disproportion Index (EDI) and Spearman correlation analysis showed a positive trend between abnormal endoscopic findings and EDI scores over 50 ($p<0.0001$). CONCLUSION: The preliminary results of this study reveal a high incidence of laryngeal injury among patients who underwent intubation and tracheostomy insertion during the COVID-19 pandemic. As these patients continue to be followed up, the evolution of these complications will be studied.

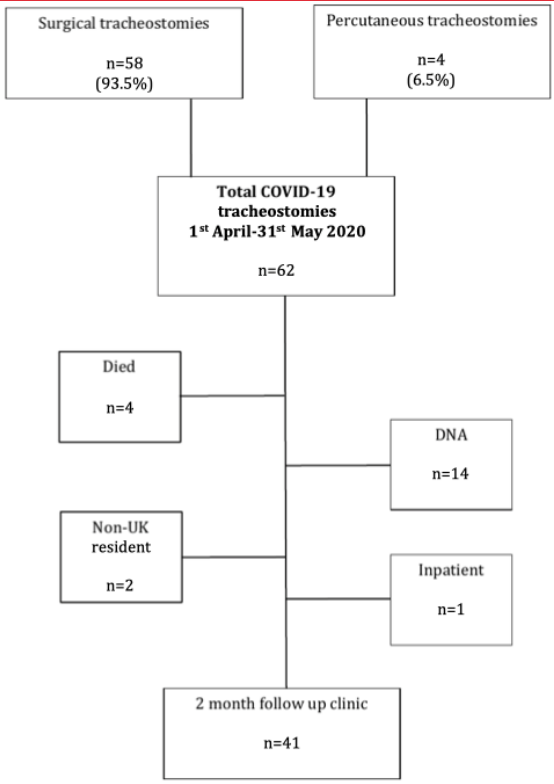


Figure 1. Voice Outcomes.

Thirty-eight patients completed the VHI-10 questionnaire; five patients (13.2%) reported a score > 11 (range 12–35), which is considered abnormal. 39 patients completed the RSI questionnaire; five patients (12.8%) reported a score > 13 (range 21–41) indicative of likely laryngopharyngeal reflux symptoms.

A total of 53.7% (22 patients) had a GRBAS score that indicated perceptual abnormalities to voice quality (grade, roughness, breathiness, asthenia, strain; score of 0 considered no audible dysphonia). The highest scoring abnormality was asthenia, indicative of overall weakness of voice. Figure 2 depicts a summary of these voice outcomes.

n=41	Median	Range
Age (years)	57	(32-77)
BMI (kg/m^2)	29.3	(18.1-47.6)
Duration of intubation (days)	24	(10-40)
Tracheostomy to decannulation (days)	15	(4-50)
Duration of intubation (days)	**n (%)**	
< 7	0	
7-14	3 (7.3)	
15-21	9 (22)	
21-35	26 (63.4)	
>35	3 (7.3)	
Tracheostomy size	**n (%)**	
7.0	1 (2.4)	
7.5	8 (19.5)	
8.0	21 (51.2)	
8.5	10 (24.4)	
9.0	1 (2.4)	

Figure 2. Swallow Outcomes.

Forty patients completed the EAT-10 questionnaire; 12 patients (30%) reported a score > 2 (range 4–33), which indicates a potentially abnormal swallow. 34 patients (82.9%) had a FOIS score of 7: total oral diet with no restrictions. Three patients (7.3%) had a score of 6: total oral diet with multiple consistencies without special preparation but with specific food limitations; two (4.9%) had a score of 5: total oral diet with multiple consistencies, but requiring special preparation or compensations; two (4.9%) had a score of 3: tube dependent with consistent oral intake of food or liquid.

Patient	EDI	Endoscopic findings
i	**76.6**	Ecchymosis of right vocal cord
ii	**51.3**	**Right vocal cord palsy**
iii	32.6	Subglottic stenosis (10-15%)
iv	65.6	Declined
v	50.4	NAD
vi	**65.7**	**Left vocal cord palsy with midline left arytenoid**
vii	85.3	NAD
viii	**71.4**	**Subglottic stenosis with granuloma**
ix	58.0	NAD
x	**76.8**	**Bilateral vocal fold immobility with subglottic granuloma**
xi	29.6	Right vocal cord palsy

Figure 3: Airway Outcomes.
A Comparison of Expiratory Disproportion Index (EDI) with Positive Endoscopic Findings (n=7). EDI is a measure of fixed upper airway obstruction as measured by spirometry.
NAD: no abnormality detected.

NEONATAL/PEDIATRIC INTENSIVE CARE

CHARACTERISTICS AND RISK FACTORS ASSOCIATED WITH CRITICAL ILLNESS IN PEDIATRIC COVID-19

Fisler G, Izard SM, Shah S, Lewis D, Kainth MK, Hagmann SHF, Belfer JA, Feld LM, Mastroianni F, Kvasnovsky CL, Capone CA, Schneider J, Sweberg T, Schleien C, Taylor MD; Northwell COVID-19 Research Consortium.. Ann Intensive Care. 2020 Dec 19;10(1):171. doi: 10.1186/s13613-020-00790-5.
Level of Evidence: 3 - Local non-random sample

BLUF

Members of the Northwell COVID-19 Research Consortium in New York conducted a retrospective cohort study of 77 SARS-CoV-2 positive pediatric patients (Table 1) admitted to two pediatric hospitals within their system between February 1 and April 24, 2020 to assess risk factors associated with PICU admission. They found patients greater than 12 years old were more likely to be admitted to the PICU than younger patients, while thrombocytopenia and leukocytosis were associated with organ dysfunction. Elevated CRP was associated with increased risk of both PICU and organ dysfunction (Tables 2, 3). Authors suggest understanding these risk factors may aid early identification of pediatric COVID-19 patients at risk for critical illness.

