April 29, 2020
Daily COVID-19 Literature Surveillance Summary

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NOW LIVE!

COVID-19 Daily Literature Surveillance

COVID19LST

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

Coming soon:

The Swab

Jasmine Rah

The untold stories of the coronavirus (COVID-19) pandemic.

April 29th, 2020
Executive Summary

Climate

- SARS-CoV-2 has had many indirect effects on the environment
    - Positive effects include: reduction in greenhouse gas emissions, air pollution, water pollution, nitrogen dioxide, and noise levels.
    - Negative effects include: decreased recycling programs, reduced sustainable waste management, and increased domestic waste such as single-use packaging and bags.
    - India, specifically, has seen a reduction in PM2.5 and an increase in O3, significantly reducing its air quality index.
- The heroic actions of medical professionals and images on social media in China are helping to restore public trust in medical professionals.

Epidemiology

- Since many epidemiological parameters are dependent on testing coverage, which has been highly variable in the case of COVID-19, researchers propose using models simply based on overall weekly deaths from any cause to estimate the probable course of the pandemic.
- There are further studies comparing infection spread to weather patterns. The latest in China found that daily average temperature and average relative humidity both showed significantly negative associations with the number of COVID-19 cases.
- COVID-19 prevalence is inversely correlated with incidence of malaria, leading researchers to propose that this is due to antimalarial drug use.
- A study of 56 COVID-19 patients found that ocular symptoms were present in 27% of patients, with 40% of these patients noting ocular symptoms prior to respiratory symptoms.

Understanding the Pathology

- One study used molecular docking software to explore binding to the SARS-CoV-2 main protease and found 17 natural marine compounds that were energetically more favorable in binding than Lopinavir and should be explored for medicinal purposes.
- One study of over 1,200 patients in China found the average incubation period of the virus to be about 7.4 days. Only 7.45% of patients had an incubation period longer than 14 days.
- Adding to previous literature, androgen regulation is thought to be related to the increased prevalence of COVID-19 in males, smokers, and the elderly.

Transmission & Prevention

- Measurements of aerosolized viral RNA in various locations in two Wuhan hospitals found the highest concentrations to be in patient toileting areas and other poorly ventilated areas.
- Physicians in Taiwan present a schematic for a homemade protective tent for aerosolizing procedures that costs less than $20 to make.
- The city of Hangzhou implemented a strict, 3-phase strategy for outbreak management involving isolation of suspected cases, quarantine of close contacts, closing of nonessential businesses, and limiting people to leaving their homes twice a week. By February 19th, there were only 2 cases in the city and quarantine was lifted.

Management

- Results from a case series led to recommendation that patients should have serial CT scans to document lung lesion resolution before discharge and a follow-up RT-PCR and CT scan after discharge to decrease risk of continued infection.
- There has been no conclusive evidence on the effect of RAS blockers or ibuprofen on headaches during infection.
- There are guidelines for management of the following in COVID-19 patients:
    - Tracheal trauma in the morbidly obese
    - Diabetic patients
    - Palliative care

- The Italian Society of Endocrinology recommends that patients with adrenal insufficiency with suspected COVID-19 should double their usual dose if the infection is mild, increase the dose to 100mg if the infection is moderate, and increase the dose to 200mg for critical infections.

Adjusting Practice during COVID-19

- Increasing case reports suggest that multiple sclerosis patients on immunosuppressants generally develop uncomplicated COVID-19, alleviating some concerns for this population.
- Guidelines and Recommendations are available for:
    - Phototherapy
    - Dermatology consultations and implementation of telemedicine.
    - Management of lung nodules and cancer screening.
- In 123 pediatric patients undergoing rheumatic disease treatment in Italy, there were zero cases of COVID-19 encouraging continuation of typical therapy and suggesting the success of current preventative measures.

R&D: Diagnosis & Treatments

- High resolution CT scans, with minimized ionizing radiation, have been proposed as an alternative to the time-consuming and lower sensitivity RT-PCR test for COVID-19 diagnosis.
- In a systematic review of nutrition-based interventions for other viral diseases, results showed that Vitamin A and D supplementation in deficient patients, as well as selenium, zinc, and probiotics may have immuno-modulatory effects for COVID-19 patients.

Mental Health & Resilience

- A cross sectional study of over 1,500 people in China found that individuals who knew someone who was quarantined or were quarantined themselves scored significantly higher in anxiety and depression metrics than those unaffected.
- Psychiatrists worry that panic and fear from the pandemic as well as limited opportunities for clinical follow up will lead to a negative impact in OCD patients.

Table of Contents

Ocular manifestation as first sign of Coronavirus Disease 2019 (COVID-19): Interest of telemedicine during the pandemic context.

Cutaneous manifestations in COVID-19: Lessons learned from current evidence.

Understanding the Pathology

May IL-17 have a role in COVID-19 infection?

COVID-19 transmission through host cell directed network of GPCR.

Hypertension prevalence in human Coronavirus: The role of ACE system in infection spread and severity.

In silico

Putative Inhibitors of SARS-CoV-2 Main Protease from A Library of Marine Natural Products: A Virtual Screening and Molecular Modeling Study.

In vitro

Covid-19, TMPRSS2, and whether android regulation affects pandemic virus gender incidence and age distribution of disease.

Transmission & Prevention

Developments in Transmission & Prevention

Aerodynamic analysis of SARS-CoV-2 in two Wuhan hospitals.

Prevention in the Community

Non-pharmaceutical intervention strategies for outbreak of COVID-19 in Hangzhou, China.

The role of community-wide wearing of face mask for control of coronavirus disease 2019 (COVID-19) epidemic due to SARS-CoV-2.

Airborne Transmission Route of COVID-19: Why 2 Meters/6 Feet of Inter-Personal Distance Could Not Be Enough.

Prevention in the Hospital

Corona-steps for tracheotomy in COVID-19 patients: A staff-safe method for airway management.

A Protection Tent for Airway Management in Patients With COVID-19 Infection.

Nepal's Response to Contain COVID-19 Infection.

3D Printed Face Shields: A Community Response to the COVID-19 Global Pandemic.

Management

Acute care

Emergency Medicine

Pulmonary thromboembolism in criticall [sic] ill COVID-19 patients.

Presepsin in risk stratification of SARS-CoV-2 patients

Performance Evaluation of UAV-Enabled LoRa Networks for Disaster Management Applications.

Diagnostic Radiology

Imaging of coronavirus disease 2019: A Chinese expert consensus statement.

Critical Care

Tracheal trauma after difficult airway management in morbidly obese patients with COVID-19.

Obesity hypoventilation syndrome and severe COVID-19.

Safe Bronchodilator Treatment in Mechanically Ventilated COVID-19 Patients: A Single Center Experience

Medical subspecialties

Serial CT features in discharged COVID-19 patients with positive RT-PCR re-test.

Allergy and immunology

Case Report: One Case of Coronavirus Desease [sic] 2019(COVID-19) in Patient Co-infected by HIV With a Low CD4+ T Cell Count

Cardiology

The role of natriuretic peptide estimation in severe COVID-19.

Endocrinology

Practical recommendations for the management of diabetes in patients with COVID-19.

Gastroenterology

Current Knowledge and Research Priorities in the Digestive Manifestations of COVID-19

Hematology and Oncology

A Quantitative Framework for Modeling COVID-19 Risk During Adjuvant Therapy Using Published Randomized Trials of Glioblastoma in the Elderly.

Age-adjusted D-dimer Cut-Off Levels to Rule Out Venous Thromboembolism in COVID-19 Patients

Palliative Care

The key role of palliative care in response to the COVID-19 tsunami of suffering.

Adjusting Practice During COVID-19

For Healthcare Professionals

Family-Centered Care During the COVID-19 Era.

An Invited Commentary on ' Evidence Based Management Guideline for the COVID-19 Pandemic- Review article'.

European Association for the Study of Obesity Position Statement on the Global COVID-19 Pandemic.

Acute care

Anti-CD20 immunosuppressive disease-modifying therapies and COVID-19.

Medical subspecialties

Dermatology

Coronavirus Disease 2019 (COVID-19) and dermatologists: Potential biological hazards of laser surgery in epidemic area.

Recommendations for Phototherapy During the COVID-19 Pandemic

Telemedicine for Inpatient Dermatology Consultations in Response to the COVID-19 Pandemic.

Geriatrics

The Need to Include Assisted Living in Responding to the COVID-19 Pandemic.

Hematology and Oncology

Management of Lung Nodules and Lung Cancer Screening During the COVID-19 Pandemic: CHEST Expert Panel Report.

Nephrology

The use of Captopril - angiotensin converting enzyme (ACE) inhibitor for cystinuria during COVID-19 pandemic.

Rheumatology

The Question of Whether to Remain on Therapy for Chronic Rheumatic Diseases in the Setting of the Covid-19 Pandemic.

Surgical Subspecialties

General Surgery

Acute care surgery and postoperative COVID-19 pneumonia: a surgical and environmental challenge.

Guidelines for infection prevention and control in perioperative patients during the COVID-19 pandemic: protocol from a tertiary general hospital in Beijing

Otolaryngology

Pediatric laryngoscopy and bronchoscopy during the COVID-19 pandemic: A four-center collaborative protocol to improve safety with perioperative management strategies and creation of a surgical tent with disposable drapes.

OBGYN

COVID-19 pandemic. Impact on hysteroscopic procedures. A consensus statement from the Global Congress of Hysteroscopy Scientific Committee.

Ophthalmology

Levels 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.**

Credit: 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

We have added Level 6 to denote papers that do not cite any sources or provide any supporting evidence.

Climate

Global

Clinical Profile of Cases of COVID-19 in Far Western Province of Nepal.

Joshi J, Mishra P, Kamar SB, Sharma ND, Parajuli J, Sharma S, Pandey HR.
J Nepal Health Res Counc
2020 Apr 20, PMID: 32335609
Level of Evidence: 4 - Case series
Type of Article: Research

BLUF: The authors of this case series of four patients who tested positive for COVID-19 in the far west province of Nepal conclude that Nepal is in stage two of disease transmission with no current local transmission and must conduct more tests, contact trace, social distance, quarantine high risk individuals, and establish dedicated COVID-19 hospitals to limit disease spread.

Abstract:
The novel coronavirus (COVID-19) cause *[sic]* various symptoms such as pneumonia, fever, breathing difficult *[sic]* and lung infection. Till now, **total 9 cases are reported in Nepal and 4 cases from this province**. This case series is to describe the initial clinical features of COVID-19 among the patients admitted in isolation ward of Seti Provincial Hospital. Oropharyngeal swab was taken from all four patients and sample *[sic]* was transfer *[sic]* to national reference laboratory. Three patients were coming from infected country *[sic]* and one is local *[sic]* transmission. Age of patients was range *[sic]* from 20 to 40 years of age with male preponderance. The patient coming from United Arab Emirate was presented with mild symptoms and others were asymptomatic. **More tests, contact tracing and keeping them in quarantine are the necessitated action need to be taken by government of Nepal** *[sic]*.

Indirect effects of COVID-19 on the environment.

Zambrano-Monserrate MA, Ruano MA, Sanchez-Alcalde L
Sci Total Environ
2020 Apr 20; PMID: 32334159
Level of Evidence: 5 - Qualitative Study
Type of Article: Research

BLUF: The SARS-CoV2 virus has both positive and negative indirect effects on the environment all around the world (most affected are China, USA, Italy, and Spain). Positive effects include: reduction in greenhouse gas emissions, air pollution, nitrogen dioxide, and noise levels. Negative effects include: decreased recycling programs, reduced sustainable waste management, and increased domestic waste such as single-use packaging and bags.

Abstract: This research aims to show the **positive and negative indirect effects of COVID-19 on the environment**, particularly in the most affected countries such as China, USA, Italy, and Spain. Our research shows that there is a **significant association between contingency measures and improvement in air quality, clean beaches and environmental noise reduction.** On the other hand, there are also negative secondary aspects such as the reduction in recycling and the increase in waste, further endangering the contamination of physical spaces (water and land), in addition to air. Global economic activity is expected to return in the coming months in most countries (even if slowly), so decreasing GHG concentrations during a short period is not a sustainable way to clean up our environment.

Environmental perspective of COVID-19.

Saadat S, Rawtani D, Hussain CM.Saadat S, et al.
Sci Total Environ.
2020 Apr 22; PMID: 32335408
Level of Evidence: Level 5 - Expert Opinion
Article Type: Review

BLUF: The COVID-19 pandemic has contributed to large amounts of medical waste in the environment due to the massive increase in use of daily masks, single-use gloves, and hand sanitizers. However, the lockdowns, reduced transportation use, and decrease in economic activities have benefited air and water quality around the world.

Abstract: The outbreak of COVID-19 has caused concerns globally. On 30 January WHO has declared it as a global health emergency. **The easy spread of this virus made people to wear [*sic*] a mask as precautionary [*sic*] route, use gloves and hand sanitizer on a daily basis that resulted in generation of a massive amount of**

medical wastes in the environment. Millions of people have been put on lockdown in order to reduce the transmission of the virus. This epidemic has also changed the people's life style; caused extensive job losses and threatened the sustenance of millions of people, as businesses have shut down to control the spread of virus. **All over the world, flights have been canceled and transport systems have been closed. Overall, the economic activities have been stopped and stock markets dropped along with the falling carbon emission. However, the lock down of the COVID-19 pandemic caused the air quality in many cities across the globe to improve and drop in water pollutions in some parts of the world.**

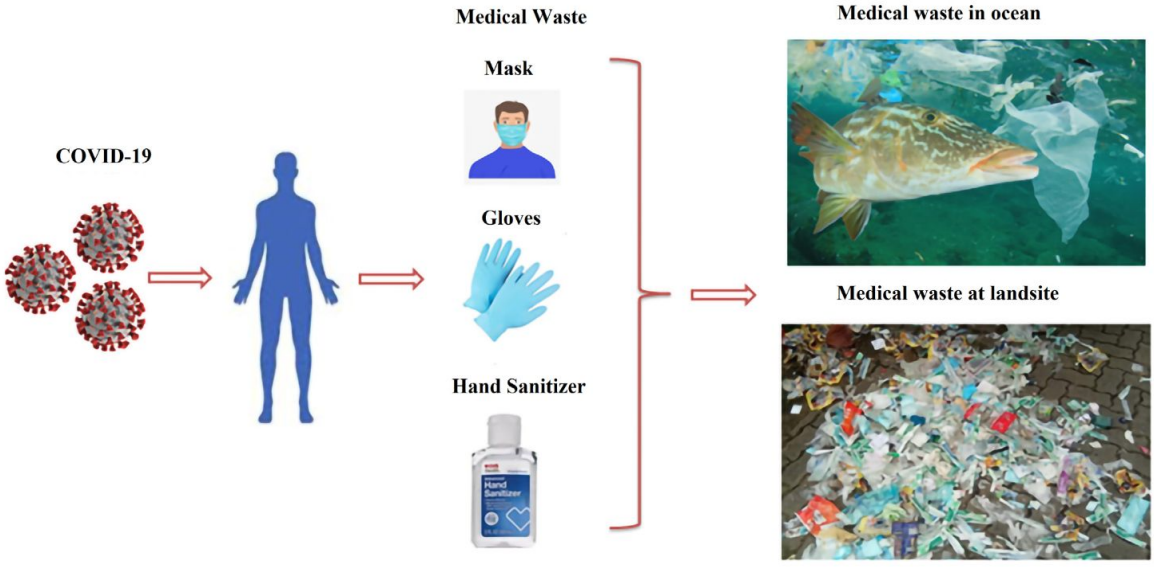


Fig. 1. Medical wastes generated during COVID-19 pandemic in the environment.

Fig. 2. Comparison of air quality in some of the biggest cities around the world before the COVID-19 pandemic and while the lockdown.

Effect of restricted emissions during COVID-19 on air quality in India.

Sharma S, Zhang M, Anshika, Gao J, Zhang H, Kota SH.
Sci Total Environ
2020 Apr 22, PMID: 32335409
Level of Evidence: 5 - Expert Opinion
Article Type: Research

BLUF: Since restrictions implemented in March in India, they have found a reduction in PM2.5 and increase in O3, significantly reducing air quality index (AQI). The authors conclude the air quality in India can continue to improve if proper plans to control the quality are implemented.

Abstract:

The effectiveness and cost are always top factors for policy-makers to decide control measures and most measures had no pre-test before implementation. Due to the COVID-19 pandemic, human activities are largely restricted in many regions in India since mid-March of 2020, and it is a progressing experiment to testify effectiveness of restricted emissions. In this study, concentrations of six criteria pollutants, PM10, PM2.5, CO, NO2, ozone and SO2 during March 16th to April 14th from 2017 to 2020 in 22 cities covering different regions of India were analysed. Overall, around 43, 31, 10, and 18% decreases in PM2.5, PM10, CO, and NO2 in India were observed during lockdown period compared to previous years. While, there were 17% increase in O3 and negligible changes in SO2. The air quality index (AQI) reduced by 44, 33, 29, 15 and 32% in north, south, east, central and western India, respectively. Correlation between cities especially in northern and eastern regions improved in 2020 compared to previous years, indicating more significant regional transport than previous years. The mean excessive risks of PM reduced by ~52% nationwide due to restricted activities in lockdown period. To eliminate the effects of possible favourable meteorology, the WRF-AERMOD model system was also applied in Delhi-NCR with actual meteorology during the lockdown period and an un-favourable event in early November of 2019 and results show that predicted PM2.5 could increase by only 33% in unfavourable meteorology. This study gives confidence to the regulatory bodies that even during unfavourable meteorology, a significant improvement in air quality could be expected if strict execution of air quality control plans is implemented.

Travel restrictions hampering COVID-19 response
Devi, Sharmila
Lancet
2020 Apr 25; PMID: 32334692
Level of Evidence: 5 - Expert Opinion
Type of Article: Comment
Summarizing Excerpt: "The coronavirus disease 2019 (COVID-19) pandemic has sparked an unprecedented shutdown of borders and airlines, which is severely restricting the movement of essential medical personnel and supplies that are vital to stem the spread of the virus and save lives."

Inter nation social lockdown versus medical care against COVID-19, a mild environmental insight with special reference to India.
Paital B, Das K, Parida SK.Paital B, et al.
Sci Total Environ.
2020, Apr 23; PMID: 32339832
Level of Evidence: 5- Literature Review
Type of Article: Review
BLUF: This article reviews the various ways that countries have approached COVID-19 and the effectiveness/limitations of specific drugs currently being used to treat patients. The authors emphasize that without an available vaccine or FDA approved medication, "**social lockdown is the only preventive found to be feasible and effective,** and therefore, it is recommended that other counties *[sic]* with low infection rate could follow this scientific but a strict social move for a considerable period to handle the CoV-19 pandemic."

Abstract:
Infection by coronavirus (CoV-19) has led to emergence of a pandemic called as Coronavirus Disease (COVID-19) that has so far affected about 210 countries. The dynamic data indicate that the pandemic by CoV-19 so far has infected 2,403,963 individuals, and among these 624,698 have recovered while, it has been fatal for 165,229. Without much experience, currently, the medicines that are clinically being evaluated for COVID-19 include chloroquine, hydroxychloroquine, azithromycin, tocilizumab, lopinavir, ritonavir, tocilizumab and corticosteroids. Therefore, countries such as Italy, USA, Spain and France with the most advanced health care system are partially successful to control CoV-19 infection. India being the 2nd largest populous country, where, the healthcare system is underdeveloped, major portion of population follow unhygienic lifestyle, is able to restrict the rate of both infection and death of its citizens from COVID-19. India has followed an early and a very strict social distancing by lockdown and has issued advisory to clean hands regularly by soap and/or by alcohol based sterilizers. Rolling data on the global index of the CoV infection is 13,306, and the index of some countries such as USA (66,148), Italy (175,055), Spain (210,126), France (83,363) and Switzerland (262,122) is high. The index of India has remained very low (161) so far, mainly due to early implementation of social lockdown, social distancing, and sanitizing hands. However, articles on social lockdown as a preventive measure against COVID-19 in PubMed are scanty. It has been observed that social lockdown has also drastic impacts on the environment especially on reduction of NO2 and CO2 emission. Slow infection rate under strict social distancing will offer time to researchers to come up with exact medicines/vaccines against CoV-19. Therefore, it is concluded that stringent social distancing via lockdown is highly important to control COVID-19 and also to contribute for self-regeneration of nature.

Deep impact of COVID-19 in the healthcare of Latin America: the case of Brazil.
Cimerman S, Chebabo A, Cunha CAD, Rodríguez-Morales AJ
Braz J Infect Dis
2020 Apr 23; PMID: 32335078
Level of Evidence: 5-Expert opinion
Type of Article: Editorial
Summary: A presentation of the spread of COVID-19 and the incidence of severe acute respiratory illness hospitalizations in Brazil through April 17. The authors express concern that Brazilian policies do not reflect current evidence-based guidelines coming from the WHO and worry about a region already recently hit by epidemics of chikungunya and Zika.

COVID-19 outbreak: Migration, effects on society, global environment and prevention.
Chakraborty I, Maity P
Sci Total Environ.
2020 Apr 22; PMID: 32335410
Level of Evidence: 5 - Expert opinion
Type of Article: Review
BLUF: The authors review the origins of the COVID-19 outbreak and its impact on global health, the economy, and the environment. They also review current strategies to control the outbreak, including limiting mass gatherings and current medical therapies, as well as potential strategies to prevent future outbreaks, such as the effects of forestation, controlling human population growth, and banning wildlife trade.

Abstract: The COVID-19 pandemic is considered as the most crucial global health calamity of the century and the greatest challenge that the humankind faced since the 2nd World War. In December 2019, a new infectious respiratory disease emerged in Wuhan, Hubei province, China and was named by the World Health Organization as COVID-19 (coronavirus disease 2019). A new class of corona virus, known as SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) has been found to be responsible for occurrence of this disease. As far as the history of human civilization is concerned there are instances of severe outbreaks of diseases caused by a number of viruses. According to the report of the World Health Organization (WHO as of April 18 2020), the current outbreak of COVID-19, has affected over 2164111 people and killed more than 146,198 people in more than 200 countries throughout the world. Till now there is no report of any clinically approved antiviral drugs or vaccines that are effective against COVID-19. It has rapidly spread around the world, posing enormous health, economic, environmental and social challenges to the entire human population. The coronavirus outbreak is severely disrupting the global economy. Almost all the nations are struggling to slow down the transmission of the disease by testing & treating patients, quarantining suspected persons through contact tracing, restricting large gatherings, maintaining complete or partial lock down etc. This paper **describes the impact of COVID-19 on society and global environment, and the possible ways in which the disease can be controlled** has also been discussed therein.

Deep impact of COVID-19 in the healthcare of Latin America: the case of Brazil.
Cimerman S, Chebabo A, Cunha CAD, Rodríguez-Morales AJ.Cimerman S, et al.Braz J Infect Dis. 2020
2020 Apr 23; PMID: 32335078
Level of Evidence: 5 - Expert Opinion
Type of Article: Editorial
Summary: Brazilian Society of Infectious Disease experts are summarizing the progression of COVID-19 in South America, particularly in Brazil. Describing it as a “complex clinical scenario” due to additional overlapping epidemics such as dengue, yellow fever, and other long term consequences of chikungunya and Zika. An epidemiological comparison of hospitalizations in Brazil from April 2019 to 2020, shows dramatic increases in hospitalizations after day 11 from the first diagnosed case in Sao Paulo. In addition to measures of quarantine, isolation and social distancing, they propose that if there is proper support and advice from scientific societies such as the Brazilian Society of Infectious Disease, international organizations such as Pan-American Health Organization (PAHO) and WHO it will help slow the progression of new cases and decrease overall cases.

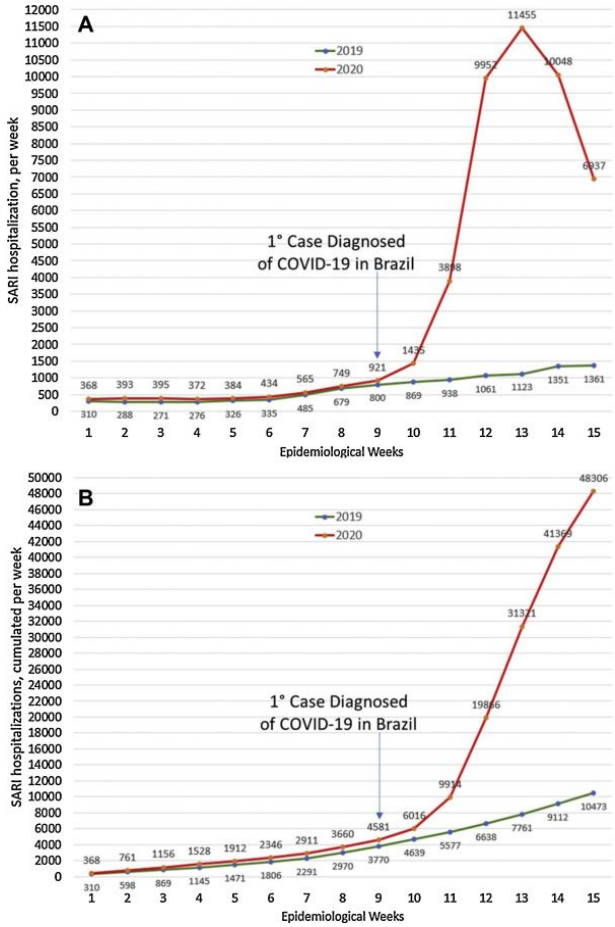


Figure 1. Hospitalizations due to Severe Acute Respiratory Infections (SARI), during the first 15 epidemiological weeks of 2019 and 2020. A. New number per week. B. Cumulative per week.

Affecting the Healthcare Workforce

-stories about how to address healthcare workforce needs that aren't directly related to workforce mental health or PPE so things like …. Much of the workforce are moms or dads who need childcare support as well as mental health support. Workforce education needs to improve- data shows most hcps don't understand disease etc etc

The Fight Against COVID-19 and the Restoration of Trust in Chinese Medical Professionals

Gan, Y., Chen, Y., Wang, C., Latkin, C., & Hall, B. J.
Asian J Psychiatr.
2020 Apr 9; PMID: 32334408
Level of Evidence: 5 - Expert opinion
Type of Article: Commentary

Summary: The authors believe that the heroic actions of medical professionals and images on social media during the COVID-19 pandemic in China have been widely applauded by the public and are helping to restore public trust in medical professionals.

COVID-19 emergency responders in FDA's Center for Drug Evaluation and Research.

Gormley LCA, Ngan CK.
J Am Pharm Assoc (2003).
2020 Apr 9; PMID: 32336674
Level of Evidence: 5- Expert opinion
Type of Article: Letter

Summary: The U.S. Public Health Service Commissioned Corps is one of the eight uniformed services and is dedicated to protecting, promoting, and advancing the health and safety of the nation. During the COVID-19 crisis, Commissioned Corps officers are currently serving many different roles. Commissioned Corps pharmacy officers are on-call 24/7 to ensure health care providers can access FDA staff to facilitate the use of investigational drugs, actively monitor global drug supply chains to anticipate and mitigate any drug shortages, and contribute to the FDA's task force dedicated to

monitoring for fraudulent products and false product claims. **Commissioned Corps pharmacy officers have a duty to help physicians and the public alike, and have taken action during this time of global crisis.**

Disparities

The vulnerability of low-and middle-income countries facing the COVID-19 pandemic: The case of Haiti.

Cénat JM.

Travel Med Infect Dis. PMID: 32334090

Level of Evidence: 5 - Expert Opinion

Type of Article: Letter

Summary: Low and middle-income countries, with Haiti as an example, are at a disadvantage in the face of the COVID-19 pandemic. **High levels of poverty, coupled with a lack of hospital equipment and infrastructure, place these countries at a higher risk of spreading the infection.** Steps need to be taken at the national and regional level to strengthen the healthcare system in these vulnerable countries.

Epidemiology

Understanding COVID-19 in Nepal.
Pun SB, Mandal S, Bhandari L, Jha S, Rajbhandari S, Mishra AK, Sharma Chalise B, Shah R.
J Nepal Health Res Counc
2020 Apr 20; PMID: 32335607
Level of Evidence: 4 - Case Series
Type of Article: Short Communication
BLUF: As of April 10, 2020 there were 9 confirmed positive COVID-19 cases in Nepal. Out of these the median age was 32 years old, 56% were male, and only one case was positive due to local transmission. There were no deaths. All infected patients showed little or no symptoms. Two cases showed persistent viral shedding 14 days after the initial positive test.

Abstract:
The novel coronavirus COVID-19 (SARS-CoV-2) was first reported in 31 December 2019 in Wuhan City, China. The first case of COVID-19 was officially announced on 24 January, 2020, in Nepal. Nine COVID-19 cases have been reported in Nepal. We aim to describe our experiences of COVID-19 patients in Nepal.

Statistical and network analysis of 1212 COVID-19 patients in Henan, China.
Wang P, Lu JA, Jin Y, Zhu M, Wang L, Chen S.
Int J Infect Dis.
2020 Apr 24; PMID: 32339715
Level of Evidence: 5 – Statistical Analysis
Type of Article: Research
BLUF: Based on a total of 1212 confirmed cases of COVID-19 in Henan, China from 1/21/20 to 2/14/20, the average incubation period of patients was estimated to be 7.4 days. About 7.45% patients were thought to have longer than 14 days of incubation periods.

Abstract:
Background: COVID-19 is spreading quickly all over the world. Publicly released data for 1212 COVID-19 patients in Henan of China was analyzed in this paper.
Methods: Various statistical and network analysis methods were employed.
Results: We found that COVID-19 patients show gender (55% vs 45%) and age (81% aged between 21 and 60) preferences, possible causes were explored; The estimated average, mode and median incubation periods are 7.4, 4 and 7 days; Incubation periods of 92% patients were no more than 14 days; The epidemic in Henan has undergone three stages and showed high correlations with the numbers of patients recently return from Wuhan; Network analysis revealed that 208 cases were clustering infected and various people's Hospitals are the main force in treating COVID-19.
Conclusions: The incubation period was statistical *[sic]* estimated and the proposed state transition diagram can well explore the epidemic stages of emerging infectious disease. We suggest that though the quarantine measures are gradually at work, strong measures might be still needed for a period of time, since ~7.45% patients may have very long incubation periods. Migrant workers or college students are with *[sic]* high risk. State transition diagram *[sic]* can help us to recognize the time-phased nature of epidemic *[sic]*. Our investigations have implications for the prevention and control of COVID-19 in other regions of the world.

COVID-19: a need for real-time monitoring of weekly excess deaths.
Leon DA, Shkolnikov VM, Smeeth L, Magnus P, Pechholdová M, Jarvis CI
Lancet.
2020 Apr 22; PMID: 32333839
Level of Evidence: 5 - Expert opinion
Type of Article: Letter
BLUF: Mounting an effective epidemiological response to COVID-19 requires estimation of key parameters like case fatality risk and reproduction number to model the probable course of the pandemic. The challenge for public health scientists is that this data relies on testing coverage. **Weekly excess deaths could be the most objective and comparable way of assessing the scale of the pandemic**, by comparing the observed weekly deaths throughout 2020 to values expected from the experience of previous non-pandemic years.

Incidence of coronavirus disease (COVID-19) and countries affected by malarial infections.
Ahmed, Anwar E
Travel Medicine and Infectious Disease

2020 Apr 22; PMID: 32334084
Level of Evidence: 5 – Expert Opinion
Type of Article: Letter to the Editor
BLUF: The author discusses the inverse relationship between incidence of COVID-19 and incidence of malaria, as portrayed by countries such as Burkina Faso and Nigeria where there are high incidences of malaria and low numbers of COVID-19 cases. One possible explanation is the use of antimalarial drugs in these populations; further studies are needed to investigate whether the use of antimalarial drugs, environmental factors, and/or different strains of COVID-19 could be contributing to the low incidence of COVID-19 infection in countries affected by malaria.

Modeling

Impact of temperature on the dynamics of the COVID-19 outbreak in China.

Shi P, Dong Y, Yan H, Zhao C, Li X, Liu W, He M, Tang S, Xi S
Sci Total Environ
2020 Apr 23; PMID: 32339844
Level of Evidence: 4 - Cross sectional study
Type of Article: Research
BLUF: Authors examining the association of daily confirmed cases of COVID-19 with daily mean temperatures using locally weighted regression and smoothing scatterplot (LOESS) and distributed lag nonlinear models (DLNMs) from 31 provincial-level regions in mainland China between January 20 and February 29 found that temperatures above 8-10°C (46.4-50°F) were associated with decreased daily incidence, suggesting that regions with temperatures above 46.4°F may experience decreased incidence of infection.

ABSTRACT: A COVID-19 outbreak emerged in Wuhan, China at the end of 2019 and developed into a global pandemic during March 2020. The effects of temperature on the dynamics of the COVID-19 epidemic in China are unknown. **Data on COVID-19 daily confirmed cases and daily mean temperatures were collected from 31 provincial-level regions in mainland China between Jan. 20 and Feb. 29, 2020.** Locally weighted regression and smoothing scatterplot (LOESS), distributed lag nonlinear models (DLNMs), and random-effects meta-analysis were used to examine the relationship between daily confirmed cases rate of COVID-19 and temperature conditions. The daily number of new cases peaked on Feb. 12, and then decreased. The daily confirmed cases rate of COVID-19 had a **biphasic relationship with temperature (with a peak at 10 °C)**, and the **daily incidence of COVID-19 decreased at values below and above these values**. The overall epidemic intensity of COVID-19 **reduced slightly following days with higher temperatures** with a relative risk (RR) was 0.96 (95% CI: 0.93, 0.99). A random-effect meta-analysis including 28 provinces in mainland China, we confirmed the statistically significant association between temperature and RR during the study period (Coefficient = -0.0100, 95% CI: -0.0125, -0.0074). The DLNMs in Hubei Province (outside of Wuhan) and Wuhan showed similar patterns of temperature. Additionally, a modified susceptible-exposed-infectious-recovered (M-SEIR) model, with adjustment for climatic factors, was used to provide a complete characterization of the impact of climate on the dynamics of the COVID-19 epidemic.

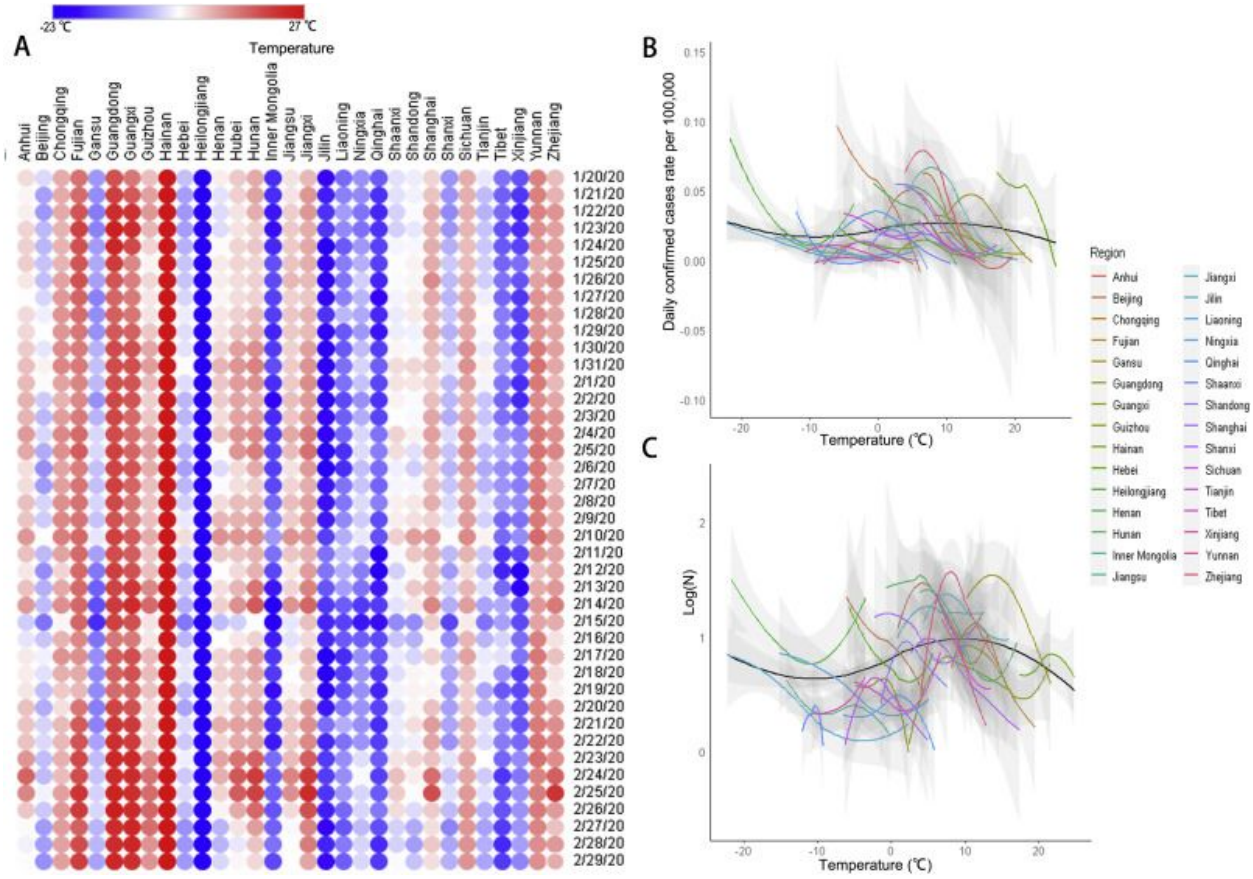


Fig. 1. (A) Temperature in 31 provincial-level regions in mainland China from Jan. 20 to Feb. 29, 2020. (B) and (C) COVID-19 daily confirmed cases indicators (daily rate and log[N]) as a function of temperature in mainland China (outside of Hubei Province) from Jan. 20 to Feb. 29. The black central line in each figure represents the expected daily confirmed cases rate and log(N) based on a LOESS regression for all days when there were available estimates. The solid colored lines represent estimated values of different regions and the gray shaded regions represent the corresponding 95% confidence intervals. Log(N): common logarithm of the number of newly confirmed cases; LOESS: locally weighted regression and smoothing scatterplot.

COVID-19 Transmission in Mainland China Is Associated With Temperature and Humidity: A Time-Series Analysis.

Qi, H., Xiao, S., Shi, R., Ward, M. P., Chen, Y., Tu, W., Su, Q., Wang, W., Wang, X., & Zhang, Z.
Sci Total Environ
2020 Apr 19; PMID: 32335405
Level of Evidence: 5 - Statistical modeling
Type of Article: Research

BLUF: A study conducted in Hubei, China, but not consistent throughout Mainland China, has shown that an increase in daily average temperature and relative humidity is associated with a decrease in daily confirmed cases of COVID-19.

Abstract:
COVID-19 has become a pandemic. The influence of meteorological factors on the transmission and spread of COVID-19 is of interest. This study sought to examine the **associations of daily average temperature (AT) and relative humidity (ARH) with the daily counts of COVID-19 cases** in 30 Chinese provinces (in Hubei from December 1, 2019 to February 11, 2020 and in other provinces from January 20, 2020 to Februarys 11, 2020). A Generalized Additive Model (GAM) was fitted to quantify the province-specific **associations between meteorological variables and the daily cases of COVID-19 during the study periods**. In the model, the 14-day exponential moving averages (EMAs) of AT and ARH, and their interaction were included with time trend and health-seeking behavior adjusted. Their spatial distributions were visualized. **AT and ARH showed significantly negative associations with COVID-19 with a significant interaction between them** (0.04, 95% confidence interval: 0.004-0.07) in Hubei. **Every 1 °C increase in the AT led to a decrease in the daily confirmed cases by 36% to 57%** when ARH was in the range from 67% to

85.5%. **Every 1% increase in ARH led to a decrease in the daily confirmed cases by 11% to 22%** when AT was in the range from 5.04 °C to 8.2 °C. However, these associations were not consistent throughout Mainland China.

GIS-based spatial modeling of COVID-19 incidence rate in the continental United States.
Mollalo A, Vahedi B, Rivera KM.
Sci Total Environ.
2020 Apr 22; PMID: 32335404
Level of Evidence: Statistical Modeling
Type of Article: Research
BLUF: The purpose of this study is to explore the relationship between 35 environmental, socioeconomic, and demographic variables and COVID-19 incidence in the US. It was stated that multiscale geographically weighted regression could explain 68.1% of the total variations of COVID-19 incidence in the US and could be a useful tool to guide policy.

Abstract:
During the first 90 days of the COVID-19 outbreak in the United States, over 675,000 confirmed cases of the disease have been reported, posing unprecedented socioeconomic burden to the country. Due to inadequate research on geographic modeling of COVID-19, we investigated county-level variations of disease incidence across the continental United States. We compiled a geodatabase of 35 environmental, socioeconomic, topographic, and demographic variables that could explain the spatial variability of disease incidence. Further, we employed spatial lag and spatial error models to investigate spatial dependence and geographically weighted regression (GWR) and multiscale GWR (MGWR) models to locally examine spatial non-stationarity. The results suggested that even though incorporating spatial autocorrelation could significantly improve the performance of the global ordinary least square model, these models still represent a significantly poor performance compared to the local models. Moreover, MGWR could explain the highest variations (adj. R^2: 68.1%) with the lowest AICc compared to the others. Mapping the effects of significant explanatory variables (i.e., income inequality, median household income, the proportion of black females, and the proportion of nurse practitioners) on spatial variability of COVID-19 incidence rates using MGWR could provide useful insights to policymakers for targeted interventions.