ABSTRACT

BACKGROUND: While much has been reported regarding the clinical course of COVID-19 in children, little is known regarding factors associated with organ dysfunction in pediatric COVID-19. We describe critical illness in pediatric patients with active COVID-19 and identify factors associated with PICU admission and organ dysfunction. This is a retrospective chart review of 77 pediatric patients age 1 day to 21 years admitted to two New York City pediatric hospitals within the Northwell Health system between February 1 and April 24, 2020 with PCR + SARS-CoV-2. Descriptive statistics were used to describe the hospital course and laboratory results and bivariate comparisons were performed on variables to determine differences. RESULTS: Forty-seven patients (61%) were admitted to the general pediatric floor and thirty (39%) to the PICU. The majority (97%, n = 75) survived to discharge, 1.3% (n = 1) remain admitted, and 1.3% (n = 1) died. Common indications for PICU admission included hypoxia (50%), hemodynamic instability (20%), diabetic ketoacidosis (6.7%), mediastinal mass (6.7%), apnea (6.7%), acute chest syndrome in sickle cell disease (6.7%), and cardiac dysfunction (6.7%). Of PICU patients, 46.7% experienced any significant organ dysfunction (pSOFA > = 2) during admission. Patients aged 12 years or greater were more likely to be admitted to a PICU compared to younger patients (p = 0.015). Presence of an underlying comorbidity was not associated with need for PICU admission (p = 0.227) or organ dysfunction (p = 0.87). Initial white blood cell count (WBC), platelet count, and ferritin were not associated with need for PICU admission. Initial C-reactive protein was associated with

both need for PICU admission (p = 0.005) and presence of organ dysfunction (p = 0.001). Initial WBC and presenting thrombocytopenia were associated with organ dysfunction (p = 0.034 and p = 0.003, respectively). CONCLUSIONS: Age over 12 years and initial CRP were associated with need for PICU admission in COVID-19. Organ dysfunction was associated with elevated admission CRP, elevated WBC, and thrombocytopenia. These factors may be useful in determining risk for critical illness and organ dysfunction in pediatric COVID-19.

FIGURES

Table 1 Demographic data and comorbidities

	Total cohort (*N* = 77)	Floor patients (*N* = 47)	PICU low acuity (*n* = 16)[a]	PICU organ dysfunction (*n* = 14)[b]
Demographic data				
Age (*n*, %)				
Age < 60 days	20 (26)	16 (34)	3 (19)	1 (7)
Age 60 days to < 5 years	10 (13)	6 (13)	2 (13)	2 (14)
Age 5 years to < 12 years	9 (12)	7 (15)	0	2 (14)
Age > = 12 years	38 (49)	18 (38)	11 (69)	9 (64)
Female sex (*n*, %)	40 (53)	23 (49)	9 (56)	8 (57)
BMI (percentile, *n*, %)[c,d]				
Underweight (< 5th percentile)	2 (4)	2 (8)	0	0
Normal weight (5–85th percentile)	26 (58)	13 (52)	7 (78)	6 (55)
Overweight (85–95th percentile)	5 (11)	3 (12)	1 (11)	1 (9)
Obese (> 95th percentile)	12 (27)	7 (28)	1 (11)	4 (36)
Race (*n*, %)				
Black	22 (29)	10 (21)	7 (44)	5 (38)
White	15 (19)	12 (26)	3 (19)	0
Asian	9 (12)	5 (11)	1 (6)	3 (21)
Multiracial/other	28 (36)	17 (36)	5 (31)	6 (43)
Unknown	3 (4)	3 (6)	0	0
Ethnicity (*n*, %)				
Hispanic	18 (23)	9 (19)	3 (19)	6 (43)
Non-Hispanic	55 (71)	37 (79)	11 (69)	7 (50)
Unknown	4 (5)	1 (2)	2 (13)	1 (7)
Comorbidities (*n*, %)				
Prematurity	7 (9)	6 (13)	1 (6)	0
Respiratory disease	16	8 (17)	5	3 (21)
Congenital heart disease	5 (6)	2 (4)	2 (13)	1 (7)
Diabetes mellitus	5 (6)	2 (4)	2 (13)	1 (7)
Immunosuppression	9 (12)	6 (13)	2 (13)	1 (7)
Autoimmune disorder	2 (3)	1 (2)	1 (6)	0
Bone marrow transplant	2 (3)	1 (2)	0	1 (2)
Kidney disease	1 (1)	1 (2)	0	0
Cancer	5 (6)	3 (6)	1 (6)	1 (7)
Genetic disorder	7 (9)	2 (4)	1 (6)	4 (29)

[a] PICU low acuity defined as pSOFA score < 2

[b] PICU organ dysfunction defined as pSOFA score > = 2

[c] BMI category presented for 45 patients (25 floor, 11 ICU organ days, 9 other). 25 missing under 2 years old, 7 missing older than 2 years

[d] BMI category for those 20–21 classified as underweight < 18.5, normal 18.5–25, overweight 25–30, obese > 30

Table 1: "Demographic data and comorbidities".