Prediction for the spread of COVID-19 in India and effectiveness of preventive measures
Tomar A, Gupta N.
Sci Total Environ.
2020 Apr 20; PMID: 32334157
Level of Evidence: Predictive modeling using AI
Type of Article: Research
BLUF: A long short-term memory (LSTM) deep learning method was used to curve fit the predicted number of cases in the future, using training data of COVID-19 confirmed cases in India from January 2020 to April 2020. The recovery rate was observed to be high, but long. **Preventative measures such as social isolation were applied to the model and were found to have a significant reduction in cases.**

Abstract:
The spread of COVID-19 in the whole world has put the humanity at risk. The resources of some of the largest economies are stressed out due to the large infectivity and transmissibility of this disease. Due to the growing magnitude of number of cases and its subsequent stress on the administration and health professionals, some prediction methods would be required to predict the number of cases in future. In this paper, we have used data-driven estimation methods like long short-term memory (LSTM) and curve fitting for prediction of the number of COVID-19 cases in India 30 days ahead and effect of preventive measures like social isolation and lockdown on the spread of COVID-19. The prediction of various parameters (number of positive cases, number of recovered cases, etc.) obtained by the proposed method is accurate within a certain range and will be a beneficial tool for administrators and health officials.

The Coronavirus Pandemic: What Does the Evidence Show?
Paudel S, Dangal G, Chalise A, Bhandari TR, Dangal O.
J Nepal Health Res Counc
2020 Apr 19; PMID: 32335585
Level of Evidence: 5 - Literature Review
Type of Article: Review Article

BLUF: As of April 17, 2020 there have been 2,074,529 confirmed cases of COVID-19 and 139,378 deaths. The clinical presentation of COVID-19 shares similarities with SARS-CoV and MERS-Cov and diagnosis is made by rRT-PCR on respiratory samples. There is currently no effective medicine or vaccine available for COVID-19. In the absence of medical treatment measures such as social distancing and community containment have been major strategies to prevent the outbreaks.

Abstract:
Coronavirus disease 2019 (COVID-19) is a newly emerged disease that has become a global public health concern as it rapidly spread around the world. The etiologic agent responsible for this disease has been named as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) by the International Committee on Taxonomy of Viruses as it shows similar genomic features to that of SARS-CoV which caused a pandemic in 2002. This disease first appeared in Hubei province of China and it follows human-to-human transmission but the path this virus took to set up human infection remains a mystery. **By 17 April 2020, globally there have been 2,074,529 confirmed cases with 139,378 deaths because of COVID-19. SARS-CoV-2 shows several similarities with SARS-CoV, and Middle East Respiratory Syndrome Coronavirus (MERS-CoV) with its clinical presentations.** This can vary from asymptomatic infection to severe disease and mortality. Real-time reverse-transcription polymerase chain reaction (rRT-PCR) screening is considered as the standard laboratory test for the diagnosis of COVID-19. There is no proven antiviral agent against SARS-CoV-2 so the treatment for COVID-19 is symptomatic, aiming for the management of the symptoms and prevention of the complications. The outbreak of COVID-19 has led to the implementation of extraordinary public health measures throughout the world. **Numerous antiviral compounds used to treat other infections are being clinically researched to find possible treatment. Similarly, the traditional public health outbreak response strategy of isolation, quarantine, social distancing and community containment has been implemented in multiple countries and has played an important role in the prevention of new outbreaks.** This review aims to enhance our understanding of COVID 19.

Real-time estimation and prediction of mortality caused by COVID-19 with patient information based algorithm.
Wang L, Li J, Guo S, Xie N, Yao L, Cao Y, Day SW, Howard SC, Graff JC, Gu T, Ji J, et al.
Sci Total Environ.
2020 Apr 8; PMID: 32334207
Level of Evidence: Proof of concept
Article Type: Research
BLUF: The authors use a new methodology to estimate the death rate of COVID-19, called the Patient Information Based Algorithm. They estimate since February 25, 2020, death rates were in the range of 0.75% to 3%. These results show that the real death numbers had fallen into the predicted ranges in Wuhan, China.

Abstract:
The global COVID-19 outbreak is worrisome both for its high rate of spread, and the high case fatality rate reported by early studies and now in Italy. We report a new methodology, the Patient Information Based Algorithm (PIBA), for estimating the death rate of a disease in real-time using publicly available data collected during an outbreak. PIBA estimated the death rate based on data of the patients in Wuhan and then in other cities throughout China. The estimated days from hospital admission to death was 13 (standard deviation (SD), 6 days). The death rates based on PIBA were used to predict the daily numbers of deaths since the week of February 25, 2020, in China overall, Hubei province, Wuhan city, and the rest of the country except Hubei province. The death rate of COVID-19 ranges from 0.75% to 3% and may decrease in the future. The results showed that the real death numbers had fallen into the predicted ranges. In addition, using the preliminary data from China, the PIBA method was successfully used to estimate the death rate and predict the death numbers of the Korean population. In conclusion, PIBA can be used to efficiently estimate the death rate of a new infectious disease in real-time and to predict future deaths. The spread of 2019-nCoV and its case fatality rate may vary in regions with different climates and temperatures from Hubei and Wuhan. PIBA model can be built based on known information of early patients in different countries.

Symptoms and Clinical Presentation

Adults

Risk factors of critical & mortal COVID-19 cases: A systematic literature review and meta-analysis.
Zheng Z, Peng F, Xu B, Zhao J, Liu H, Peng J, Li Q, Jiang C, Zhou Y, Liu S, Ye C, et al.
J Infect.
2020 Apr 23; PMID: 32335169
Level of Evidence: Level 1- Systematic Metaanalysis
Article Type: Research

Summary: The data of COVID-19 patients until March 20, 2020 were retrieved from four databases and the risk factors for critical/mortal and non-critical COVID-19 patients were analyzed. The authors found that males, those over 65, and smoking patients showed a greater risk of developing the critical or mortal condition and that the comorbidities such as hypertension, diabetes, cardiovascular disease, and respiratory diseases could also greatly affect the prognosis of the COVID-19. Clinical manifestations such as fever, shortness of breath or dyspnea and laboratory findings such as WBC, AST, Cr, PCT, LDH, hs-cTnI and D-dimer could predict the progression of COVID-19.

Background: An epidemic of Coronavirus Disease 2019 (COVID-19) began in December 2019 and triggered a Public Health Emergency of International Concern (PHEIC). We aimed to find risk factors for the progression of COVID-19 to help [in] reducing the risk of critical illness and death for clinical help.
Methods: The data of COVID-19 patients until March 20, 2020 were retrieved from four databases. We statistically analyzed the risk factors of critical/mortal and non-critical COVID-19 patients with metaanalysis.
Results: Thirteen studies were included in Meta-analysis, including a total number of 3027 patients with SARS-CoV-2 infection. **Male, older than 65, and smoking were risk factors for disease progression in patients with COVID-19** (male: OR = 1.76, 95% CI (1.41, 2.18), P < 0.00001; age over 65 years old: OR =6.06, 95% CI(3.98, 9.22), P < 0.00001; current smoking: OR =2.51, 95% CI(1.39, 3.32), P = 0.0006). **The proportion of underlying diseases such as hypertension, diabetes, cardiovascular disease, and respiratory disease were statistically significant higher in critical/mortal patients compared to the non-critical patients** (diabetes: OR=3.68, 95% CI (2.68, 5.03), P < 0.00001; hypertension: OR = 2.72, 95% CI (1.60,4.64), P = 0.0002; cardiovascular disease: OR = 5.19, 95% CI(3.25, 8.29), P < 0.00001; respiratory disease: OR = 5.15, 95% CI(2.51, 10.57), P < 0.00001). Clinical manifestations such as fever, shortness of breath or dyspnea were associated with the progression of disease [fever: OR = 0.56, 95% CI (0.38, 0.82), P = 0.003;shortness of breath or dyspnea: OR=4.16, 95% CI (3.13, 5.53), P < 0.00001]. Laboratory examination such as aspartate aminotransferase (AST) > 40U/L, creatinine(Cr) ≥ 133mol/L, hypersensitive cardiac troponin I(hs-cTnI) > 28pg/mL, procalcitonin(PCT) > 0.5ng/mL, lactatede *[sic]* hydrogenase(LDH) > 245U/L, and D-dimer > 0.5mg/L predicted the deterioration of disease while white blood cells(WBC)<4 × 109/L meant a better clinical status[AST > 40U/L:OR=4.00, 95% CI (2.46, 6.52), P < 0.00001; Cr ≥ 133μmol/L: OR = 5.30, 95% CI (2.19, 12.83), P = 0.0002; hs-cTnI > 28 pg/mL: OR = 43.24, 95% CI (9.92, 188.49), P < 0.00001; PCT > 0.5 ng/mL: OR = 43.24, 95% CI (9.92, 188.49), P < 0.00001;LDH > 245U/L: OR = 43.24, 95% CI (9.92, 188.49), P < 0.00001; D-dimer > 0.5mg/L: OR = 43.24, 95% CI (9.92, 188.49), P < 0.00001; WBC < 4 × 109/L: OR = 0.30, 95% CI (0.17, 0.51), P < 0.00001].
Conclusion: Male, aged over 65, smoking patients might face a greater risk of developing into the critical or mortal condition and the comorbidities such as hypertension, diabetes, cardiovascular disease, and respiratory diseases could also greatly affect the prognosis of the COVID-19. Clinical manifestation such as fever, shortness of breath or dyspnea and laboratory examination such as WBC, AST, Cr, PCT, LDH, hs-cTnI and D-dimer could imply the progression of COVID-19.

Diabetes mellitus is associated with increased mortality and severity of disease in COVID-19 pneumonia - A systematic review, meta-analysis, and meta-regression.

Huang I, Lim MA, Pranata R
Diabetes Metab Syndr
2020 Apr 17; PMID: 32334395
Level of Evidence: 1 - Systematic Review
Type of Article: Research

BLUF: A systematic literature review shows that diabetes mellitus (DM) was associated with poor outcomes including increased mortality, severe COVID-19, ARDS, and disease progression in patients with COVID-19. Poor outcome in patients with COVID-19 was also influenced by age and hypertensive status.

Abstract:
Aims and background: Diabetes Mellitus (DM) is chronic conditions with devastating multi-systemic complication and may be associated with severe form of Coronavirus Disease 2019 (COVID-19). We conducted a systematic review and meta-analysis in order to investigate the association between DM and poor outcome in patients with COVID-19 pneumonia.
Methods: Systematic literature search was performed from several electronic databases on subjects that assess DM and outcome in COVID-19 pneumonia. The outcome of interest was composite poor outcome, including mortality, severe COVID-19, acute respiratory distress syndrome (ARDS), need for intensive care unit (ICU) care, and disease progression.
Results: There were a total of 6452 patients from 30 studies. Meta-analysis showed that DM was associated with composite poor outcome (RR 2.38 [1.88, 3.03], p < 0.001; I2: 62%) and its subgroup which comprised of mortality (RR 2.12 [1.44, 3.11], p < 0.001; I2: 72%), severe COVID-19 (RR 2.45 [1.79, 3.35], p < 0.001; I2: 45%), ARDS (RR 4.64 [1.86, 11.58], p = 0.001; I2: 9%), and disease progression (RR 3.31 [1.08, 10.14], p = 0.04; I2: 0%). Meta-regression showed that the association with composite poor outcome was influenced by age (p = 0.003) and hypertension (p < 0.001). Subgroup

analysis showed that the association was weaker in studies with median age ≥55 years-old (RR 1.92) compared to <55 years-old (RR 3.48), and in prevalence of hypertension ≥25% (RR 1.93) compared to <25% (RR 3.06). Subgroup analysis on median age <55 years-old and prevalence of hypertension <25% showed strong association (RR 3.33).
Conclusions: **DM was associated with mortality, severe COVID-19, ARDS, and disease progression in patients with COVID-19.**

Factors Associated With Negative Conversion of Viral RNA in Patients Hospitalized With COVID-19.
Hu, X., Xing, Y., Jia, J., Ni, W., Liang, J., Zhao, D., Song, X., Gao, R., & Jiang, F.
Sci Total Environ
2020 Apr 22; PMID: 32335406
Level of Evidence: 4 - Case series
Type of Article: Research
BLUF: A case series of COVID-19 patients in Qingdao, China showed that hospitalized patients older than 45 years or those presenting with chest tightness or headache showed delayed clearance of SARS-CoV-2 RNA, suggesting that these patients may need extended isolation.

Abstract:
Factors associated with negative conversion of SARS-CoV-2 RNA in hospitalized patients have not yet been systematically determined. We conducted a retrospective cohort study of COVID-19 patients in Qingdao, China. Both univariate and multivariate analysis were performed to identify independent factors for time to viral RNA negative conversion. Data on patients with re-detectable viral RNA after showing negative on RT-PCR test (intermittent negative status) were also analyzed. A total of 59 patients confirmed with COVID-19 were included in this study, with a median duration of 1 (interquartile range, IQR: 0-2) day from symptom onset to hospital admission. Median communicable period (from first day of positive nucleic acid test to first day of consecutive negative results) was 14 (IQR: 10-18) days, and 7 (IQR: 6-10) days for 10 patients with intermittent negative results. Age older than 45 years (hazard ratio, HR: 0.378; 95% confidence interval, CI: 0.205-0.698) and chest tightness (HR: 0.290; 95%CI: 0.091-0.919) were factors indecently affecting negative conversion of SARS-CoV-2 RNA. Headache (odds ratio: 7.553; 95%CI: 1.011-28.253) was significantly associated with intermittent negative status, with a predicted probability of 60%. Older age and chest tightness were independently associated with delayed clearance of SARS-CoV-2 RNA in hospitalized patients. These predictors would provide a new perspective on early identification of patients with prolonged viral shedding and facilitate optimal isolation protocols and treatment strategies.

Evaluation of ocular symptoms and tropism of SARS-CoV-2 in patients confirmed with COVID-19.
Hong N, Yu W, Xia J, Shen Y, Yap M, Han W.
Acta Ophthalmol.
2020 Apr 26; PMID: 32336042
Level of Evidence: 4 - Case Series
Type of Article: Research
BLUF: In 56 patients infected with SARS-CoV-2, researchers administered two questionnaires to assess ocular symptoms. Ocular symptoms were present in 27% of patients of whom 40% presented with ocular symptoms before the onset of respiratory symptoms (n=56, p<0.05)

Abstract:
Purpose: The SARS-CoV-2 RNA has been detected in tears and conjunctival samples from infected individuals. Conjunctivitis is also reported in a small number of cases. We evaluated ocular symptoms and ocular tropism of SARS-CoV-2 in a group of patients with COVID-19.
Method: Fifty-six patients infected with SARS-CoV-2 were recruited as subjects. Relevant medical histories were obtained from the electronic medical record system. Ocular history and ocular symptoms data were obtained by communicating directly with the subjects. The Ocular Surface Disease Index (OSDI) and Salisbury Eye Evaluation Questionnaire (SEEQ) were used to assess the anterior ocular surface condition before and after the onset of disease.
Results: Patients classified as severe COVID-19 cases were more likely to have hypertension compared to mild cases (p = 0.035). Of the 56 subjects, thirteen patients (23%) were infected in Wuhan, 32 patients (57%) were community-infected, 10 patients (18%) were unknown origin, 1 (2%) was a physician likely infected by a confirmed patient. Three patients wore face mask with precaution when contacting the confirmed patients. Fifteen **(27%) had aggravated ocular symptoms, of which 6 (11%) had prodromal ocular symptoms before disease onset.** The differences in mean scores of OSDI questionnaire and SEEQ between before and after onset of COVID-19 were all significant (p < 0.05 for both).
Conclusions: Ocular symptoms are relatively common in COVID-19 disease and may appear just before the onset of respiratory symptoms. Our data provided the anecdotal evidences of transmission of SARS-CoV-2 via ocular surface.

[Characterization of Acute Acro-Ischemic Lesions in Non-Hospitalized Patients: A Case Series of 132 Patients During the COVID-19 Outbreak]

Fernandez-Nieto D, Jimenez-Cauhe J, Suarez-Valle A, Moreno-Arrones OM, Saceda-Corralo D, Arana-Raja A, Ortega-Quijano D
J Am Acad Dermatol
2020 Apr 24; PMID: 32339703
Level of Evidence: 4 – Case Series
Type of Article: Letter to the Editor

BLUF: This article reports two patterns of acro-ischemic lesions, chilblaine like and erythema multiforme like, observed in 132 young outpatients who were consulted on by dermatology during a month of the COVID-19 pandemic (March-April 2020). They suspect these lesions could be late manifestations of mild COVID-19, with mild being defined as COVID-19 without pneumonia.

Summary: A case series of 132 outpatients (mean age = 19.9 years old) from March 5 – April 15 performed in Spain found **two different patterns of acute acro-ischemic lesions as suspected late manifestations of SARS-CoV-2 infection in patients without atypical pneumonia**. Of the two patterns, those with the **chilblain-like lesions** (n = 95) were statistically more likely to have lesions that were ventrally located, on the feet and heels/wrists, and had a mean duration of 9.2 days. Those with the **erythema multiforme-like lesions** (n = 37) were also statistically likely to display the same location characteristics, although the mean duration of skin lesions was found to be 7.4 days. **It is important to note that the groups included in the study were not all diagnosed with COVID-19;** 54 patients had close contact with a confirmed COVID-19 patient, 28 patients had close contact with a healthcare worker, 19 patients were clinically diagnosed with COVID-19, and 2 patients were confirmed to be positive for the virus via RT-PCR from a nasopharyngeal swab.

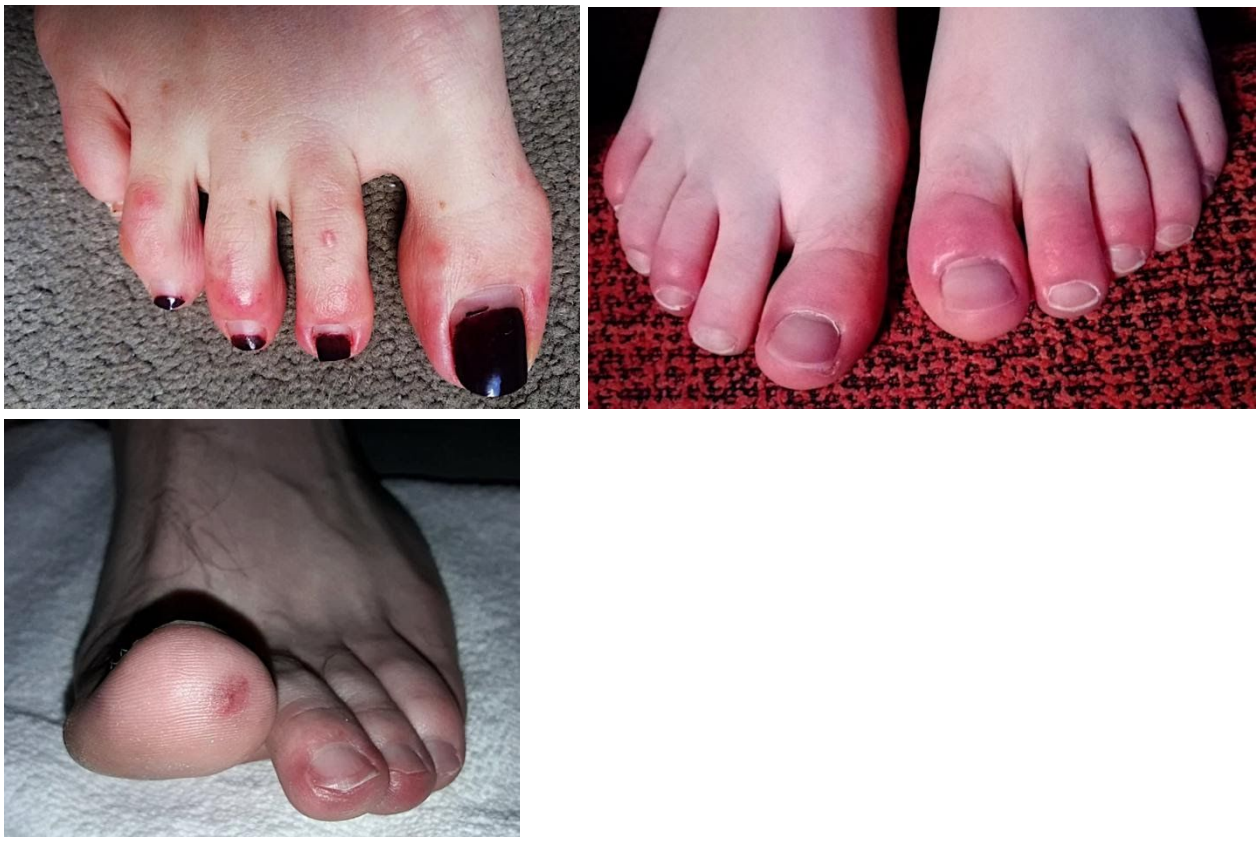


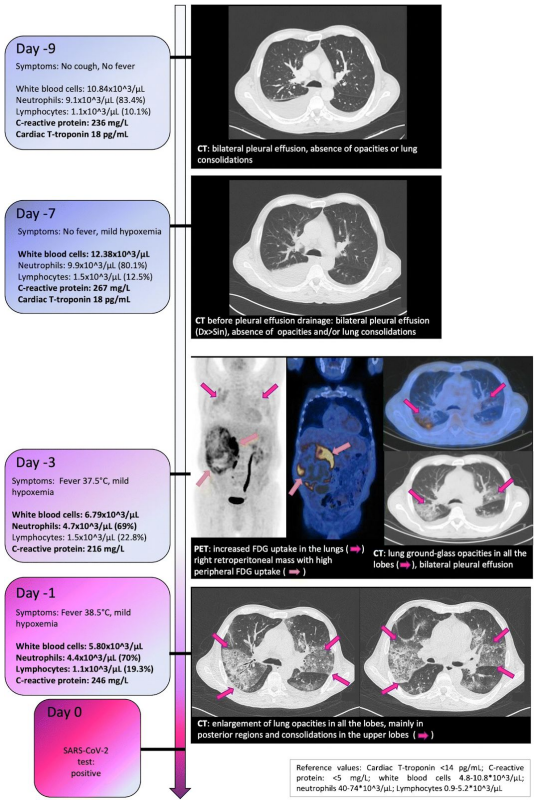
Figure 1. Chilblain-like acro-ischemia. A) Ecchymotic plaques and nodules with a bruising appearance over the distal aspects of toes. B) Confluent erythemato-violaceous diffuse plaques sparing some toes and the dorsal feet. C) Close-up view of the lateral and plantar aspects of toes.

Figure 2. Erythema multiforme-like acro-ischemia. A) Erosion and crust formation over dusky plaques in the dorsal aspects of digits. A Koebner phenomenon is present over the hallux valgus. B) Circular lesions, some of them with a targetoid appearance over the plantar surface. C) Confluent vesicles over a dusky area.

CT, [^{18}F]FDG-PET/CT and clinical findings before and during early Covid-19 onset in a patient affected by vascular tumour.

Kirienko M, Padovano B, Serafini G, Marchianò A, Gronchi A, Seregni E, Alessi A.Kirienko M
J Nucl Med Mol Imaging
2020 April 25; PMID: 32335706
Level of Evidence: 4 - Case Report
Type of Article: Research

Summary: A proactive approach for managing patients with SARS-CoV-2 infection includes early identification, appropriate imaging studies, and obtaining a history of neoplastic disease. This case report emphasizes this approach by performing imaging studies such as high-resolution CT and fluoro-deoxyglucose PET/CT during a patient's initial workup to monitor their symptoms and progression from the disease (figure 1). This proactive approach allowed healthcare workers to be prepared, anticipate diagnosis, and select safe and effective interventions for the patient.



Ocular manifestation as first sign of Coronavirus Disease 2019 (COVID-19): Interest of telemedicine during the pandemic context.

Daruich A, Martin D, Bremond-Gignac D.Daruich A, et al.
J Fr Ophtalmol.
2020 Apr 17; PMID: 32334847
Level of Evidence: 4 – Case Report
Article Type: Case Report

Summary: A 27 year-old male contacted a telemedicine service with left eye foreign body sensation, conjunctival hyperemia, and eyelid edema. Within 12 hours he developed fever to 39C, cough, and dyspnea. Nasopharyngeal RT-PCR was positive for COVID-19. Conjunctiva/tears were not tested for COVID-19. 11 days later a telemedicine consult confirmed his ocular and respiratory symptoms had resolved. The case illustrates a rare example of conjunctivitis or "red eye" as the presenting sign of COVID-19 infection.

Cutaneous manifestations in COVID-19: Lessons learned from current evidence.

Suchonwanit P, Leerunyakul K, Kositkuljorn C.Suchonwanit P, et al.
J Am Acad Dermatol.
2020 Apr 24; PMID: 32339706
Level of Evidence: 5 – Expert Opinion
Article Type: Letter to the Editor

Summarizing excerpt: "…We can speculate that cutaneous manifestations in COVID-19 may present in 2 major groups regarding their pathomechanisms: (1) clinical features similar to viral exanthems, an immune response to viral nucleotides; and (2) cutaneous eruptions secondary to systemic consequences caused by COVID-19, especially vasculitis and thrombotic vasculopathy."

Understanding the Pathology

May IL-17 have a role in COVID-19 infection?
Megna M, Napolitano M, Fabbrocini G.
Med Hypotheses.
2020 Apr 22; PMID: 32339777
Level of Evidence: 5 – Mechanism-Based Reasoning
Type of Article: Letter to the Editor
Summary: The author makes a case for targeting IL-17 to potentially improve COVID-19's aberrant immune response and ARDS-related mortality, as tocilizumab (IL-6 blocker) is currently being investigated for similar reasons. Recent studies have shown IL-17 to be related to IL-6 in the context of viral infections, as well as elevated IL-17 in intensive-care COVID-19 patients compared to non-intensive-care patients.

COVID-19 transmission through host cell directed network of GPCR.
Singh Y, Gupta G, Satija S, Pabreja K, Chellappan DK, Dua K.
Drug Dev Res.
2020 Apr 23; PMID: 32329083
Level of Evidence: 5 - Mechanism-based reasoning
Type of Article: Research
BLUF: The COVID-19 virus is thought to activate JNK and JAK–STAT mediated mechanisms in the lungs, leading to the proliferation and transmission of viral cells. It is possible that both JNK and JAK–STAT pathways could be targeted pharmacologically to inhibit a COVID-19 infection, while keeping in mind potential risks of cardiac hypertrophy and fibrosis.

How Could This Happen? : Narrowing Down the Contagion of COVID-19 and Preventing Acute Respiratory Distress Syndrome (ARDS)
Allaerts W
Acta Biotheor
2020 Apr 25; PMID: 32335749
Level of Evidence: 5 – Expert Opinion
Type of Article: Review
BLUF: This article summarizes key genetic, biochemical, and early pathological similarities between the SARS-CoV and SARS-CoV-2, while noting the divergence in each respect from MERS (see bullets). The author further delves into risk factors for COVID-19 ARDS complications, including COPD among other lung diseases, and potential impacts that ACEIs may pose, given that SARS-CoV viruses use this receptor for entry.

- SARS-CoV and SARS-CoV-2 enter cells via ACE2; MERS via DPP4
- SARS-CoV viruses (including bat varieties) have different spike proteins from MERS
- SARS-CoV-2 is more infectious than SARS-CoV or MERS, but has a lower case fatality rate (2.3% vs 36% for MERS)

Abstract:
In this rapid commentary, a mini-review is given of the present state-of-knowledge regarding the etiology and epidemiology of the new coronavirus 2019-nCoV and the risks for developing Acute respiratory distress syndrome (ARDS). The available knowledge on the viral genomics, molecular biology and pathogenicity of viruses of the Coronaviridae family and other Nidovirales, forms a helpful template for understanding the present pandemic outbreak. However, important questions remain unanswered about the underlying mechanism causing the very high case fatality ratios (CFR) and mechanisms regarding severe reactions like ARDS, fatal cardiac and renal failures, associated with a number of important comorbidity factors. Immunological reactions to lung alveoles in particular (involving lung macrophages and alveolar epithelial cell damage) in late phase ARDS in SARS-like CoV diseases, so far may not have received enough attention. Finally a shortlist of questions for high priority further research is suggested.

Hypertension prevalence in human Coronavirus: The role of ACE system in infection spread and severity.
Ruocco G, Feola M, Palazzuoli A.
Int J Infect Dis
2020 Apr 23; PMID: 32335337
Level of Evidence: 5 - Mechanism Based Reasoning

Type of Article: Editorial

Summary: The authors discuss initial epidemiological data that suggests that hypertension is a risk factor for COVID-19 infection, noting that worldwide there are significant differences in the prevalence of hypertension. They also discuss potential mechanisms by which COVID-19 might interact with the ACE system (see Figure below), commenting that it remains unknown how ACE inhibitors and angiotensin receptor blockers might modulate the infectious process. They call for additional studies on this subject.

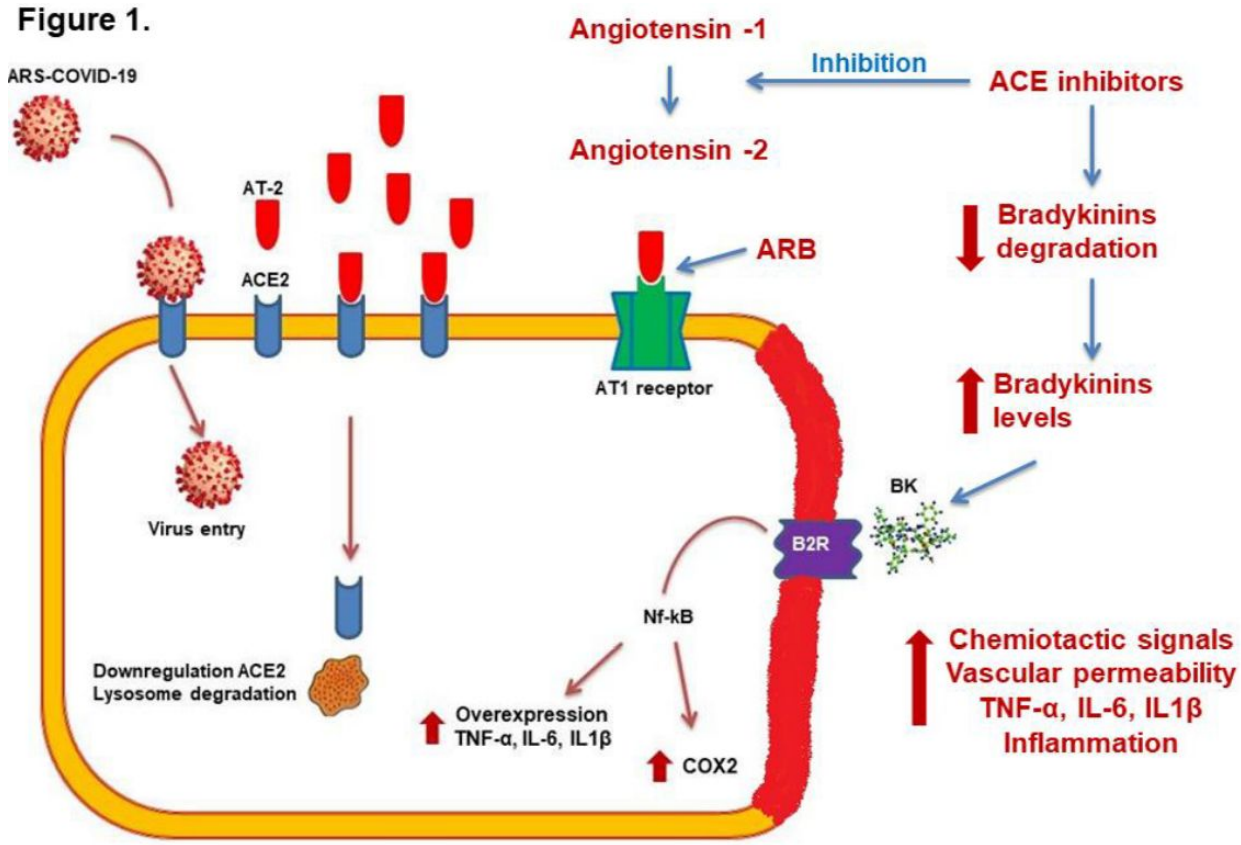


Figure: "Schematic view of potential mechanisms linking ACE system and COVID-19 infection. Virus could enter directly inside the epithelial cell of respiratory system by ACE2 receptor or induce inflammatory cascade by bradykinins escape related to ACEi therapy. The subsequent increase of prostaglandins and cyclooxygenases leads to interleukines production which cause membrane cell inflammation up to apoptosis. Abbreviations: ACE: angiotensin converting enzyme; ARB: angiotensin receptor Blocker; AT: Angiotensin; B2R: Bradykinin-2 receptor; BK: Bradykinin; COX: cyclooxygenase"

In silico

Putative Inhibitors of SARS-CoV-2 Main Protease from A Library of Marine Natural Products: A Virtual Screening and Molecular Modeling Study.

Gentile D, Patamia V, Scala A, Sciortino MT, Piperno A, Rescifina A

Mar Drugs

2020 Apr 23; PMID: 32340389

Level of Evidence: 5 - Mechanism-Based Reasoning

Type of Article: Research

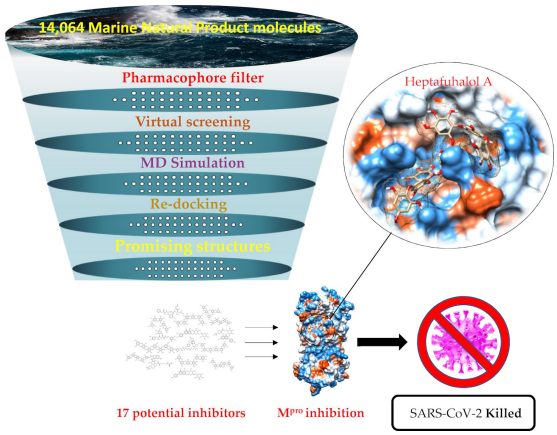
BLUF: Using molecular docking software to simulate binding to SARS-CoV-2 MPro (the main protease enzyme that has been validated as a pharmacological target for COVID-19 in recent studies) the authors found 17 natural marine compounds that have produced more favorable free binding energy scores than Lopinavir (HIV protease inhibitor currently gaining popularity in potential treatment of COVID-19). They conclude that these compounds could thus play a role in the development of novel COVID-19 medications.

Abstract:

The current emergency due to the worldwide spread of the COVID-19 caused by the new severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a great concern for global public health. Already in the past, the outbreak of severe acute respiratory syndrome (SARS) in 2003 and Middle Eastern respiratory syndrome (MERS) in 2012

demonstrates the potential of coronaviruses to cross-species borders and further underlines the importance of identifying new-targeted drugs. An ideal antiviral agent should target essential proteins involved in the lifecycle of SARS-CoV. Currently, some HIV protease inhibitors (i.e., Lopinavir) are proposed for the treatment of COVID-19, although their effectiveness has not yet been assessed. The main protease (Mpr) provides a highly validated pharmacological target for the discovery and design of inhibitors. We identified potent Mpr inhibitors employing computational techniques that entail the screening of a Marine Natural Product (MNP) library. MNP library was screened by a hyphenated pharmacophore model, and molecular docking approaches. Molecular dynamics and re-docking further confirmed the results obtained by structure-based techniques and allowed this study to highlight some crucial aspects. Seventeen potential SARS-CoV-2 Mpr inhibitors have been identified among the natural substances of marine origin. As these compounds were extensively validated by a consensus approach and by molecular dynamics, the likelihood that at least one of these compounds could be bioactive is excellent.

Graphical Abstract:



In vitro

Covid-19, TMPRSS2, and whether android regulation affects pandemic virus gender incidence and age distribution of disease.

Brenner SR.Brenner SR.
Med Hypotheses.
2020 Apr 22; PMID: 32339776
Level of Evidence: 5 - Mechanism Based Reasoning
Type of Article: Commentary

BLUF: Androgen regulation via Transmembrane Serine Protease 2 (TMPRSS2) may play a role in pathogenesis and treatment of SARS-COV-2.

Summary: The author believes androgen regulation may play a role in epidemiological trends showing increased prevalence in males, smokers, and the elderly. This claim is supported mainly by three articles. The first determined that TMPRSS2 is involved in ACE2 mediated pathways for viral cellular entry. The second study showed high TMPRSS2 concentrations in prostate epithelium and the third demonstrated an increased androgen:estrogen ratio in smokers. Based on these studies, he also proposes TMPRSS2 inhibitors as a potential therapy for SARS-COV-2.

Transmission & Prevention

Developments in Transmission & Prevention

Aerodynamic analysis of SARS-CoV-2 in two Wuhan hospitals.

Liu Y, Ning Z, Chen Y, Guo M, Liu Y, Gali NK, Sun L, Duan Y, Cai J, Westerdahl D, Liu X, Xu K, Ho KF, Kan H, Fu Q, Lan K.

Nature.

2020 Apr 27; PMID: 32340022

Level of Evidence: 5 – Qualitative Data

Type of Article: Research

Summary: The authors found that samples of aerosol deposition from areas used for protective apparel removal had relatively high levels of airborne SARS-CoV-2 RNA, particularly in aerosol sizes of between 0.25 to 1.0 micrometers. The areas with the highest concentration of SARS-CoV-2 RNA were inside patient mobile toilet rooms without ventilation. Thus, the authors recommend surface sanitization of apparel before they are taken off to help reduce potential infection risk of medical staff.

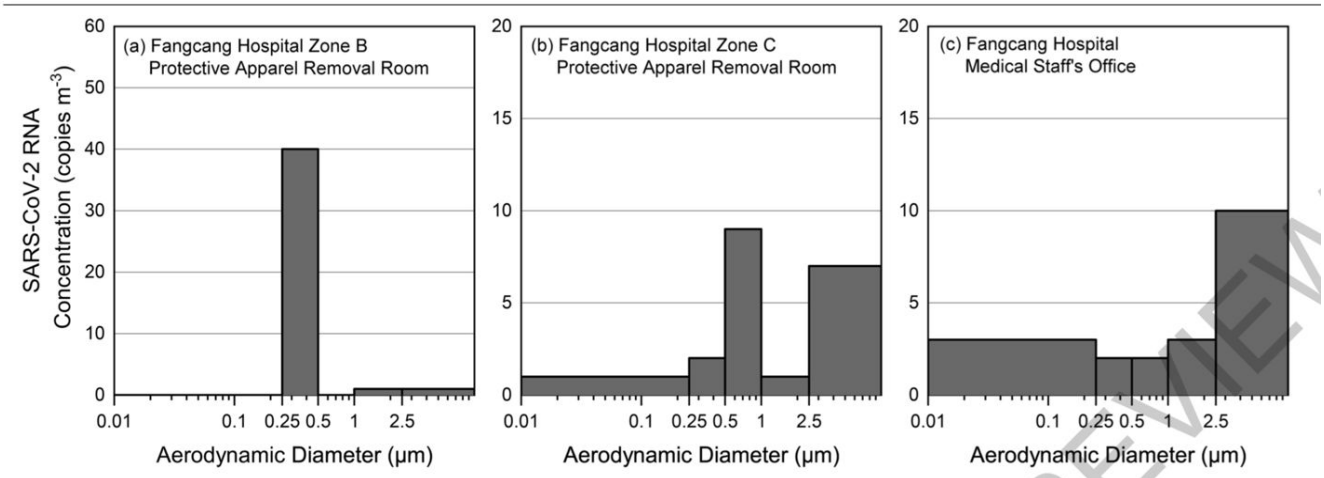


Fig. 1 | Concentration of airborne SARS-CoV-2 RNA in different aerosol size bins. The *x* axis represents aerodynamic diameter in logarithmic scale to cover the multiple magnitude of measured aerosol diameter..

Addressing the corona virus outbreak: will a novel filtered eye mask help?

Douglas, David; Douglas, Robert

International Journal of Infectious Diseases

2020 Apr 22; PMID: 32334119

Level of Evidence: 5 - Mechanism-based Reasoning

Type of Article: Research

BLUF: Following a review of eye protection currently available on the market (hermetically vs non-hermetically sealed eye protection), this paper introduces a novel filtered eye mask (FEM) that was developed with a filter to maintain a virus-free air mass in front of the eye while simultaneously limiting condensation build up of standard hermetically sealed eyewear. The FEM was tested against a hermetically-sealed standard eye mask (SEM) and out performed the SEM based on fog, revealing increased clarity with the FEM at 1 minute, 5 minutes, and 60 minutes after wear.

Abstract:

Objective: Non-hermetically sealed eye protection does not fully protect the eyes from airborne particles. Hermetically sealed eye protection fully protects the eyes from particles, but tend to fog up rendering unusable. The purpose of this study was build and test a filtered eye mask (FEM) to protect the eyes from airborne particles while being usable without excessive fog build up.

Methods: The steps performed to build the FEM were described. A hermetically-sealed standard eye mask (SEM) and a FEM were examined at 1 minute, 5 minutes and 60 minute period for performance metrics relating to fog.

Results: The SEM showed minimal fog at 1-minute, very foggy at 5-minutes and dripping with condensation at 60minutes. The FEM was clear at 1-minute, 5-minutes and showed minimal fog at 60minutes.

Conclusion: The FEM may play an important role in preventing novel coronavirus (COVID-19) exposure by protecting the eyes from airborne particles and preventing fog, rendering it usable. Further research is strongly recommended.

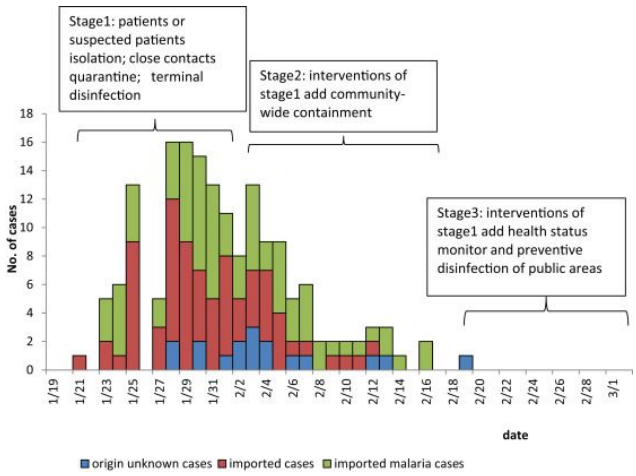
Prevention in the Community

Non-pharmaceutical intervention strategies for outbreak of COVID-19 in Hangzhou, China.