Reason(s) for PICU admission *n* (%)			Total PICU cohort (*N* = 30)
Hypoxia			15 (50)
Hemodynamic instability			6 (20)
DKA			2 (7)
Cardiac dysfunction			2 (7)
Mediastinal mass			2 (7)
Apnea			2 (7)
Acute chest syndrome in sickle cell disease			2 (7)
Other			6 (20)
Outcomes			
Length of ICU stay, days [mean (median, IQR)][a]			8.8 (3.6, 2.5–14.7)
ICU discharge (*n*, %)			29 (97)
Deceased (*n*, %)			1 (3)
Respiratory failure			**Intubated cohort (*N* = 8)**
OSI at intubation [mean (median, IQR)]			14 (15, 5.5–20)
Maximum PEEP [mean (median)]			12 (13.5)
Ventilator-free days [mean (median, IQR)]			14 (15, 13–23)
PICU admission characteristics	**Total cohort (*N* = 30)**	**PICU low acuity (*n* = 16)**	**PICU organ dysfunction (*n* = 14)**
pSOFA [mean (median, IQR)]	2.3 (1.0, 1.0–3.0)	0.6 (1.0, 0–1.0)	44 (3.0, 2.0–7.0)
PELOD-2 [mean (median, IQR)]	2.0 (2.0, 0–3.0)	0.6 (0, 0–2.0)	3.6 (3.5, 2.0–6.0)
System failure (*n*, %)[b]			
Cardiovascular dysfunction	14 (47)	3 (19)	11 (79)
Respiratory dysfunction	9 (30)	0	9 (64)
Hematalogic dysfunction	6 (20)	0	6 (43)
Neurologic dysfunction	5 (17)	0	5 (36)
Hepatic dysfunction	5 (17)	2 (13)	3 (21)
Renal dysfunction	5 (17)	0	5 (36)

[a] Among survivors

[b] System failure defined as pSOFA > = 1 for system category(18)

Table 2: "PICU admittance and characteristics".

	PICU admission N = 30	No PICU admission N = 47	p value
Outcome: PICU admission			
Age			0.0152
> = 12 years	20 (66.67)	18 (38.30)	
< 12 years	10 (33.33)	29 (61.70)	
Any comorbidity			0.2267
Yes	17 (56.67)	20 (42.55)	
No	13 (43.33)	27 (57.45)	
BMI category (N = 45)[a]			0.7310
Overweight/obese	7 (35.00)	10 (40.00)	
Underweight/normal weight	13 (65.00)	15 (60.00)	
Laboratory data			
Initial CRP (N = 37)			0.0053
Median (IQR)	54.10 (13.90, 161.90)	9.30 (4.00, 33.10)	
Initial ferritin (N = 42)			0.8495
Median (IQR)	446.05 (307.35, 809.35)	525.30 (160.20, 1003.00)	
Initial WBC (N = 69)			0.1455
Median (IQR)	7.8 (5.4–17.1)	7.8 (4.9–12.3)	
Initial platelets			0.0612
Median (IQR)	231 (182–206)	267 (200–419)	
	Organ dysfunction N = 14	**No organ dysfunction N = 63**	***p* value**
Outcome: organ dysfunction			
Age			0.2166
> = 12 years	9 (64.29)	29 (46.03)	
< 12 years	5 (35.71)	34 (53.97)	
Any comorbidity			0.8719
Yes	7 (50.00)	30 (47.62)	
No	7 (50.00)	33 (52.38)	
BMI category (N = 45)[1]			0.7224
Overweight/obese	5 (45.45)	12 (35.29)	
Underweight/normal weight	6 (54.55)	22 (64.71)	
Laboratory data			
Initial CRP[c]			0.0011
Median (IQR)	109.70 (54.25, 218.15)	13.90 (4.50, 46.70)	
Initial ferritin[b]			0.2125
Median (IQR)	454.60 (373.70, 1039.00)	487.10 (178.90, 592.40)	
Initial WBC (N = 69)			0.0341
Median (IQR)	15.7 (6.4–18.5)	7.8 (4.8–11.4)	
Initial platelets			
Median (IQR)	149 (100–280)	268 (203–392)	0.0025

Organ dysfunction defined as pSOFA > = 2, No organ dysfunction included floor patients and ICU patients with pSOFA < 2

[a] Patients < 2 years old excluded (n = 25) and n = 7 missing > = 2 years old

[b] Ferritin collected for 42 patients

[c] CRP collected for 37 patients

Table 3: "Outcomes for PICU admission and organ dysfunction".

MEDICAL SUBSPECIALTIES

DERMATOLOGY

SEVERE HYPERALGESIA AND PAIN DURING BOTULINUM TOXIN INJECTION AVOIDING APPLICATION IN A PATIENT 1 WEEK AFTER COVID-19 INFECTION

Akdogan N.. J Cosmet Dermatol. 2020 Dec 19. doi: 10.1111/jocd.13897. Online ahead of print.
Level of Evidence: 5 - Case report

BLUF

A dermatologist of Hacettepe University in Turkey discusses the case of a 55-year-old female who presented for botulinum injections to address facial wrinkles in the setting of three weeks of facial pain that started several days after a positive SARS-CoV-2 RT-PCR. Despite a negative repeat PCR test prior to the appointment and having tolerated the procedure well every 4-6 months for the last 7 years, the patient only tolerated one of glabellar injections without the use of local anesthetic due to severe pain. The author suggests chronic pain and hyperalgesia may persist after SARS-CoV-2 infection and waiting for at least one month prior to botulinum toxin injection or using topical anesthetics.

ADJUSTING PRACTICE DURING COVID-19

HEMATOLOGY AND ONCOLOGY

AS PANDEMIC CONTINUES, SCREENING CONCERNS GROW

. Cancer Discov. 2020 Dec 22. doi: 10.1158/2159-8290.CD-NB2020-116. Online ahead of print.
Level of Evidence: 5 - Expert Opinion

BLUF

Several interviews conducted with oncologists across the United States reveal their concerns for skipped screenings amidst the COVID-19 pandemic, and found that these canceled screening appointments have led to decreased cancer diagnoses. The physicians fear that patients may present at later disease stages and with worse prognoses, suggesting the benefit of these screenings outweighs the risks of attending them during the pandemic.

SUMMARY

Oncologists in this article cite examples of skipped cancer screenings leading to fewer cancer diagnoses, including:
1. There was a 90% decrease in colonoscopies performed, leading to a 32% decrease in colorectal cancer diagnoses
2. There were decreased breast cancer screenings leading to half as many breast cancer diagnoses

ABSTRACT

When the COVID-19 pandemic began, oncologists were mildly concerned about how it might affect cancer screening. Many months later, amid the continuing pandemic, their concerns about how extensively COVID-19 has disrupted screening have grown-along with their fears about the consequences.

SURGICAL SUBSPECIALTIES

OPERATIONAL IMPACTS OF THE CORONAVIRUS DISEASE OF 2019 (COVID-19) PANDEMIC AND EARLY RECOVERY TRENDS: UNIVERSITY OF WASHINGTON ANATOMIC PATHOLOGY EXPERIENCE

Miller TI, Smith KD, Gonzalez-Cuyar LF, Swanson PE.. Arch Pathol Lab Med. 2020 Dec 14. doi: 10.5858/arpa.2020-0639-SA. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

Pathologists from the University of Washington analyzed changes in accessioned pathology specimens in their hospital system during the COVID-19 pandemic between January and June 2020. They found a significant reduction in accessioned pathology specimens (up to 79% from pre-pandemic levels) after the ban on non-urgent procedures with specimens received increasing to 89% of pre-COVID-19 levels after non-urgent procedures resumed (Figure 2). Gastrointestinal and dermatological samples were most impacted; breast, head/neck, and pulmonology services were least impacted (Table 3). These findings highlight the importance of workflow monitoring in all departments and labs when making policy changes that might affect resource planning or management.

ABSTRACT

CONTEXT: The novel coronavirus virus severe acute respiratory syndrome coronavirus (SARS-CoV2) causing the coronavirus disease of 2019 (COVID-19) pandemic has resulted in worldwide disruption to the delivery of patient care. The Seattle Washington metropolitan area was one of the first in the United States affected by the pandemic. As a result, the anatomic pathology services at the University of Washington experienced significant changes in operational volumes early in the pandemic. OBJECTIVE: To assess the impact of COVID-19 and both state and institutional policies implemented to mitigate viral transmission (including institutional policies on non-urgent procedures) on anatomic pathology volumes. DESIGN: Accessioned specimens from January 2020 to June 2020 was evaluated as COVID-19 and institutional policies changed. The

data were considered in these contexts: subspecialty, billable CPT codes, and intraoperative consultation. Comparable data were retrieved from 2019 as a historical control. RESULTS: There was a significant reduction in overall accessioned volume (up to 79%) from pre-pandemic levels, during bans on non-urgent procedures when compared to 2020 pre- COVID-19 volumes and historical controls. The gastrointestinal and dermatopathology services were most impacted, while breast and combined head&neck/pulmonary services were least impacted. CPT code 88305, for smaller/biopsy specimens, had a 63% reduction during non-urgent procedure bans. After all bans on procedures were lifted, the overall volume plateaued at 89% of pre-pandemic levels. CONCLUSIONS: A significant decrease in specimen volume was most strongly associated with bans on non-urgent procedures. While all departmental areas had a decrease in volume, the extent of change varied across subspecialty and specimen types. Even with removing all bans, service volume did not reach pre-pandemic levels.

FIGURES

Pathology Service	Baseline 2020 (before Mar. 16th/bans)	Strict Ban (3/16/2020–04/12/2020)	Less Strict Ban (04/13/2020–05/17/2020)	No Ban (05/18/2020–06/28/2020)
Breast	15.1	8.6 (-43%)	7.6 (-50%)	13.1 (-13%)
Bone & Soft Tissue	16.3	6.5 (-60%)	6.4 (-61%)	11.5 (-29%)
Cardiac	5.9	2.6 (-60%)	4.1 (-31%)	6.4 (+8.5%)
Cytology	35.1	14.1 (-60%)	16.7 (-52%)	32.9 (-6.3%)
Dermatopathology	32.6	7.6 (-77%)	10.0 (-69%)	25.0 (-23%)
Gastrointestinal	58.7	17.0 (-71%)	20.1 (-66%)	46.2 (-21%)
Genitourinary	21.6	10.2 (-53%)	13.1 (-39%)	19.0 (-12%)
Gynecology	26.7	13.2 (-51%)	16.0 (-40%)	23.6 (-12%)
Hematopathology	13.7	7.7 (-44%)	7.2 (-47%)	11.0 (-20%)
Head & Neck/Lung	17.4	8.8 (-49%)	10.0 (-43%)	14.9 (-14%)
Neuropathology	8.5	3.4 (-60%)	4.6 (-46%)	6.8 (-20.0%)
Renal (medical)	6.9	2.2 (-68%)	4.2 (-39%)	5.0 (-28%)

Table 3: Mean Cases per Workday and Percentage Change from Baseline for Each Pathology Subspecialty Service over Intervals of Different Policies on Suspension of Non-urgent Procedures.