Kong Q, Jin H, Sun Z, Kao Q, Chen J.
Public Health
2020 Apr 24; PMID: 32339883
Level of Evidence: Level 5 - Statistical analysis
Type of Article: Letter to the Editor

BLUF: Strict quarantine measures were implemented in Hangzhou, China shortly after the first confirmed case in the city. These measures were incredibly effective and controlled the outbreak within a month of the first confirmed case.

Summary: The authors outline the three stages of interventions which were implemented in Hangzhou, a city in southern China with a population of more than 9.86 million. The first stage, beginning when the first confirmed case was reported on January 21, consisted of **isolation of patients/suspected patients, quarantine of close contacts, and disinfection of locations** where the patients had been previously. The second stage, from February 3-18, consisted of **closing of non-essential business and only allowing people to go out twice per week to buy necessities.** The third stage began February 19 and is currently in effect, and allowed businesses to resume normal function and people to stop their quarantine. These steps were very effective, as **by the time stage three went into effect there were less than 2 cases in the entire city.**



The role of community-wide wearing of face mask for control of coronavirus disease 2019 (COVID-19) epidemic due to SARS-CoV-2.

Cheng VCC, Wong SC, Chuang VWM, So SYC, Chen JHK, Sridhar S, To KKW, Chan JFW, Hung IFN, Ho PL, Yuen KY
J Infect
2020 Apr 23; PMID: 32335167
Level of Evidence: 4- Population study
Type of Article: Research

BLUF: The authors attempt to evaluate the effects of universal masking on COVID-19 spread by looking at the number of case clusters in "mask on" vs "mask off" settings in Hong Kong as well as the difference in case load in Hong Kong vs Singapore in the first 100 days (which they argue is a good control based on similar size, population density, development of health system, and COVID-19 tests/million people). They find **Hong Kong has significantly fewer cases and a smaller proportion of "mask off" cases than Singapore and that more clusters in Hong Kong were related to "mask off settings" than "mask on settings."**

Abstract

Background: Face mask usage by the healthy population in the community to reduce risk of transmission of respiratory viruses remains controversial. We assessed the effect of community-wide mask usage to control coronavirus disease 2019 (COVID-19) in Hong Kong Special Administrative Region (HKSAR).

Methods: Patients presenting with respiratory symptoms at outpatient clinics or hospital wards were screened for COVID-19 per protocol. Epidemiological analysis was performed for confirmed cases, especially persons acquiring COVID-19 during mask-off and mask-on settings. The incidence of COVID-19 per-million-population in HKSAR with community-wide masking was compared to that of non-mask-wearing countries which are comparable with HKSAR in

terms of population density, healthcare system, BCG vaccination and social distancing measures but not community-wide masking. Compliance of face mask usage in the HKSAR community was monitored.
Findings: Within first *[sic]* 100 days (31 December 2019 to 8 April 2020), 961 COVID-19 patients were diagnosed in HKSAR. The COVID-19 incidence in HKSAR (129.0 per-million-population) was significantly lower ($p<0.001$) than that of Spain (2983.2), Italy (2250.8), Germany (1241.5), France (1151.6), U.S. (1102.8), U.K. (831.5), Singapore (259.8), and South Korea (200.5). The compliance of face mask usage by HKSAR general public was 96.6% (range: 95.7% to 97.2%). **We observed 11 COVID-19 clusters in recreational 'mask-off' settings compared to only 3 in workplace 'mask-on' settings ($p = 0.036$ by Chi square test of goodness-of-fit).**
Conclusion: Community-wide mask wearing may contribute to the control of COVID-19 by reducing virus shedding in saliva and respiratory droplets from individuals with subclinical or mild COVID-19.

Airborne Transmission Route of COVID-19: Why 2 Meters/6 Feet of Inter-Personal Distance Could Not Be Enough.
Setti, Leonardo; Passarini, Fabrizio; Gennaro, Gianluigi D; Barbieri, Pierluigi; Perrone, Maria G; Borelli, Massimo; Palmisani, Jolanda; Gilio, Alessia D; Piscitelli, Prisco; Miani, Alessandro
International Journal of Environmental Research and Public Health
2020 Apr 23; PMID: 32340347
Level of Evidence: 5 – Expert Opinion
Type of Article: Editorial
BLUF: There is recent evidence, including on-field studies in Wuhan Hospitals and Nebraska University Hospital, that supports the hypothesis of airborne diffusion of droplets from person to person of SARS-CoV-2 at a distance greater than two meters. This position paper emphasizes the airborne transmission route as a potential explanation for the anomalous outbreaks in northern Italy, which is characterized as one of the most polluted areas in Europe; recommendations are made with the possibility of airborne transmission in mind, including the mandatory adoption of face masks during lockdown and phase 2, and more extensive distancing measures.

Abstract:
The COVID-19 pandemic caused the shutdown of entire nations all over the world. In addition to mobility restrictions of people, the World Health Organization and the Governments have prescribed maintaining an inter-personal distance of 1.5 or 2 m (about 6 feet) from each other in order to minimize the risk of contagion through the droplets that we usually disseminate around us from nose and mouth. However, recently published studies support the hypothesis of virus transmission over a distance of 2 m from an infected person. Researchers have proved the higher aerosol and surface stability of SARS-COV-2 as compared with SARS-COV-1 (with the virus remaining viable and infectious in aerosol for hours) and that airborne transmission of SARS-CoV can occur besides close-distance contacts. Indeed, there is reasonable evidence about the possibility of SARS-COV-2 airborne transmission due to its persistence into aerosol droplets in a viable and infectious form. Based on the available knowledge and epidemiological observations, it is plausible that small particles containing the virus may diffuse in indoor environments covering distances up to 10 m from the emission sources, thus representing a kind of aerosol transmission. On-field studies carried out inside Wuhan Hospitals showed the presence of SARS-COV-2 RNA in air samples collected in the hospitals and also in the surroundings, leading to the conclusion that the airborne route has to be considered an important pathway for viral diffusion. Similar findings are reported in analyses concerning air samples collected at the Nebraska University Hospital. On March 16th, we have released a Position Paper emphasizing the airborne route as a possible additional factor for interpreting the anomalous COVID-19 outbreaks in northern Italy, ranked as one of the most polluted areas in Europe and characterized by high particulate matter (PM) concentrations. The available information on the SARS-COV-2 spreading supports the hypothesis of airborne diffusion of infected droplets from person to person at a distance greater than two meters (6 feet). The inter-personal distance of 2 m can be reasonably considered as an effective protection only if everybody wears face masks in daily life activities.

Prevention in the Hospital

Corona-steps for tracheotomy in COVID-19 patients: A staff-safe method for airway management.
D'Ascanio L, Latini G, Pandolfini M, Giardini D.D'Ascanio L, et al.
Oral Oncol.
2020 Apr 20; PMID: 32335007
Level of Evidence: 4 - Case series
Type of Article: Research / Letter
BLUF: The authors recommend a number of updates (summarized below) to Pichi et al.'s previously published editorial, "CORONA-steps for tracheostomy in COVID-19 patients: A staff-safe method for airway management". These updates were recommended based on preliminary results from a case series involving 22 patients who underwent surgical tracheostomy between 2/3/2020 and 3/14/2020 after orotracheal intubation for SARS-CoV-2.

Summary: Based on preliminary findings from their case series **(no health care worker infections and decreased air exposure time to contaminated aerosols)**, the authors **recommend the following updates** to Pichi et al.'s standardized steps for tracheostomy:

1. Instead of pushing the ET tube caudally when opening the trachea: "**push the endotracheal tube forward along the tracheal lumen until its cuff is placed just above the carina** before surgery to erase this contamination risk".
2. Instead of reducing the O2 saturation of air to 21%: "once the anterior tracheal wall is exposed…**carry out an adequate preoxygenation (100% oxygen for 3 min) and then stop mechanical ventilation 30 s before the tracheal anterior wall is opened**…[this] prevents the expired infected air to come out under pressure".
3. "In order **to minimize** HCWs' intraoperative time **exposure to patients' aerosolized secretions…connect the tracheostomy cannula with a Halyard closed suction system®** (which is attached to the ventilator at the end of the procedure)"

A Protection Tent for Airway Management in Patients With COVID-19 Infection.
Fang PH, Lin YY, Lin CH.Fang PH, et al.
Ann Emerg Med.
2020 Apr 11; PMID: 32334882
Level of Evidence: 5 – Expert Opinion
Article Type: Letter to the Editor
Summary: A schematic for a protection tent using a home-made $20 USD frame and accompanying disposable plastic sheet film is presented. It is light, portable, and designed with holes for arms. The goal is to provide a cheap, mobile barrier that allows doctors and nurses to perform aerosolizing procedures (e.g. intubation) on COVID-19 patients with greater safety.

Nepal's Response to Contain COVID-19 Infection.
Piryani RM, Piryani S, Shah JN.
J Nepal Health Res Counc
2020 Apr 20, PMID: 32335608
Level of Evidence: 5 - Review of events
Type of Article: Research
BLUF: Since the start of the pandemic, Nepal has dedicated COVID-19 spaces in hospitals, updated the capacity of lab confirmatory testing, disseminated PPE, released information to the public, strengthened the health sector's preparedness, and improved lab services for COVID-19.

Abstract:
Nepal is a landlocked country bordering two most populous countries, India and China. Nepal shares open border with India from three sides, east, south and west. And, in north with China, where the novel coronavirus infection (CVOVID-19) began in late December 2019. The first confirmed imported case in Nepal was reported in 2nd week of January 2020. The initial response of Nepal to COVID-19 were comparably slow but country geared efforts after it was declared a 'global pandemic' by WHO on 11 March, 2020. **Government of Nepal's steps from 18 March, 2020 led to partial lock down and countrywide lockdown imposed on 24 March, 2020**. Government devised comprehensive plan on 27 March, 2020 for **quarantine for peoples who arrived in Nepal from COVID-19 affected countries**. This article covers summary of global status, South Asian Association of Regional Cooperation (SAARC) status, and Nepal's response to contain COVID-19 infection discussed under three headings: Steps taken before and after WHO declared COVID-19 a global pandemic and lab services regarding detection of COVID-19. Nepal has **documented five confirmed cases of COVID-19 till the end of March 2020**, first in second week of 15 January, 2020 and 2nd case 8-weeks thereafter and 3rd case two days later, 4th on 27 March and 5th on 28 March. Four more cases detected during first week of April. **Non-Pharmacological interventions like social distancing and excellent personal habits are widely practiced**. Country has to enhance testing and strengthen tracing, isolation and quarantine mechanism and care of COVID-19 patients as **Nepal is in risk zone because of comparably weak health system and porous borders with India**. The time will tell regarding further outbreak and how it will be tackled.

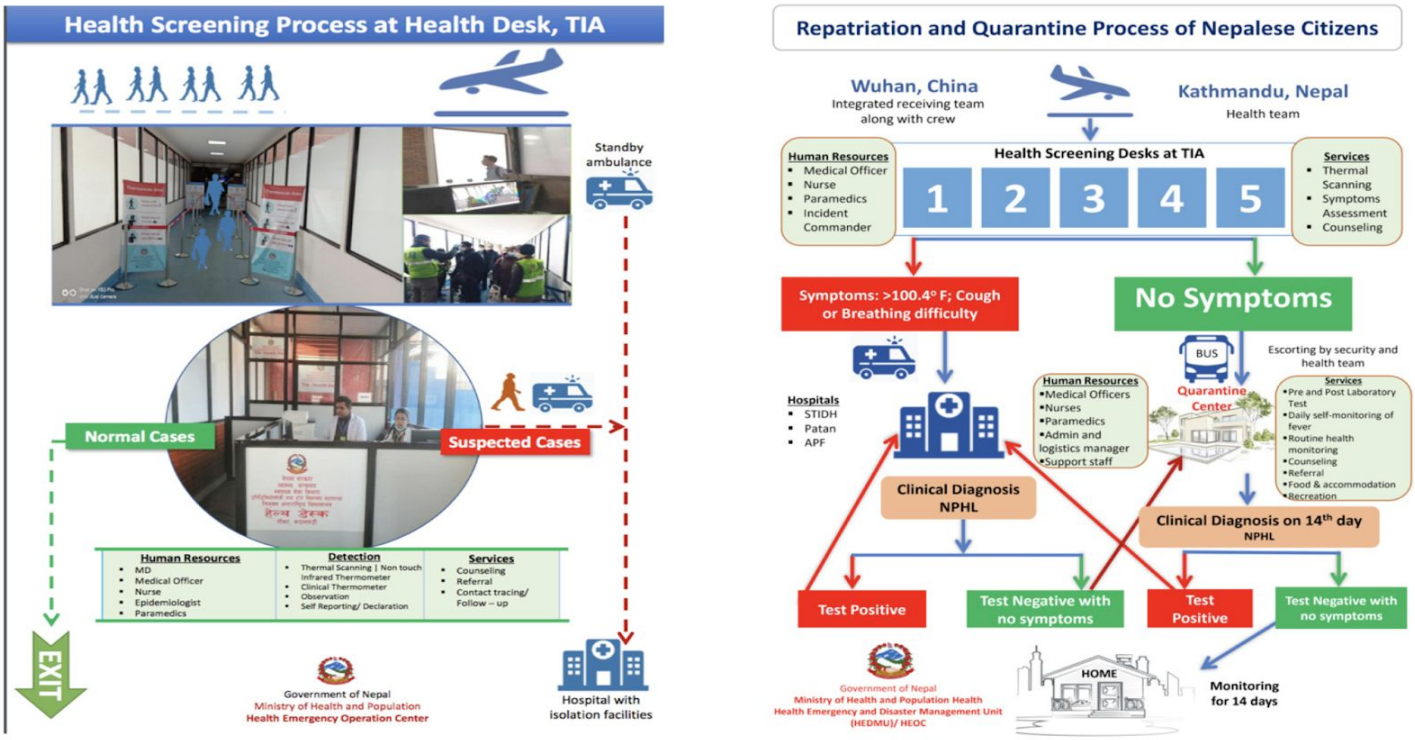


Figure: (a) Health screening at the Tribhuvan International Airport (TIA) in Kathmandu to isolate and treat travelers with COVID-19 (b) Repatriation and quarantine process of Nepalese citizens.

[3D Printed Face Shields: A Community Response to the COVID-19 Global Pandemic.](#)
Flanagan ST, Ballard DH.
Acad Radiol.
2020 Apr 17; PMID: 32335004
Level of Evidence: 5-Expert Opinion
Type of Article: Letter to the Editor
BLUF: Amidst critical shortages for PPE, 3D printing industries are meeting the demand by rapidly producing face shields for healthcare providers.

Summary: Three-dimensional printing has evolved greatly over the last decade, and its uses have since expanded to many healthcare applications. Now, in the midst of a global pandemic, there is a collective need to re-supply the critical shortages of personal protective equipment (PPE). Healthcare providers across the globe are improvising and rationing PPE, often outside the lines of CDC and FDA guidelines. While providers should ideally don an N95 mask when caring for COVID-19-positive patients, a face shield and surgical mask are now identified as an acceptable alternative. With relaxed guidelines on face shield production, there is a clear role for 3D printed face shields to meet the critical shortages. **Hobbyists, technology companies, and 3D printing industries are rapidly producing face shields to meet this demand for PPE.**

Management

Acute care

Emergency Medicine

Pulmonary thromboembolism in criticall *[sic]* ill COVID-19 patients.

Scialpi M, Scialp S, Piscioli I, Scalera G, Longo F.
Int J Infect Dis
2020 Apr 24; PMID: 32339717
Level of Evidence: Level 5 - Expert opinion
Type of Article: Letter to the Editor

BLUF: Death in COVID-19 patients is caused by not only pneumonia but multi-system organ failure. Pulmonary thromboembolism should be considered in critically ill patients, and should be monitored via contrast-enhanced chest CT to assess parenchymal patterns and diagnose PTE.

Presepsin in risk stratification of SARS-CoV-2 patients

Zaninotto, M; Maria Mion, M; Cosma, C; Rinaldi, D; Plebani, M
Clin Chim Acta
2020 Apr 22; PMID: 32333860
Level of Evidence: 4 - Case Series
Type of Article: Research

BLUF: In a study of 75 patients with COVID-19 who were admitted to the intensive care unit (ICU) or infectious disease ward in Japan, **presepsin (PSP) concentration was found to be correlated with longer ICU stays than those who did not meet the cut-off value (17 day median hospital stay versus 10 day median, respectively).**

Abstract:

Background: A severe form of pneumonia, is the leading complication of the respiratory Coronavirus disease 2019 (COVID-19), recently renamed SARS-CoV-2. Soluble cluster of differentiation (CD)14 subtype (sCD14-ST also termed presepsin PSP) is a regulatory factor that modulates immune responses by interacting with T and B cells, useful for early diagnosis, prognosis and risk stratification prediction.

Methods: In 75 consecutive patients suffering from COVID-19 microbiology proven infection, admitted to intensive care unit (ICU, n=21, 28%) and/or in infectious disease ward (IW, n=54, 72%), PSP (Pathfast, Mitsubishi, Japan) has been measured in addition to routine laboratory tests performed during the period of hospitalization (from January to March 2020).

Results: PSP demonstrates: -statistically significant higher values (Mann-Whitney test) in 6 patients died (median, IQR= 1046, 763-1240; vs 417, 281-678 ng/L, $p<0.05$); -statistically significant but poor correlations with CRP (r= 0.59 $p<0.001$), LDH (r=0.52, $p<0.001$) and PCT (r=0.72, $p<0.001$) measured at the same day; -a significant relationship between concentrations and ICU stay. In fact *[sic]* patients showing PSP values higher than 250 ng/L (cut-off for risk stratification) did stay in ICU for a significantly longer time (median 17 days, IQR 12-31; $p<0.001$) than those exhibiting lower values (median 10 days, IQR 7-18).

Conclusions: The data obtained seems to demonstrate the role of PSP in providing prognostic information in COVID-19 patients, allowing to *[sic]* identify, during the early phase of the monitoring, the patients suffering from a more severe disease which will be hospitalized for a more long *[sic]* time.

Performance Evaluation of UAV-Enabled LoRa Networks for Disaster Management Applications.

Saraereh OA, Alsaraira A, Khan I, Uthansakul P.
Sensors (Basel).
2020 Apr 23; PMID: 32340268
Level of Evidence: 5 - Mechanism-based
Type of Article: Research

BLUF: A novel Unmanned Aerial Vehicle-Enabled Long Range Nodes (UAV-Enabled LoRa) network architecture is suggested for disaster management, including the COVID-19 pandemic. The model utilizes an efficient distributed topology algorithm to manage connectivity with a drone between the LoRa and base station (BS). Measures such as average packet reception rate, average buffered packets, and total delay were used to ensure high quality performance. **Possible uses of the drone include travel to quarantined areas, delivery of medical supplies, and communication.**

Abstract:

In hostile and remote environments, such as mountains, forests or suburban areas, traditional communications may not be available, especially after a disaster, such as a flood, a forest fire or an earthquake. In these situations, the wireless networks may become congested or completely disrupted and may not be adequate to support the traffic generated by rescuers. It is also considered as the key tool in Corona Virus (COVID-19) battle. Moreover, the conventional approaches with fixed gateways may not work either, and this might lead to decoding errors due to the large distance between mobile nodes and the gateway. To avoid the decoding errors and improve the reliability of the messages, we propose to use intermediate Unmanned Aerial Vehicles (UAVs) to transfer messages from ground-based Long Range (LoRa) nodes to the remote base station (BS). Specifically, this UAV-enabled LoRa architecture is based on the ad hoc WiFi network, wherein, UAVs act as relays for the traffic generated between LoRa nodes and BS. To make the architecture more efficient, a distributed topology control algorithm is also proposed for UAVs. The algorithm is based on virtual spring forces and movement prediction technique that periodically updates the UAV topology to adapt to the movement of the ground-based LoRa nodes that move on the surface. The simulation results show the feasibility of the proposed approach for packet reception rate and average delay quality of service (QoS) metrics. It is observed that the mechanisms implemented in a UAV-enabled LoRa network effectively help to improve the packet reception rate with nominal buffer delays.

Diagnostic Radiology

Imaging of coronavirus disease 2019: A Chinese expert consensus statement.

Yang Q, Liu Q, Xu H, Lu H, Liu S, Li H.
European Journal of Radiology.
2020 Apr 18; PMID: 32335426
Level of Evidence: 5 - Expert opinion
Type of Article: Opinion

BLUF: This article details the characteristics of chest CT imaging in COVID-19 patients with pneumonia. The authors suggest that the use of artificial intelligence would significantly increase the finding of ground glass opacity which is a frequently missed feature of COVID-19.