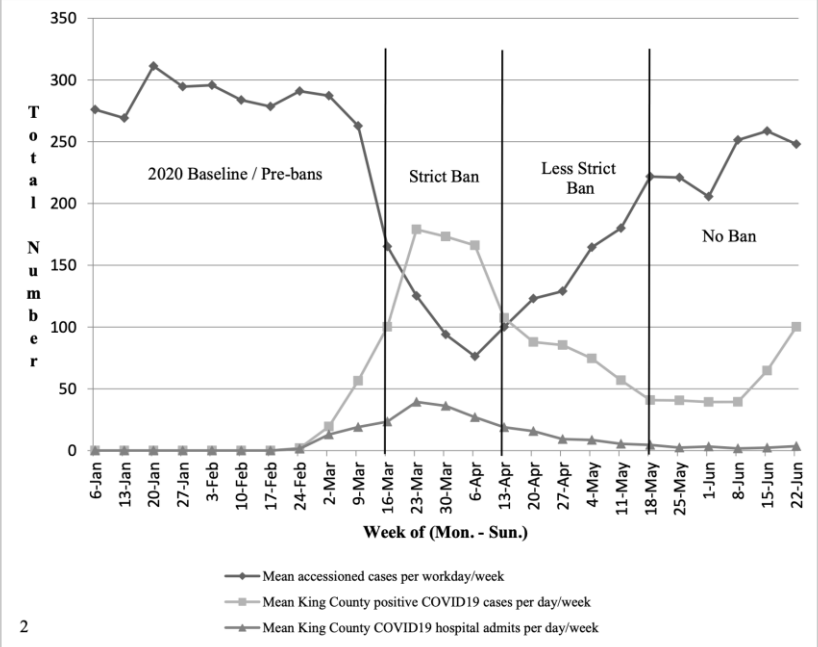


Figure 2. For the weeks of 01/06/2020 to 06/28/2020, mean accessioned cases per workday/week and King County coronavirus disease of 2019 (COVID-19) case trends. There was a strict ban on non-urgent procedures in place from 03/16/2020 to 04/12/2020, less strict ban from 04/13/2020 to 05/17/2020, and no ban after 05/18/2020.

EFFICACY AND SAFETY OF LOPINAVIR/RITONAVIR IN THE TREATMENT OF COVID-19: A SYSTEMATIC REVIEW

Joseph BA, Dibas M, Evanson KW, Paranjape G, Vegivinti CTR, Selvan PT, Saravu K, Gupta N, Pulakurthi YS, Keesari PR, Varsha S, Chittajallu S, Dmytriw AA, Reierson NL, Mikoff N, Kamrowski S, Schmidt M, Davis AR, Pederson JM, Mishra HK, Touchette JC, Kallmes K.. Expert Rev Anti Infect Ther. 2020 Dec 21:1-9. doi: 10.1080/14787210.2021.1848545. Online ahead of print.

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

BLUF

An international research team from Nested Knowledge, Inc conducted a systematic review of 16 studies assessing the effectiveness and safety of lopinavir/ritonavir (LPV/r) in the treatment of COVID-19 published between before May 2020 (Figure 1). They found the majority of included studies showed no significant improvement in clinical outcomes (RT-PCR negativity, chest-CT findings, mortality, adverse events) following LPV/r treatment (Tables 2, 3), though they could not perform meta-analysis due to the high heterogeneity of the comparison groups. Though their review suggests little survival or clinical benefit of LPV/r in COVID-19, authors recommend larger clinical trials are needed to more definitively explore its potential benefits due to the limitations of currently available data.

ABSTRACT

Objectives: To systematically review the clinical literature reporting the use of Lopinavir/ritonavir (LPV/r) for the treatment of patients with COVID-19 to assess the efficacy of LPV/r for the treatment of Cornonavirus disease 19 (COVID-19). Methods: The authors systematically searched PubMed and MedRxiv databases for studies describing treatment of COVID-19 patients using LPV/r compared to other therapies. Articles were excluded if they were case reports, opinion editorials, preclinical studies, single-armed studies, not written in English, not relevant to the topic, or published before May 2020. The included outcomes were viral clearance as measured by reverse-transcription polymerase chain reaction (RT-PCR) negativity and/or improvement on chest computed tomography (CT), mortality, and adverse events (AEs). Results: Among 858 total studies, 16 studies met the inclusion criteria and were included in the qualitative review. These studies consisted of 3 randomized control trials, 3 open-label trials, and 10 observational studies. Most of these studies did not report positive clinical outcomes with LPV/r treatment. Conclusion: The systematic review revealed insufficient evidence of effectiveness and clinical benefit of LPV/r in the treatment of patients with COVID-19. Specifically, LPV/r does not appear to improve clinical outcome, mortality, time to RT-PCR negativity, or chest CT clearance in patients with COVID-19.

FIGURES

Author	Follow-Up Length (days)	Mortality	RT-PCR negativity	Days to RT-PCR negativity Mean (±SD); Median [IQR]	Chest CT improvement	Conclusions
Li et al [20](China)	14	N/A	29/34 (85.3%)	9 (±5)	21/28 (75.0%)	Neither LPV/r nor UMF/ improved outcomes compared to SOC
	14	N/A	32/35 (91.4%)	9.1 (±4.4)	23/33 (69.7%)	
	14	N/A	13/17 (76.5%)	9.3 (±5.2)	13/14 (92.9%)	
Cao et al [18](China)	28	19/99 (19.2%)	39/99 (39.4%)	N/A	N/A	No difference in outcomes between LPV/r and SOC
	28	25/100 (25.0%)	41/100 (41.0%)	N/A	N/A	
Hung et al [19](China)	30	N/A	N/A	7 [5–11]	N/A	Favors LPV/r + RV+IFNβ1b over LPV/r in time to viral clearance
	30	N/A	N/A	12 [8–15]	N/A	

Data are presented as Mean(SD); median[IQR]; n/N (%).
N/A = not available, LPV/r = lopinavir/ritonavir, UMF = Umifenovir (arbidol), FPV = favipiravir, CQ = chloroquine, IFN = interferon, SOC = standard of care, RV = ribavirin, HCQ = hydroxychloroquine, TZ = tocilizumab, AZ = azithromycin, DP = danoprevir, SAE = serious adverse events; CT = computed tomography

Table 2: "Outcomes from the randomized control trials".