Abstract:
Coronavirus disease 2019 (COVID-19) is highly contagious, mainly causing inflammatory lesions in the lungs, and can also cause damage to the intestine and liver. The rapid spread of the virus that causes coronavirus disease 2019 (COVID-19) pneumonia has posed complex challenges to global public health. Early detection, isolation, diagnosis, and treatment are the most effective means of prevention and control. At present, the epidemic situation of new coronavirus infection has tended to be controlled in China, and it is still in a period of rapid rise in much of the world. The current gold standard for the diagnosis of COVID-19 is the detection of coronavirus nucleic acids, but **imaging has an important role in the detection of lung lesions, stratification, evaluation of treatment strategies, and differentiation of mixed infections.** This Chinese expert consensus statement summarizes the imaging features of COVID-19 pneumonia and may help radiologists across the world to understand this disease better.

Critical Care

Tracheal trauma after difficult airway management in morbidly obese patients with COVID-19.

Abou-Arab O, Huette P, Berna P, Mahjoub Y
Br J Anaesth
2020 Apr 11; PMID: 32334809; No abstract available
Level of Evidence: 4 - Case series
Type of Article: Correspondence

Summary: Two case reports of patients with the SARS-CoV-2 infection had **airway trauma during tracheal intubation** after failing noninvasive oxygen therapy. Both cases evolved to severe ARDS refractory to prone positioning and met the criteria for **difficult tracheal intubation owing to severe obesity** (in this case, BMI's were 41 and 34). As a result, it is highly recommended to perform a videolaryngoscopy to allow for successful intubation at first attempt thus avoiding potential tracheal trauma and worsening respiratory failure.

Obesity hypoventilation syndrome and severe COVID-19.

Huang JF, Wang XB, Zheng KI, Liu WY, Chen JJ, George J, Zheng MH.Huang JF, et al.
Metabolism.
2020 Apr 22; PMID: 32333938
Level of Evidence: 4 - Case Report
Type of Article: Research

BLUF: Until now only type I acute respiratory failure cases have been reported in COVID-19 patients. However, this case report is of a 23 y/o patient, with obesity and metabolic associated fatty liver disease, who developed type II acute respiratory failure. The authors explore the lack of management guidelines for these cases and postulate increased risk of obesity hypoventilation syndrome.

Summary: This case report aimed to highlight how **obesity commonly causes aggravation of respiratory disease severity** and that COVID-19 complications should be likewise considered. The authors' case involved a 23 year old **COVID-19 patient, with comorbidities of obesity and metabolic associated fatty liver disease, who was diagnosed with type II acute respiratory failure.** They reported that up until that time, which was January of 2020, severe COVID-19 patients had been diagnosed with type 1 acute respiratory failure. With this, they identified a **lack of strategies to manage COVID-19 patients with obesity, chronic obstructive pulmonary disease or other diseases that may predispose them to a type II diagnosis**. Futhermore, they speculated that COVID-19 in an obese patient may also put them at risk for obese hypoventilation syndrome or other severe conditions.

Safe Bronchodilator Treatment in Mechanically Ventilated COVID-19 Patients: A Single Center Experience
Miller, Asaf; Epstein, Danny
J Crit Care
2020 Apr 21; PMID: 32339975
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter to the Editor
Summary: Authors detail a closed system for delivering bronchodilation to intubated COVID-19 patients. They propose this method will reduce staff handling and does not require an open circuit, therefore reducing the risk of COVID-19 transmission.

Medical subspecialties
Serial CT features in discharged COVID-19 patients with positive RT-PCR re-test.
Dou P, Zhang S, Wang C, Cai L, Liu Z, Xu Q, Li X, Meng Y, Rong Y, Li S, Hu C, Xu K.
Eur J Radiol.
2020, Apr 18: PMID: 32334369
Level of Evidence: 4- Case Series
Type of Article: Letter to the Editor
BLUF: Given the possibility of false negative COVID-19 tests, all patients should have serial CT scans to document the resolution of lung lesions prior to discharge. Additionally, **all discharged patients should follow-up with RT-PCR and CT to avoid the risk of persistent infection.**

Summary: The authors review **serial CT scans of two COVID-19 patients** who met discharge criteria after testing negative with two consecutive RT-PCR, but tested positive at follow-up two weeks later. They explain that this could be a result of either false negative tests or re-infection, however, both patients followed strict quarantine regimens for 14 days after discharge. Authors suggest that patients with unresolved lung lesions seen on CT need additional time before discharge, and strict follow up with RT-PCR and imaging should be required for all COVID-19 patients.

Allergy and immunology
Case Report: One Case of Coronavirus Desease *[sic]* 2019(COVID-19) in Patient Co-infected by HIV With a Low CD4+ T Cell Count
Wang M, Luo L, Bu H, Xia H
Int J Infect Dis.
2020 Apr 23; PMID: 32335339
Level of Evidence: 4 - Case report
Type of Article: Case report
Summary: Wang et al describe a patient co-infected with HIV and SARS-Cov-2. The patient was admitted to a tertiary care center in Wuhan, China for a fever of one month and typical changes of viral pneumonia on lung CT. COVID-19 was diagnosed by nasopharyngeal swab that was positive for the ORF1ab gene. Eight markers of infectious diseases were also checked and showed antibodies to HIV and syphilis. This patient exhibited a long disease course of over 2 months as well as late development of IgM which may be due to cooperative impairment of the immune system by both viruses.
Cardiology
The role of natriuretic peptide estimation in severe COVID-19.
Mahajan K, Negi P

Monaldi Arch Chest Dis
2020 Apr 27; PMID: 32340429
Level of Evidence: 5- Expert opinion
Type of Article: Perspective
Summary: An argument for the use of BNP and NT-proBNP as biomarkers as a way to distinguish cardiac vs pulmonary causes of dyspnea in COVID-19 especially in resource limited settings like India. Acknowledging that their recommendations differ from the American College of Cardiology, the authors argue that normal to moderate values of BNP and NT-proBNP could be used to rule out heart failure, while elevated levels could support the decision to begin HF medications, taking the place of invasive hemodynamic monitoring.

Endocrinology

Practical recommendations for the management of diabetes in patients with COVID-19.
Bornstein SR, Rubino F, Khunti K, Mingrone G, Hopkins D, Birkenfeld AL, Boehm B, Amiel S, Holt RI, Skyler JS, DeVries JH, Renard E, Eckel RH, Zimmet P, Alberti KG, Vidal J, Geloneze B, Chan JC, Ji L, Ludwig B.
Lancet Diabetes Endocrinol.
2020 Apr 23; PMID: 32334646
Level of Evidence: 5 – Expert Opinion
Type of Article: Recommendations
Summary: Diabetes is one of the most important comorbidities linked to the severity of all three known human pathogenic coronavirus infections, including SARS-CoV-2. This international panel of experts of diabetes and endocrinology provide recommendations for the management of diabetes during the pandemic.

- Optimize outpatient management of diabetes mellitus, hypertension and dyslipidemia.
- Type 1 diabetics particularly at risk for immune function compromise with poor glycemic control.
- Patients with type 2 diabetes and concomitant fatty liver disease will be at increased risk for a more pronounced inflammatory response including the so-called cytokine storm.
- Patients with obesity at high risk of ventilatory failure and complications and pro-inflammatory state.
- Anti-diabetic drugs associated with lactic acidosis should be discontinued for patients with severe symptoms of COVID-19 to reduce risk of acute metabolic decompensation.

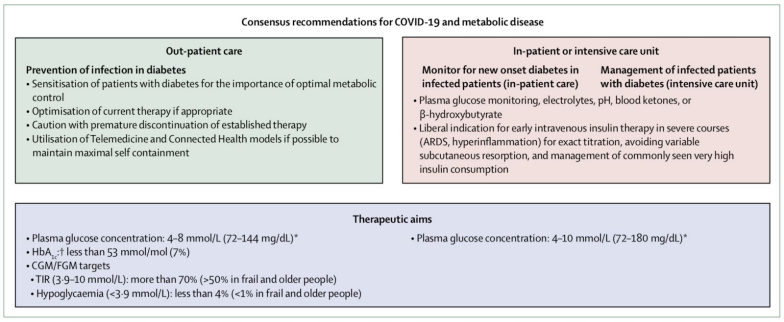


Figure: **Flowchart for metabolic screening and type 1 and 2 diabetes management of patients with COVID-19**
Older patients refers to those aged 70 and above. ARDS=Acute Respiratory Distress Syndrom. CGM=Continous Glucose Measurement. FGM=Flash Glucose Measurement. HbA_{1c}=haemoglobin A_{1c}. TIR=time in range. *Target concentrations for lower plasma glucose can be adjusted to 5 mmol/l (90 mg/dl) in frail patients. †HbA_{1c} testing might not be possible at the time, but previous measurements if available allow for differentiation of chronic and acute decompensation.

Panel: **Consideration of potential metabolically interfering effects of drugs in suspected or COVID-19 positive patients with type 2 diabetes**

Metformin

- Dehydration and lactic acidosis will probably occur if patients are dehydrated, so patients should stop taking the drug and follow sick day rules
- During illness, renal function should be carefully monitored because of the high risk of chronic kidney disease or acute kidney injury

Sodium-glucose-co-transporter 2 inhibitors

- These include canagliflozin, dapagliflozin, and empagliflozin
- Risk of dehydration and diabetic ketoacidosis during illness, so patients should stop taking the drugs and follow sick day rules
- Patients should avoid initiating therapy during respiratory illness
- Renal function should be carefully monitored for acute kidney injury

Glucagon-like peptide-1 receptor agonists

- These include albiglutide, dulaglutide, exenatide-extended release, liraglutide, lixisenatide, and semaglutide
- Dehydration is likely to lead to a serious illness so patients should be closely monitored
- Adequate fluid intake and regular meals should be encouraged

Dipeptidyl peptidase-4 inhibitors

- These include alogliptin, linagliptin, saxagliptin, and sitagliptin
- These drugs are generally well tolerated and can be continued

Insulin

- Insulin therapy should not be stopped
- Regular self-monitoring of blood-glucose every 2–4 hours should be encouraged, or continuous glucose monitoring
- Carefully adjust regular therapy if appropriate to reach therapeutic goals according to diabetes type, comorbidities, and health status

Connected Health models and Telemedicine should be used to continue regular reviews and self-management education programmes virtually and ensure patients are adherent to therapy.

Gastroenterology

Current Knowledge and Research Priorities in the Digestive Manifestations of COVID-19

Aroniadis, OC; DiMaio, CJ; Dixon, RE; Elmunzer, BJ; Kolb, JM; Mendelsohn, R; Singal, AG; Ordiah, CO; Rockey, DC; Spitzer, RL; Tierney, WM; Wani, S; Yadav, D

Clin Gastroenterol Hepatol

2020 Apr 22; PMID: 32334083

Level of Evidence: 4 - Expert Review of Case Studies

Type of Article: Correspondence

Summary: Authors review the latest gastrointestinal (GI) findings thought to be associated with COVID-19 and provide suggestions to the gastroenterology community.

- Current Understanding
    - COVID-19 infects the GI tract
        - High incidence of GI symptoms in infected patients
        - High expression of angiotensin converting enzyme (ACE) receptors in the GI tract
        - Prior experience with other viruses of the coronavirus family
        - Stool samples showing COVID-19, even when upper respiratory tract is negative
    - Abnormal liver function tests in approximately 15-50% of patients in one large study, suggesting hepatocellular involvement
        - A case of postmortem liver biopsy with findings suggestive of viral infection
- Take home points for the GI community
    - Suspect COVID-19 in patients with diarrhea, even with absence of typical symptoms
    - Endoscopy should be treated as a high-risk procedure

Hematology and Oncology

A Quantitative Framework for Modeling COVID-19 Risk During Adjuvant Therapy Using Published Randomized Trials of Glioblastoma in the Elderly.

Tabrizi S, Trippa L, Cagney D, Tanguturi S, Ventz S, Fell G, Wen PY, Alexander BM, Rahman R

Neuro Oncol

2020 Apr 27; PMID: 32339235

Level of Evidence: 2 - Meta analysis

Type of Article: Research

BLUF: Authors used published data from randomized clinical trials of elderly glioblastoma (GBM) patients with incorporation of COVID-19-associated infection and mortality risk to create a quantitative framework that can serve as a model for assessing COVID-19 risk associated with elderly GBM treatment:

- Hypofractionated radiation (RT) with concurrent and adjuvant temozolomide (TMZ)
- In frail, elderly patients, shorter courses of RT are preferable.
- TMZ alone may be a reasonable option for frail, elderly MGMT methylated patients suitable for single modality treatment in high risk settings.
- In MGMT unmethylated frail patients, a hypofractionated course of radiation is recommended.
- In areas of very high infection risk and mortality, supportive care only may be considered.

ABSTRACT:

Background: During the ongoing COVID-19 pandemic, contact with the healthcare system for cancer treatment can increase risk of infection and associated mortality. Treatment recommendations must consider this risk for elderly and vulnerable cancer patients. **We re-analyzed trials in elderly glioblastoma (GBM) patients, incorporating COVID-19 risk, in order to provide a quantitative framework for comparing different radiation (RT) fractionation schedules on patient outcomes.**

Methods**:** We extracted individual patient-level data (IPLD) for **1,321 patients** from Kaplan-Meier curves from **five randomized trials on treatment of elderly GBM patients** including available subanalyses based on MGMT methylation status. We simulated trial data with **incorporation of COVID-19 associated mortality risk** in several scenarios (low, medium, and high infection and mortality risks). Median overall survival and hazard ratios were calculated for each simulation replicate.

Results: Our simulations reveal how COVID-19-associated risks affect survival under different treatment regimens. **Hypofractionated RT with concurrent and adjuvant temozolomide (TMZ)** demonstrated the best outcomes in **low and medium risk scenarios**. In **frail elderly patients**, **shorter courses of RT** are preferable. In patients with **methylated MGMT** receiving single modality treatment, **TMZ-alone treatment approaches** may be an option in settings with high COVID-19-associated risk.

Conclusions: Incorporation of COVID-19-associated risk models into analysis of randomized trials can help guide clinical decisions during this pandemic. In elderly GBM patients, our results support **prioritization of hypofractionated RT** and highlight the **utility of MGMT methylation status** in decision-making in pandemic scenarios. Our quantitative framework can serve as a model for assessing COVID-19 risk associated with treatment across neuro-oncology.

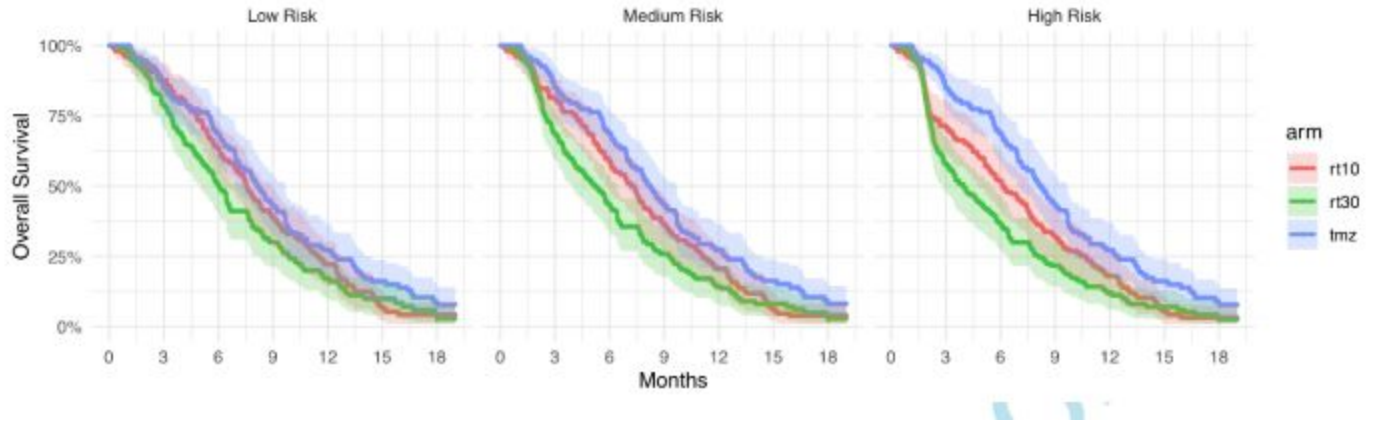


Figure 1: Survival curves from simulations of the Nordic trial with low risk, medium risk, and high risk COVID-19 pandemic scenarios. One thousand replicates were generated for each scenario, and the shaded bands represent the upper and lower 95% confidence interval bounds for Kaplan-Meier estimates across the replicates.

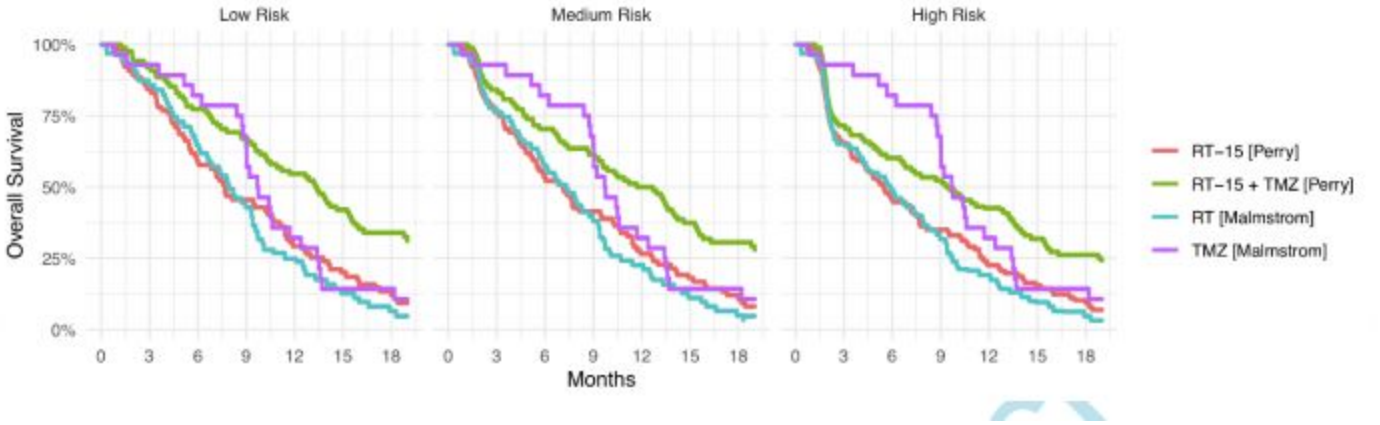


Figure 2: Survival curves from simulations for MGMT methylated patients enrolled in the CCTG/EORTC hypofractionated chemoradiation trial and the Nordic trial, under low risk, medium risk, and high risk COVID-19 pandemic scenarios.

Age-adjusted D-dimer Cut-Off Levels to Rule Out Venous Thromboembolism in COVID-19 Patients
Roncon L, Zuin M, Zonzin P
Thromb Res
2020 Apr 21; PMID: 32335420
Level of Evidence: 5 - Expert opinion
Type of Article: Letter
Summary: The authors pen a **response** to "*Incidence of thrombotic complications in critically ill ICU patients with COVID-19, Thromb Res (2020)*" by Klok et al. which concluded that there was an **elevated incidence of thrombotic complications** in **ICU patients with COVID-19** (n = 184). The authors comment on the **lack of D-dimer levels reported** in the study, and further **suggest risk stratification of D-dimer levels by age** to determine which individuals receive thromboprophylaxis.

Palliative Care
The key role of palliative care in response to the COVID-19 tsunami of suffering.
Radbruch L, Knaul FM, de Lima L, de Joncheere C, Bhadelia A.
Lancet
2020 Apr 22; PMID: 32333842
Level of Evidence: 5 - Expert Opinion
Type of Article: Comment
Summary: This article presents a series of recommendations to ensure availability of palliative healthcare services - including prescription of opioids to mitigate symptoms of pain and shortness of breath - during the pandemic. These recommendations include:

- Train all medical providers in palliative care needs for COVID-19 patients, potentially via online training programs
- Use telehealth platforms to perform home-based palliative care
- Engage families and patients in end of life decision making
- Ensure a supply of opioid medications is available, especially in lower income countries, by using the International Narcotics Control Board's simplified procedures for medication export, transport, and provision
- Mobilize a volunteer workforce for social support of patients via teleconnection applications
- Include assessment of social suffering in contact tracing and data collection activities
- In order to be better prepared in the future, the authors also recommend including palliative care competencies in healthcare training curriculum

Adjusting Practice During COVID-19

For Healthcare Professionals

Family-Centered Care During the COVID-19 Era.

Hart JL, Turnbull AE, Oppenheim IM, Courtright KR
J Pain Symptom Manage
2020 Apr 22; PMID: 32333961
Level of Evidence: 5 - Expert Opinion
Type of Article: Guideline

BLUF: In light of the physical distancing hospital regulations that have disrupted family-centered care during the COVID-19 pandemic, the authors present a framework of strategies for promoting family engagement with the use of technology to overcome communication/family engagement barriers (table 2) that could potentially enhance future aspects of family-centered care in post-pandemic settings.