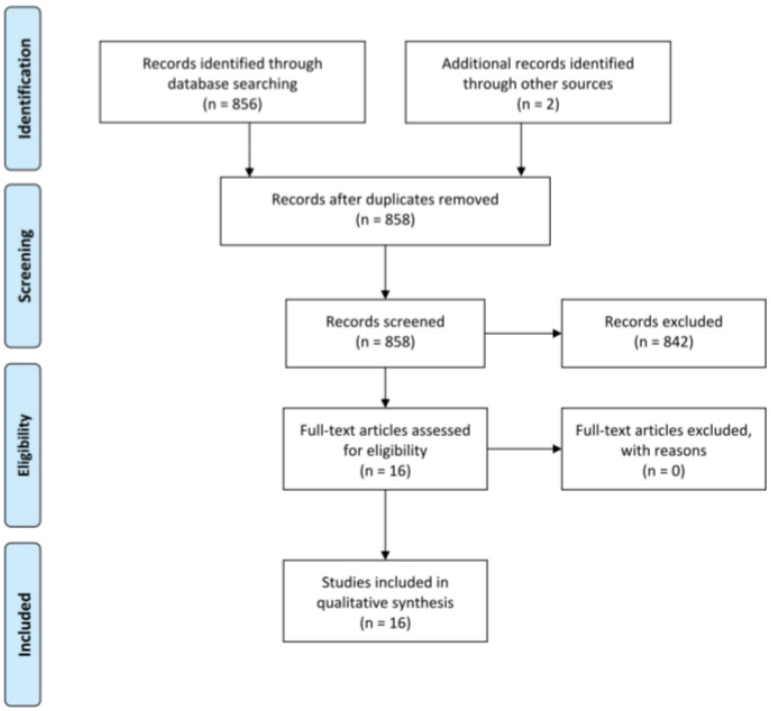


Figure 1: "PRISMA Diagram of search records and inclusions (The template for the flow chart is adapted from Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097)".

Author	Follow-Up Length (days)	Mortality	Mortality	RT-PCR negativity	Days to RT-PCR negativity Mean (±SD); Median [IQR]	Chest CT improvement	Conclusions
Cai et al [21](China)	14 14	N/A N/A	N/A N/A	N/A N/A	4 [2.5–9] 11 [8–13]	32/35 (91.4%) 28/45 (62.2%)	FPV was more effective than LPV/r in limiting disease progression and enhancing viral clearance
Ye et al [23](China)	N/A N/A	N/A N/A	N/A N/A	N/A N/A	7.8 (±3.09) 12 (±0.82)	N/A N/A	Favors LPV/r over UMF/for viral clearance
Huang et al [22](China)	14 14	N/A N/A	N/A N/A	10/10 (100%) 11/12 (91.7%)	N/A N/A	10/10 (100%) 9/12 (75.0%)	No difference in outcomes between CQ and LPV/r

Data are presented as Mean(SD); median[IQR]; n/N (%).
N/A = not available, LPV/r = lopinavir/ritonavir, UMF = umifenovir, FPV = favipiravir, CQ = chloroquine, IFN = interferon, SOC = standard of care, RV = ribavirin, HCQ = hydroxychloroquine, TZ = tocilizumab, AZ = azithromycin, DP = danoprevir, SAE = serious adverse events; CT = computed tomography

Table 3: "Outcomes from the non-randomized clinical trials".

DEVELOPMENTS IN TREATMENTS

EVALUATING THE EFFICACY OF COVID-19 VACCINES

Lin DY, Zeng D, Mehrotra DV, Corey L, Gilbert PB.. Clin Infect Dis. 2020 Dec 19:ciaa1863. doi: 10.1093/cid/ciaa1863. Online ahead of print.
Level of Evidence: 5 - Mechanism-based reasoning

BLUF

Researchers at the Fred Hutch Institute in Seattle, WA collaborate with the University of North Carolina Department of Biostatistics to discuss limitations of current COVID-19 vaccination trials. The main critique of current study designs is the primary endpoint of "virologically confirmed symptomatic COVID-19 disease", which does not provide accurate data on mild or asymptomatic individuals. The authors propose an alternative model that includes 3 primary endpoints: 1) SARS-CoV-2 infection 2) Symptomatic COVID-19 disease 3) Severe COVID-19 disease. They assert that this strategy would provide important data on the vaccine's ability to protect against severe disease and also prevent mild and asymptomatic disease. Simulation studies are included to demonstrated these advantages (Table 1-2).

SUMMARY

The authors conclude, "Rapid introduction of effective vaccines in the US and other countries with high numbers of COVID-19 cases would be a major step toward halting the global pandemic. However, deployment of a non-effective vaccine could actually worsen the pandemic because public acceptance of a COVID-19 vaccine might diminish the implementation of other control measures. Thus, we need speedy and reliable evaluation of the efficacy of COVID-19 vaccines on the basis of clinically relevant endpoints."

ABSTRACT

A large number of studies are being conducted to evaluate the efficacy and safety of candidate vaccines against novel coronavirus disease-2019 (COVID-19). Most Phase 3 tri- als have adopted virologically confirmed symptomatic COVID-19 disease as the primary efficacy endpoint, although laboratory-confirmed SARS-CoV-2 is also of interest. In addi- tion, it is important to evaluate the effect of vaccination on disease severity. To provide a full picture of vaccine efficacy and make efficient use of available data, we propose using SARS-CoV-2 infection, symptomatic COVID-19, and severe COVID-19 as dual or triple pri- mary endpoints. We demonstrate the advantages of this strategy through realistic simulation studies. Finally, we show how this approach can provide rigorous interim monitoring of the trials and efficient assessment of the durability of vaccine efficacy.

FIGURES

Table 1. Statistical Power (%) for Testing the Null Hypothesis of At Most 30% Vaccine Efficacy Against Infection (I), Disease (D), and Severe Disease (S) Over 6 Months

Vaccine Efficacy			Single Endpoint			Combined Test			Multiple Testing			Bonferroni		
VE_I	VE_D	VE_S	I	D	S	I-D	D-S	I-D-S	I-D	D-S	I-D-S	I-D	D-S	I-D-S
40%	60%	60%	21	80	27	51	77	53	75	75	72	73	74	69
40%	60%	70%	21	80	45	51	83	57	75	78	75	73	77	72
40%	60%	80%	21	80	69	51	88	61	75	85	82	73	84	79
40%	60%	90%	21	80	91	51	93	65	75	94	92	73	93	90
50%	60%	60%	65	80	27	78	77	78	79	75	76	77	74	73
50%	60%	70%	65	80	45	78	83	81	79	78	78	77	77	75
50%	60%	80%	65	80	69	78	88	83	79	85	84	77	84	81
50%	60%	90%	65	80	91	78	93	86	79	94	93	77	93	91
55%	60%	60%	84	80	27	87	77	86	86	75	83	84	74	80
55%	60%	70%	84	80	45	87	83	89	86	78	84	84	77	82
55%	60%	80%	84	80	69	87	88	91	86	85	88	84	84	87
55%	60%	90%	84	80	91	87	93	93	86	94	95	84	93	94
60%	60%	60%	96	80	27	94	77	93	94	75	92	93	74	91
60%	60%	70%	96	80	45	94	83	94	94	78	93	93	77	92
60%	60%	80%	96	80	69	94	88	96	94	85	95	93	84	94
60%	60%	90%	96	80	91	94	93	97	94	94	98	93	93	97

Note: VE_I, VE_D, and VE_S denote, respectively, the vaccine efficacy for infection, disease, and severe disease. I-D, D-S, and I-D-S denote, respectively, the dual endpoints of infection and disease, the dual endpoints of disease and severe disease, and the triple endpoints of infection, disease, and severe disease. The power pertains to a single test at the one-sided nominal significance level of 2.5%.

Table 1

Table 2. Statistical Power (%) for Testing the Null Hypothesis of No Vaccine Efficacy Against Infection (I), Disease (D), and Severe Disease (S) Over 12 Months

Vaccine Efficacy			Single Endpoint			Combined Test			Multiple Testing			Bonferroni		
VE_I	VE_D	VE_S	I	D	S	I-D	D-S	I-D-S	I-D	D-S	I-D-S	I-D	D-S	I-D-S
10%	30%	30%	22	84	26	54	80	57	79	78	75	76	77	72
10%	30%	40%	22	84	44	54	85	60	79	80	77	76	79	74
10%	30%	50%	22	84	65	54	89	64	79	84	81	76	83	79
10%	30%	60%	22	84	84	54	92	67	79	90	88	76	89	86
20%	30%	30%	70	84	26	82	80	81	83	78	78	80	77	76
20%	30%	40%	70	84	44	82	85	84	83	80	80	80	79	78
20%	30%	50%	70	84	65	82	89	86	83	84	84	80	83	82
20%	30%	60%	70	84	84	82	92	88	83	90	90	80	89	88
25%	30%	30%	88	84	26	90	80	89	89	78	86	87	77	84
25%	30%	40%	88	84	44	90	85	91	89	80	87	87	79	85
25%	30%	50%	88	84	65	90	89	93	89	84	89	87	83	88
25%	30%	60%	88	84	84	90	92	94	89	90	93	87	89	92
30%	30%	30%	97	84	26	96	80	95	96	78	94	95	77	93
30%	30%	40%	97	84	44	96	85	96	96	80	95	95	79	94
30%	30%	50%	97	84	65	96	89	97	96	84	96	95	83	95
30%	30%	60%	97	84	84	96	92	97	96	90	97	95	89	96

Note: VE_I, VE_D, and VE_S denote, respectively, the vaccine efficacy for infection, disease, and severe disease. I-D, D-S, and I-D-S denote, respectively, the dual endpoints of infection and disease, the dual endpoints of disease and severe disease, and the triple endpoints of infection, disease, and severe disease. The power pertains to a single test at the one-sided nominal significance level of 2.5%.

Table 2

EXPERIENCES OF NEW ZEALAND REGISTERED NURSES OF CHINESE ETHNICITY DURING THE COVID-19 PANDEMIC

Song J, McDonald C.. J Clin Nurs. 2020 Dec 21. doi: 10.1111/jocn.15607. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

Nurses from the Waikato Institute of Technology in New Zealand conducted an anonymous online questionnaire of 51 Chinese nurses (Table 1) between July 28 and August 28, 2020 to assess their experiences at work during the COVID-19 pandemic. They found 47.06% experienced racial hostility due to being Chinese, 41.18% were concerned about catching SARS-CoV-2, and 57.14% felt supported in the workplace by their colleagues. Authors suggest that because New Zealand has a large ethnic-minority nursing base, health organizations must understand and support healthcare workers experiencing racial discrimination during the COVID-19 pandemic to adequately meet the demands on the healthcare system.

ABSTRACT

AIMS: This study aimed to investigate the experiences and challenges of New Zealand registered nurses of Chinese ethnicity who have been working during the COVID-19 pandemic. BACKGROUND: New Zealand's nursing workforce is becoming increasingly multicultural as foreign nurses make up an essential part of the New Zealand health workforce. The ongoing COVID-19 pandemic has highlighted the contributions that nurses have made in providing frontline services to the public. However, little has been documented about challenges and experiences of this minority ethnic group - Chinese nurses - who have been working as registered nurses in New Zealand during the COVID-19 pandemic. METHODS: This study utilised an anonymous online questionnaire and a thematic approach to establishing understandings of the experiences of New Zealand registered nurses of Chinese ethnicity in working through the COVID-19 pandemic. A total of 51 Chinese nurses completed this survey. A self-explanatory checklist for reporting results of internet e-surveys (CHERRIES) was used for the purpose of the quality of this online survey. RESULTS: The result showed that 47.06% participants (n=24) reported negative experiences including racial discrimination, workplace bullying and judgement, while 52.94% (n=27) participants reported positive working experiences including supports received in the workplace and positive recognition by the pubic in New Zealand. CONCLUSION: Ethnic-minority nurses are key assets to the New Zealand health system. It is important to understand their experiences and challenges, particularly during the COVID-19 pandemic to make sure they are supported and protected from any physical and emotional injury. RELEVANCE TO CLINICAL PRACTICE: COVID-19 has brought additional challenges and concerns to nurses who are working on the frontline of health services. Having knowledge of nurses' working experiences will help with their job satisfaction and has potential implications for the sustainability of the New Zealand nursing workforce and retention strategies to address nursing workforce shortages which is foreseeable in New Zealand.