Abstract:
Family support is more, not less, important during crisis *[sic]*. However, during the COVID-19 pandemic, maintaining public safety necessitates restricting the physical presence of families for hospitalized patients. In response, health systems must rapidly adapt family-centric procedures and tools to circumvent restrictions on physical presence. Strategies for maintaining family integrity must acknowledge clinicians' limited time and attention to devote to learning new skills. Internet-based solutions can facilitate the routine, predictable, and structured communication which is central to family-centered care. But the reliance on technology may compromise patient privacy and exacerbate racial, socioeconomic, and geographic disparities for populations that lack access to reliable internet access, devices or technological literacy. We provide a toolbox of strategies for supporting family-centered inpatient care during physical distancing responsive to the current clinical climate. Innovations in the implementation of family involvement during hospitalizations may lead to long-term progress in the delivery of family-centered care.

Barrier	*Mitigation*
Family spokesperson or healthcare proxy unavailable during daytime hours	Utilize night and weekend coverage to continue seamless family communication
Family members without internet access or device capable of videoconferencing	Engage using telephone and teleconferencing Provide a hospital-issued phone with free outgoing calls to patients, including pre-paid calling cards as needed Provide the family with resources for low-cost or free internet programs, if available Describe visual scene, care provided, and patient behavior in more detail to family
Patient without device capable of videoconferencing	Provide patients with access to videoconferencing via a hospital-owned device (e.g., equip a workstation on wheels with a camera and videoconferencing platform software or use tablets) Encourage and facilitate family delivery of device to the hospital for patient use, if available
Family members do not speak the same primary language as clinical team	Access translation services during video- or teleconferencing
Family members or patient have limited technological literacy	Provide instructions for use of the preferred videoconferencing platform tailored to all technological literacy levels Teach the use of the preferred platform for videoconferencing Engage using telephone and teleconferencing
Patient lacks communication aids such as glasses or hearing aids	Facilitate delivery of essential items from the family to the patient

Table 2: Strategies for communication with and engagement of families during physical distancing

An Invited Commentary on ' Evidence Based Management Guideline for the COVID-19 Pandemic- Review article'.

Atogebania JW, Chen H
Int J Surg
2020 Apr 23; PMID: 32335244
Level of Evidence: 5 - Opinion
Type of Article: Commentary

BLUF: The authors review and comment on Evidence Based Management Guideline for the COVID-19 Pandemic - Review article by Maria Nicola et al, and conclude with their opinion that the best strategies to deal with COVID-19 should be centered around non pharmacological interventions such as using PPE and continued social distancing measures.

Abstract:
COVID 19 been *[sic]* declared recently as a pandemic, to date has affected over 1,8881,365 with over 119,403 deaths in accordance to the global pandemic Real-Time Report. In this paper, the prime motive is to enlighten the key variables to the public on the pandemic and essential key points to note and practice in accordance to standard regulation to curb the aggressive COVID-19 pandemic.

European Association for the Study of Obesity Position Statement on the Global COVID-19 Pandemic.
Frühbeck, Gema; Baker, Jennifer L; Busetto, Luca; Dicker, Dror; Goossens, Gijs H; Halford, Jason CG; Handjieva-Darlenska, Teodora; Hassapidou, Maria; Holm, Jens-Christian; Lehtinen-Jacks, Susanna; Mullerova, Dana; O'Malley, Grace; Sagen, Jorn V; Rutter, Harry; Ximena, Salas R; Woodward, Euan; Yumuk, Volkan; Farpour-Lambert, Nathalie J
The European Journal of Obesity
2020 Apr 27; PMID: 32340020
Level of Evidence: 5 - Expert Opinion
Type of Article: Position Statement
Summary: This position statement discusses the impact that the COVID-19 pandemic is having on those experiencing obesity and the essential role the European Association for the Study of Obesity Position Statement (EASO) has in (1) identifying the needs of people living with obesity, (2) disseminating science-based information, and (3) sharing knowledge, evidence-based recommendations, and guidance toward the community.

Acute care

Anti-CD20 immunosuppressive disease-modifying therapies and COVID-19.
Giovannoni G.
Mult Scler Relat Disord.
2020 Apr 18; PMID: 32339915
Level of Evidence: 5 - Expert Opinion
Type of Article: Commentary
Summary: Case reports have reported how **multiple sclerosis (MS) patients on immunosuppressive drugs such as ocrelizumab (Anti-CD20) develop uncomplicated COVID-19.** These drugs might be helpful in reducing the inflammatory cytokines of COVID-19 induced acute respiratory disease syndrome. Since being on these immunosuppressive therapies seem less likely to lead to severe COVID-19, the author proposes that we **reevaluate our decision of withholding these drugs from MS patients**.

Medical subspecialties

Dermatology

Coronavirus Disease 2019 (COVID-19) and dermatologists: Potential biological hazards of laser surgery in epidemic area.
Emadi SN, Abtahi-Naeini B.
Ecotoxicol Environ Saf.
2020 Apr 6; PMID: 32335416
Level of Evidence: 5 - Expert opinion
Type of Article: Letter
Summarizing excerpt: "Regarding the outbreaks of COVID-19, in area with sustained community transmission, special consideration on laser safety with focus on potential biological hazards of moderate and high-power laser surgery is needed to reduce potential risks of laser airborne contaminants that provide more laser safety profiles and it is preferred that elective laser procedures postponed."

Recommendations for Phototherapy During the COVID-19 Pandemic
Lim HW, Feldman SR, Van Voorhees AS, Gelfand JM
J Am Acad Dermatol
2020 Apr 24; PMID: 32339700
Level of Evidence: 5 – Expert opinion
Type of Article: Letter to the Editor

Summary: This letter of correspondence outlines several ways that dermatologic units may offer phototherapy to patients while minimizing risk of spreading and contracting COVID-19 during the pandemic. The authors suggest:

Patients

- Be screened for symptoms prior to entering unit
- Attend phototherapy appointment alone
- Wear a mask
- Apply hand sanitizer upon entering and leaving unit
- Use individualized goggles per patient that are cleaned prior to storage in a bag
- Store clothes in a bag that is then disposed of after treatment
- Practice social distancing

Staff

- Schedule patients for every 30mins
- Arrange seating in waiting area such that it is 6 feet apart
- Wear a mask
- Apply hand sanitizer upon entering and leaving unit
- Avoid turning on the fan in the phototherapy room if possible
- Disinfect high touch surface areas in changing rooms and phototherapy equipment after each patient

Telemedicine for Inpatient Dermatology Consultations in Response to the COVID-19 Pandemic.

Trinidad J, Kroshinksy D, Kaffenberger BH, Rojek N
J Am Acad Dermatol
2020 Apr 24; PMID: 32339708
Level of Evidence: 5 - Expert Opinion
Type of Article: Commentary

BLUF: The authors present a decision-making algorithm for triaging telemedicine consults in dermatology based on expert consensus within the Society of Dermatology Hospitalists. The algorithm suggests telemedicine consults be provided if the case is deemed appropriate. If the consultation must be done in person, the algorithm suggests pre-rounding with pictures, limiting the number of people in the room, and donning appropriate PPE. The guidelines aim to limit exposure of patients and consulting dermatologists to Covid-19 while maintaining access to inpatient dermatological care.

Summarizing Statement: "**Herein, we provide a practical algorithm to implement triaging telemedicine consults within multiple hospital settings in the context of the ongoing COVID-19 pandemic. (Figure 2).** These guidelines may evolve as data on COVID-19 transmission improves, testing becomes faster, and improved telemedicine platforms emerge. However, given the state of our current crisis, it is imperative to implement guidelines in the interest of public health. **This algorithm will maintain access to inpatient dermatologic care, reduce patient and provider exposure to COVID-19, and decrease unnecessary utilization of PPE.** Given the current paucity of data, the following goals are based on expert consensus within the Society of Dermatology Hospitalists, and have been adopted by a plurality of member institutions within this society.

Goals:

1)Prioritize the use of telemedicine consultation in order to minimize risk of COVID-19 exposure to both patients and consulting dermatologists.

2) Identify patients who are high-risk for exposing consulting dermatologists to COVID-19.

3) Limit the utilization of resources for low-risk in-person dermatology consults.

4) Provide a framework for predominantly outpatient dermatologists to utilize in the event that they are required to staff inpatient dermatology consultations."

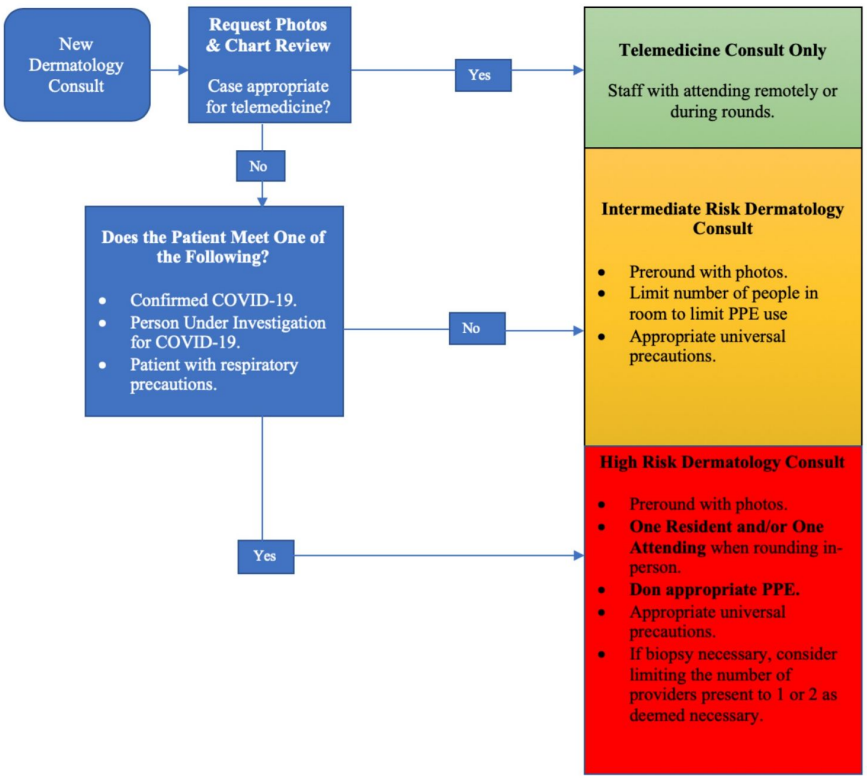


Figure 2) Inpatient Dermatology Consult Decision-Making Algorithm

Geriatrics

The Need to Include Assisted Living in Responding to the COVID-19 Pandemic.

Zimmerman S, Sloane PD, Katz PR, Kunze M, O'Neil K, Resnick B..

J Am Med Dir Assoc.

2020 May; PMID: 32334770

Level of Evidence: 5 - Expert Opinion

Type of Article: Editorial

Summary: Assisted living (AL) facilities are distinct from nursing homes and the differences between them highlight how AL needs attention, especially during the COVID-19 pandemic. There needs to be continuous communication between caretakers, medical providers, and family members. **Telehealth from providers and more training should be promoted for the limited AL staff. The effects of social distancing should be mitigated and monitored in AL patients, especially those with dementia.**

Hematology and Oncology

Management of Lung Nodules and Lung Cancer Screening During the COVID-19 Pandemic: CHEST Expert Panel Report.

Mazzone PJ, Gould MK, Arenberg DA, Chen AC, Choi HK, et al.

Chest.

2020 Apr 22; PMID: 32335067

Level of Evidence: 5 - Expert opinion

Type of Article: Expert panel report

BLUF: The following was recommended by 24 panelists on the management of lung nodules during the pandemic:

- Unanimous consensus to delay baseline or repeat annual screening.
- Over 95% agreed to delay the evaluation of pulmonary nodules detected incidentally or by screening that are <8 mm in diameter
- Strong consensus to delay or modify the evaluation and management of patients with nodules measuring >8 mm in average diameter.
- Evaluation with PET or non-surgical biopsy should occur when the pCA is 25% to 85%, with subsequent referral for treatment when cancer is confirmed or more strongly suspected.

Abstract:
Background: The risks from potential exposure to COVID-19, and resource reallocation that has occurred to combat the pandemic, have altered the balance of benefits and harms that informed current (preCOVID-19) guideline recommendations for lung cancer screening and lung nodule evaluation. We developed consensus statements to guide clinicians managing lung cancer screening programs and patients with lung nodules during the COVID-19 pandemic.
Methods: An expert panel of 24 members, including pulmonologists (17), thoracic radiologists (5), and thoracic surgeons (2) was formed. The panel was provided with an overview of current evidence, summarized by recent guidelines related to lung cancer screening and lung nodule evaluation. The panel was convened by video teleconference to discuss then vote on statements related to 12 common clinical scenarios. A predefined threshold of 70% of panel members voting agree or strongly agree was used to determine if there was a consensus for each statement. Items that may influence decisions were listed as notes to be considered for each scenario.
Results: Twelve statements related to baseline and annual lung cancer screening (2), surveillance of a previously detected lung nodule (5), evaluation of intermediate and high risk lung nodules (4), and management of clinical stage I non-small cell lung cancer (1) were developed and modified. All 12 statements were confirmed as consensus statements by voting results. The consensus statements provide guidance about situations where it was felt to be appropriate to delay screening, defer surveillance imaging of lung nodules, and minimize non-urgent interventions during the evaluation of lung nodules and stage I non-small cell lung cancer.
Conclusions: There was consensus that during the COVID-19 pandemic it is appropriate to defer enrollment in lung cancer screening and modify the evaluation of lung nodules due to the added risks from potential exposure and the need for resource reallocation. There are multiple local, regional, and patient related factors that should be considered when applying these statements to individual patient care.

Mitigating the effect of the COVID-19 pandemic on sickle cell disease services in African countries.
Dexter, Daniel; Simons, David; Kiyaga, Charles; Kapata, Nathan; Ntoumi, Francine; Kock, Richard; Zumla, Alimuddin
Lancet Haematology
2020 Apr 23; PMID: 32334676
Level of Evidence: 5 – Expert Opinion
Type of Article: Comment
BLUF: Healthcare strategies for patients with sickle cell disease in sub-saharan Africa include identifying people who are at risk through targeted screening for sickle-cell disease, scaling up diagnostic and treatment resources targeted at this population, and prioritizing sickle-cell patients for immunization when a SARS-CoV-2 vaccine becomes available.

Summary: Acute respiratory illnesses are a major cause of morbidity and mortality in patients with sickle cell disease who have an increased risk of respiratory complications and pulmonary vaso-occlusive disease, such as acute chest syndrome. In places such as sub-saharan Africa, where the burden of sickle cell disease is extremely high, there is a need for consideration to be given to this population when developing local preventative and health-care strategies in this pandemic. This includes taking steps such as identifying people who are at risk through targeted screening for sickle-cell disease, scaling up diagnostic and treatment resources in conjunction with public health campaigns targeted to the at-risk sickle cell disease population, and prioritizing sickle-cell patients for immunization when a SARS-CoV-2 vaccine becomes available. Additionally, with the overlapping epidemiological and clinical association of sickle-cell disease with malaria, bacterial, and viral infections (including SARS-CoV-2), there is an opportunity to include sickle cell disease in the Integrated Management of Childhood Illness program and incorporate it into national health systems programing in order to scale up sickle cell disease-related health-care infrastructure.

Nephrology
The use of Captopril - angiotensin converting enzyme (ACE) inhibitor for cystinuria during COVID-19 pandemic.
Biyani CS, Palit V, Daga S.
Urology
2020 Apr 22; PMID: 32333991
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter to the Editor
Summary: It has been suggested that ACE inhibitors may exacerbate symptoms in COVID-19 because ACE2 functions as a receptor for the COVID-19 virus. Despite this there is scarce data to support any change in practice. Until further data are available the authors recommend that Captopril continue to be used to treat stone disease associated with cystinuria.

Rheumatology

The Question of Whether to Remain on Therapy for Chronic Rheumatic Diseases in the Setting of the Covid-19 Pandemic.

Cron RQ, Chatham WW.
J Rheumatol.
2020 Apr 25; PMID: 32335514
Level of Evidence: 4 - Case Series
Type of Article: Comment

BLUF: In 123 pediatric patients undergoing rheumatic disease therapy surveyed over 7 weeks in Milan, Italy, there were zero cases of COVID-19, encouraging continuation of typical therapy in this population and suggesting success of current preventative measures.

Abstract: We appreciate our Italian colleagues' interest in our editorial denoting the rheumatologist's role in helping to diagnose and treat cytokine storm syndrome (CSS) in the setting of the Covid-19 pandemic (1). It is encouraging that none of the 123 pediatric rheumatology patients (primarily juvenile idiopathic arthritis) on background biological disease modifying anti-rheumatic drug (bDMARD) therapies in Milan, Italy surveyed over a 7-week period from February 25 through April 14, 2020 (during which time Covid-19 was hyper-endemic there) had either confirmed or suspected Covid-19 (2).

Surgical Subspecialties

General Surgery

Acute care surgery and postoperative COVID-19 pneumonia: a surgical and environmental challenge.

Lepre L, Costa G, Virno VA, Dalsasso G, Campa RD, Clavarino F, Petrucciani N.
ANZ J Surg
2020 Apr 25, PMID: 32336012
Level of Evidence: 4 - Case study
Type of Article: Research

Summary: This is a single case report of a 64 year old female with no reported COVID-19 contacts who presented to an Emergency Department with intense abdominal pain secondary to a distal ileal volvulus. The patient was hospitalized and underwent an ileocolic resection and anastomosis with a **postoperative course complicated by COVID-19 pneumonia** seen on CT and confirmed by RT-PCR. Despite hospitals' efforts to "organize specific pathways for patients with documented COVID-19 infections, the virus is highly contagious and can spread to other patients, facilitated by the lower efficiency of the immune system in the postoperative period" or "some patients may be already infected at admission, but totally asymptomatic." The authors "suggest **active surveillance** with a **liberal use of RT-PCR test and thoracic CT scan** in [acute surgery departments], to rule out COVID-19 infection, in the effort to offer prompt treatment to infected patients and to protect other patients and health workers."

Guidelines for infection prevention and control in perioperative patients during the COVID-19 pandemic: protocol from a tertiary general hospital in Beijing

Du, Zhe; Wang, Tianbing
J Minim Invasive Gynecol
2020 Apr 22; PMID: 32334041
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter to the Editor, Clinical Guidelines

Summarizing Excerpt: "For patients requiring surgery, especially emergency patients, on the one hand *[sic]*, strict screening can reduce the incidence of nosocomial infection and medical staff infection, on the other hand *[sic]*, tedious screening may delay operation. Thus, finding a balance is the challenge." See figure 1 below on protocol schematic.

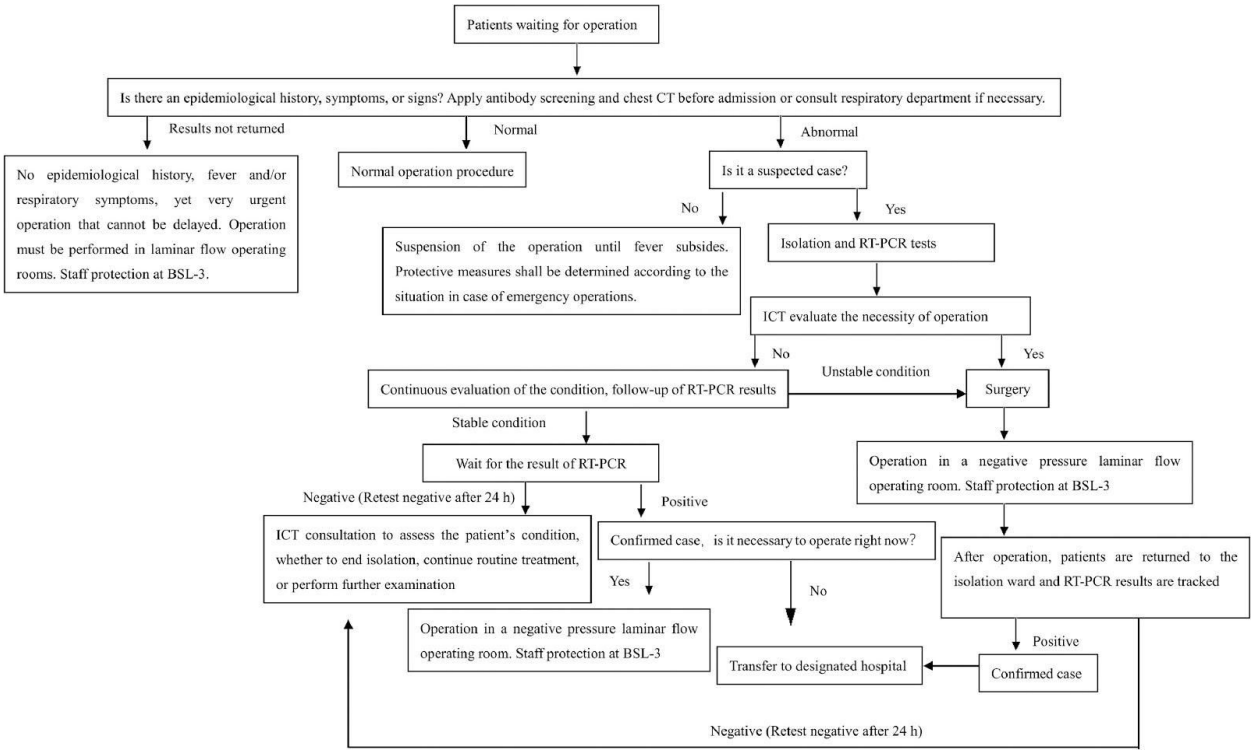


Figure 1. Algorithm for screening patients awaiting operation ICT: infection control team; BSL-3: biosafety level 3

Otolaryngology

Pediatric laryngoscopy and bronchoscopy during the COVID-19 pandemic: A four-center collaborative protocol to improve safety with perioperative management strategies and creation of a surgical tent with disposable drapes.