Experiences of New Zealand Registered Nurses of Chinese Ethnicity During the COVID-19 Pandemic

Table 1: Demographic data

	Numbers (n=51)	Valid %
Gender		
Female	49	96.08%
Male	2	3.92%
Age		
Less than 20	0	0%
20-29	9	17.65%
30-39	29	56.86%
40-49	11	21.57%
50-59	2	3.92%
60 and over	0	0%
Years of professional nursing practice in New Zealand		
Less than one year	3	5.88%
1 to 5 years	14	27.45%
6 to 10 years	15	29.41%
More than 10 years	19	37.25%
Highest qualification in nursing		
Diploma	1	1.96%
Bachelor's degree	21	41.18%
Post graduate certificate	18	35.29%
Post-graduate diploma	10	19.61%
Master's degree	1	1.96%
Doctorate	0	0%
Working areas		
Public hospital	26	50.98%
Private hospital	1	1.96%
Medical centre	5	9.8%
Aged care facility	7	13.73%
Community home care	5	9.8%
Others (including specialty clinic)	7	13.72%

RESOURCES

RETURN TO WORK: MANAGING EMPLOYEE POPULATION HEALTH DURING THE COVID-19 PANDEMIC

Fragala MS, Goldberg ZN, Goldberg SE.. Popul Health Manag. 2020 Dec 21. doi: 10.1089/pop.2020.0261. Online ahead of print.
Level of Evidence: 5 - Guidelines and Recommendations

BLUF

An article conducted in New Jersey by employees of Quest Diagnostics provides evidence-based strategies for self-insured employers to lower the risk of COVID-19 transmission in the workplace. This strategy includes ensuring proper screening, access to diagnostics/testing, work space modifications, and masking (See Figure 1) to mitigate the spread of infection. This article also focuses on the effects of employer-sponsored health insurance, employee health benefits, cost-effective chronic care management, health screenings, influenza vaccination administration, and mental health support. They propose that implementing these strategies can help employers manage the new occupational environment.

ABSTRACT

Coronavirus disease-2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), has abruptly transformed the outlook of employer health benefits plans for 2020 and 2021. Containing the spread of the virus and facilitating care of those infected have quickly emerged as immediate priorities. Employers have adjusted health benefits coverage to make COVID-19 testing and treatment accessible and remove barriers to care in order to facilitate the containment of the disease. Employers also are introducing strategies focused on testing, surveillance, workplace modifications, and hygiene to keep workforces healthy and workplaces safe. This paper is intended to provide evidence-based perspectives for self-insured employers for managing population health during the COVID-19 pandemic. Such considerations include (1) return to work practices focused on mitigating the spread of COVID-19 through safety practices, testing and surveillance; and (2) anticipating the impact of COVID-19 on health benefits and costs (including adaptations in delivery of care, social and behavioral health needs, and managing interrupted care for chronic conditions).

FIGURES

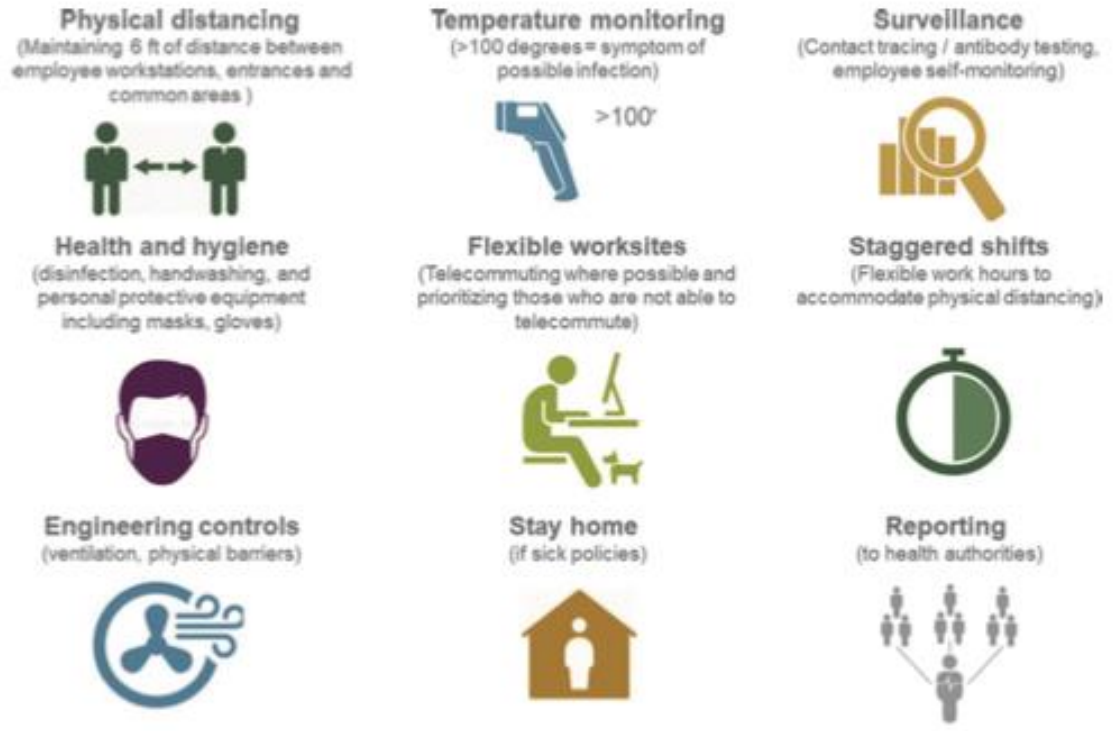


FIG. 1. Workplace measures to contain the spread of COVID-19.[23,24]

FIG. 1. Workplace measures to contain the spread of COVID-19.23,24

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