Francom CR, Javia LR, Wolter NE, Lee GS, Wine T, Morrissey T, Papsin BC, Peyton JM, Matava CT, Volk MS, Prager JD, Propst EJ.Francom CR, et al.
Int J Pediatr Otorhinolaryngol.
2020 Apr 21;PMID: 32339971
Level of Evidence: Level 5 - Expert Opinion
Article Type: Editorial

BLUF: This article presents a protocol for pediatric laryngoscopy and bronchoscopy with a focus on the use of surgical tents**.** The protocol suggests approaches for pre-operation (PPE use, COVID-19 testing, imaging with non-contrast CT), intra-operation (surgical tent usage and adjustments, full PPE preferably with PAPRs, anesthetic induction, flexible bronchoscopy use prior to rigid bronchoscopy), and post-operation (management of airway under the drape, safe drape removal, doffing PPE).

Abstract: Aerosolization procedures during the COVID-19 pandemic place all operating room personnel at risk for exposure. **We offer detailed perioperative management strategies and present a specific protocol designed to improve safety during pediatric laryngoscopy and bronchoscopy. Several methods of using disposable drapes for various procedures are described**, with the goal of constructing a tent around the patient to decrease widespread contamination of dispersed droplets and generated aerosol. **The concepts presented herein are translatable to future situations where aerosol generating procedures increase risk for any pathogenic exposure.** This protocol is a collaborative effort based on knowledge gleaned from clinical and simulation experience from Children's Hospital Colorado, Children's Hospital of Philadelphia, The Hospital for Sick Children in Toronto, and Boston Children's Hospital.

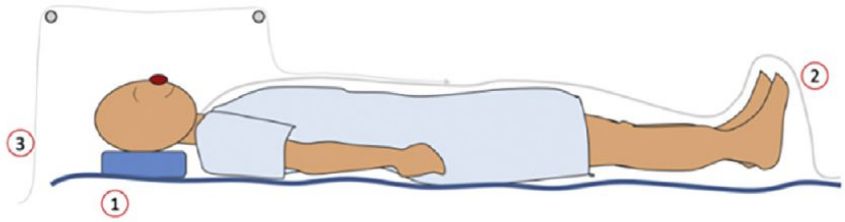


Fig. 1. Surgical tent for containing droplet and aerosolized particles during unsecured airway procedure. Three disposable drapes are used to prevent contamination, including 1) drape covering bed, 2) drape covering patient's body, 3) drape suspended over patient's head and chest to create contained working space or tent.

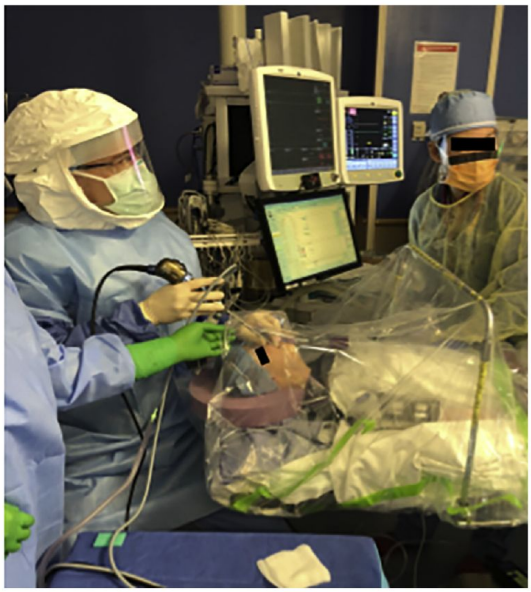


Fig. 6. Rigid bronchoscopy for foreign body removal. Surgical tent is constructed from an ether screen (cross bar) and an O-arm drape. The surgeon works through a small slit in the drape. There is a 1010 drape over the patient's chest and a smoke evacuator overtop to filter aerosolized product from under the tent.

OBGYN

COVID-19 pandemic. Impact on hysteroscopic procedures. A consensus statement from the Global Congress of Hysteroscopy Scientific Committee.

Carugno J, Sardo ADS, Alonso L, Haimovich S, Campo R, De Angelis C, Bradley L, Bettocchi S, Arias A, Isaacson K, Okohue J, Farrugia M, Kumar A, Xue X, Cavalcanti L, Laganà AS, Grimbizis G.

J Minim Invasive Gynecol.

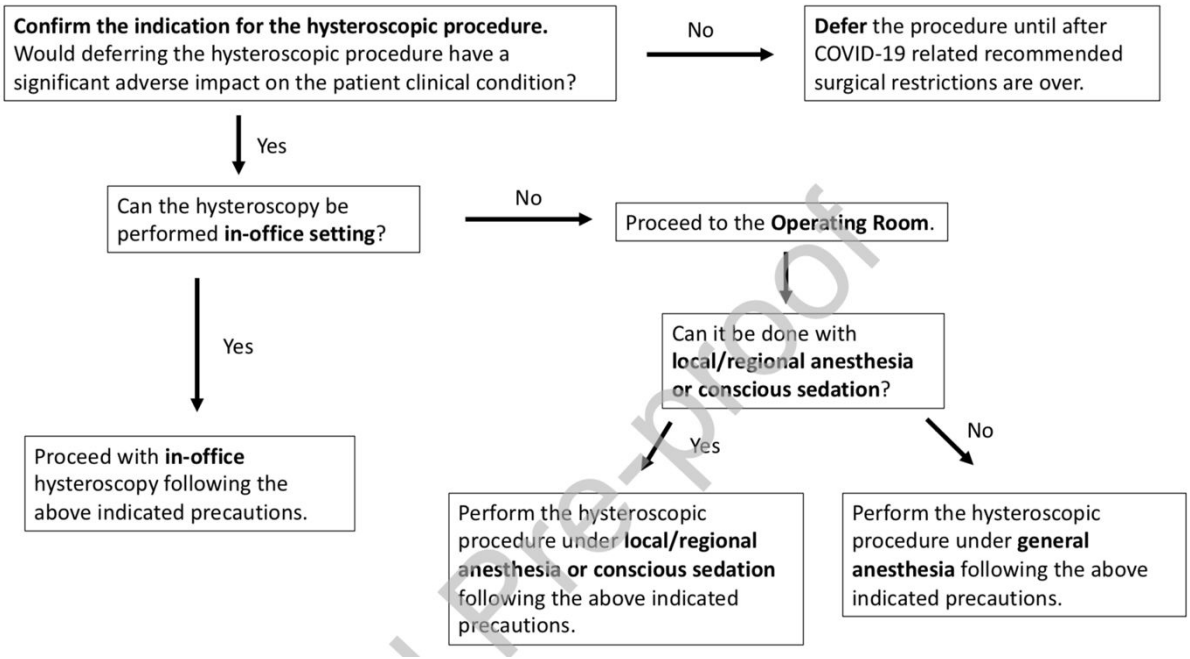
2020 Apr 24; PMID: 32339754

Level of Evidence: 5 – Expert Opinion

Type of Article: Recommendations

Summary: Hysteroscopy is a quick diagnostic and therapeutic procedure that can be performed with very little risk of infection during the COVID-19 pandemic provided that preventive measures are taken. There is a favor for use of instruments that do not produce surgical smoke and avoids multiple insertion and removal of hysteroscopes from inside the uterine cavity. Use of conscious sedation or regional anesthesia is recommended instead of general anesthesia when appropriate.

Figure 1. Algorithm for the triage of the patient requiring hysteroscopic procedures during the COVID-19 pandemic.



Ophthalmology

Contact Lens Wear During the COVID-19 Pandemic.

Morgan PB.

Cont Lens Anterior Eye.
2020 Apr 22; PMID: 32334933
Level of Evidence: 3 – Local, non-random sample
Type of Article: Letter to the Editor

BLUF: Most regular contact lens wearers find no supposed benefit of wearing contacts while in 'lockdown' quarantine; fear of SARS-CoV-2 infection from contact lens wearing is uncommon.

Summary: Recent investigations have found no relationship between contact lens use and COVID-19 infection, perhaps because it is rare to find the SARS-CoV-2 infection in the tear films of patients who have tested positive. However, in spite of these studies, many media reports suggest that ceasing contact lens wear is recommended during the pandemic. A survey was administered between April 9-12, 2020 amongst 433 contact lens wearers to identify the reasons for any changes in their contact lens usage. One hundred people responded to the survey, of which 89 were living in a 'lockdown situation.' In the lockdown group, 64 (72%) people were using their lenses less often than normal. The most common explanation (75%) was that there was a perception of 'less need' to wear them in the house. **Only 8% of the 64 people reporting less use cited concerns of infection. The findings presented herein offer a reasonable estimate of contact lens use during the COVID-19 pandemic.**

R&D: Diagnosis & Treatments

Developments in Diagnostics

COVID-19 Evaluation by Low-Dose High Resolution CT Scans Protocol.

Radpour A, Bahrami-Motlagh H, Taaghi MT, Sedaghat A, Karimi MA, Hekmatnia A, Haghighatkhah HR, Sanei-Taheri M, Arab-Ahmadi M, Ashideh A.
Acad Radiol.
2020 Apr 17; PMID: 32335002
Level of Evidence: 5 - Expert opinion
Type of Article: Letter to the Editor

BLUF: A low-dose HRCT protocol may be advantageous in detecting COVID-19 in highly-probable patients (with minimal ionizing radiation exposure), compared to RT-PCR, which remains time-consuming and has sub-optimal sensitivity.

Summary: The diagnosis of COVID-19 infection consists of detecting the viral RNA through swab samples via reverse-transcription polymerase chain reaction (RT-PCR). However, RT-PCR is quite time-consuming and has sub-optimal sensitivity. The hallmark of COVID-19 on chest CT is interstitial pneumonia, even in asymptomatic patients. Several studies have demonstrated higher sensitivity of CT compared to RT-PCR in detecting COVID-19 infected patients, and thus an increasing number of chest CT scans are being requested by physicians. There is now a need to reduce the risks of ionizing radiation; the Iranian Society of Radiology designed a low-dose High Resolution Computed Tomography (HRCT) protocol that can be used to evaluate individuals with a high probability of COVID-19. The protocol is described herein, with the following **suggested parameters to minimize radiation dose: Kvp: 100-120, mAs: 50-100, Pitch: 0.8-1.5, thickness: 1-3 mm.**

Developments in Treatments

Update on treatment of COVID-19: ongoing studies between promising and disappointing results.

Esposito S, Noviello S, Pagliano P
Infez Med
2020 June 1 (Ahead of Print); PMID: 32335561
Level of Evidence: 1 - Systematic Review
Type of Article: Systematic Review

BLUF: Authors reviewed articles published on PubMed and clinical trials on ClinicalTrials.gov and the Chinese Clinical Trial Registry regarding the treatment of COVID-19, with the following findings:

- Results of treatment with chloroquine (CQ) and hydroxychloroquine (HCQ) are varied, and potentially indicate patients with mild COVID-19 infections may show better outcomes when treated with CQ/HCQ compared to those with moderate-severe infections.
- Remdesivir has shown clinical improvement in hospitalized patients with severe infections, with greater efficacy reported in those requiring non-invasive ventilation.
- Compared to arbidol, favipiravir has improved time-to-relief for fever and cough, but has not been shown to significantly improve clinical recovery rate.
- Treatment with lopinavir/ritonavir has not shown any difference in clinical improvement when compared to standard care alone.
- Previous treatment with tocilizumab for another condition or treatment in conjunction with steroids may decrease symptom severity, and repeated doses of tocilizumab may improve the condition of critically ill COVID-19 patients.
- Several case reports of convalescent plasma with another therapy show improved conditions in patients with severe COVID-19 infections.

ABSTRACT:
The COVID-19 pandemic represents the greatest global public health crisis since the pandemic influenza outbreak of 1918. We are facing a new virus, so several antiviral agents previously used to treat other coronavirus infections such as SARS and MERS are being considered as the first potential candidates to treat COVID-19. Thus, several agents have been used by the beginning of the current outbreak in China first and all over the word successively, as reported in several different guidelines and therapeutic recommendations. At the same time, a great number of clinical trials have been launched to investigate the potential efficacy therapies for COVID-19 highlighting the urgent need to get as quickly as possible high-quality evidence. **Through PubMed, we explored the relevant articles published on treatment of COVID-19 and on trials ongoing up to April 15, 2020.**

Current status of potential therapeutic candidates for the COVID-19 crisis.
Zhang J, Xie B, Hashimoto K.Zhang J, et al.
Brain Behav Immun.
2020 Apr 22; PMID: 32334062
Level of Evidence: 5- Literature Review
Type of Article: Review
BLUF: Authors within the fields of Critical Care and Clinical Neuroscience draw from 240 publications to review current theories on the pathophysiological mechanisms of the SARS-CoV-2 virus and associated COVID-19 disease. They also summarize the current status of potential therapeutic candidates with focus on the mechanism of action, safety, evidence, and efficacy of these treatments.

Abstract: As of April 15, 2020, the ongoing coronavirus disease 2019 (COVID-2019) pandemic has swept through 213 countries and infected more than 1,870,000 individuals, posing an unprecedented threat to international health and the economy. There is currently no specific treatment available for patients with COVID-19 infection. The lessons learned from past management of respiratory viral infections have provided insights into treating COVID-19. Numerous potential therapies, including supportive intervention, immunomodulatory agents, antiviral therapy, and convalescent plasma transfusion, have been tentatively applied in clinical settings. A number of these therapies have provided substantially curative benefits in treating patients with COVID-19 infection. Furthermore, intensive research and clinical trials are underway to assess the efficacy of existing drugs and identify potential therapeutic targets to develop new drugs for treating COVID-19. Herein, we summarize the current potential therapeutic approaches for diseases related to COVID-19 infection and introduce their mechanisms of action, safety, and effectiveness.

Can dapagliflozin have a protective effect against COVID-19 infection? A hypothesis.
Cure E, Cumhur Cure M.Cure E, et al.
Diabetes Metab Syndr
2020 Apr 21; PMID: 32335366
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter
BLUF: A letter describing how COVID-19 is associated with low cytosolic pH through increased lactate dehydrogenase (LDH) levels causing cellular destruction, and are proposing dapagliflozin (sodium-glucose co-transporter-2), could help reduce lactate levels and prevent damage of cells by its various mechanisms: reduce lactate release from epicardial adipose tissue, reduce oxygen consumption in tissues and cause use of glucose in aerobic pathway, and increase urinary lactate excretion.

Abstract: It has been reported that frequent occurrence of COVID-19 infection in these patients is associated with low cytosolic pH. During virus infection, serum lactate dehydrogenase (LDH) level excessively rises. LDH is a cytosolic enzyme and the serum level increases as the cell break down. When anaerobic conditions develop, lactate formation increases from pyruvate. Cell pH is regulated by very complex mechanisms. When lactate increases in the extracellular area, this symporter carries lactate and H+ ion into the cell, and the intracellular pH quickly becomes acidic. Paradoxically, Na+/H+ exchanger activation takes place. While H+ ion is thrown out of the cell, Na+ and Ca+2 enter the cell. When Na+ and Ca+2 increase in the cell, the cells swell and die. **Dapagliflozin is a sodium-glucose cotransporter-2 inhibitor. Dapagliflozin has been reported to reduce lactate levels by various mechanisms.** Also, it reduces oxygen consumption in tissues and causes the use of glucose in the aerobic pathway, thereby reducing lactate production. A lactate decrease in the environment reduces the activation of lactate/H+ symporter. Thus, the H ion pumping into the cell by this symporter is reduced and the cytosolic pH is maintained. Dapagliflozin also directly inhibits NHE. Thus, Na+ and Ca+2 flow to the cell are inhibited. Dapagliflozin provides the continuation of the structure and functions of the cells. **Dapagliflozin can prevent the severe course of COVID-19 infection by preventing the lowering of cytosolic pH and reducing the viral load.**

[Improving the efficacy of Chloroquine and Hydroxychloroquine against SARS-CoV-2 may require Zinc additives - A better synergy for future COVID-19 clinical trials.]

Shittu MO, Afolami OI.Shittu MO

Infez Med
2020 Ahead of print Jun 1; PMID: 32335560
Level of Evidence: 5 - Mechanism based reasoning
Type of Article: Expert Opinion

BLUF: A synergistic effect of zinc and chloroquine/hydroxychloroquine can be used to treat patients with COVID-19 infection. Chloroquine/hydroxychloroquine utilizes zinc ions to inhibit RNA-dependent RNA polymerase, increase pH levels, disrupt cell signal transduction, and induce apoptosis resulting in impairment of viral replication and survival.

Abstract:
The recent outbreak of coronavirus disease 2019 (COVID-19), is now officially declared as a pandemic by the World Health Organization. As of now, there is no known effective pharmaceutical agent against the SARS-CoV-2 virus. However, several precautionary measures have been prescribed to prevent further spread of the virus, which include avoidance of social gatherings, proper handwashing, frequently disinfecting of used items and surfaces and so on. More recent studies have highlighted the possibility of treating patients infected with the novel SARS-CoV-2 virus with chloroquine and hydroxychloroquine, of which mechanism of action is not completely understood. We seek to draw the attention of the scientific community to the possibility of drastically reducing the effects of the virus on the affected patients and improving clinical trials outcome through the synergistic action of zinc and chloroquine in patients suffering from the coronavirus disease.

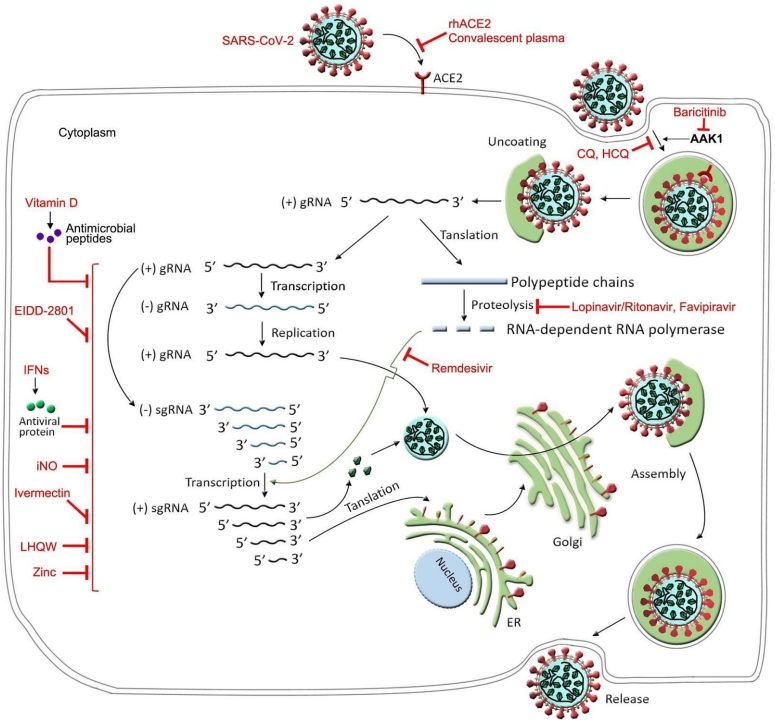


Fig. 2. The hypothetical replication cycle of SARS-CoV-2 and the possible targets of anti-COVID-19 drugs.

Table 1

Potential therapeutic drugs for COVID-19.

Intervention	Type	Status and mechanisms	Recommendations
Remdesivir	Antiviral	Remdesivir interferes with virus RNA polymerases to inhibit virus replication, and was used for Ebola virus outbreak	Being tested in clinical trials
Lopinavir/Ritonavir	Antiviral	Lopinavir/ritonavir are approved protease inhibitors for HIV	Inconsistent results in completed clinical trials
Favipiravir	Antiviral	Favipiravir inhibits viral RNA polymerase, thus interfering with viral replication	Proven efficacy in completed clinical trials
EIDD-2801	Antiviral	EIDD-2801 is incorporated during RNA synthesis and then drives mutagenesis, thus inhibiting viral replication	Prepared for clinical trials
Convalescent plasma	Antiviral	Convalescent plasma from cured patients provides protective antibody against SARS-CoV-2	Proven efficacy
rhACE2	ACE2 blocker	rhACE2 completely binds to virus S-protein, thus protects host lungs from virus attack	Being tested in clinical trials
Chloroquine Hydroxychloroquine	Antimalaria	Endosomal acidification fusion inhibitor anti-inflammatory activity	Proven efficacy in completed clinical trials (clinical data partly not shown)
Tocilizumab	mAb	Humanized mAb targeting IL-6	Being tested in clinical trials
Sarilumab	mAb	Humanized mAb targeting IL-6	Being tested in clinical trials
Bevacizumab	mAb	Humanized mAb targeting VEGF	Being tested in clinical trials
Baricitinib	JAK inhibitor	Baricitinib attenuates proinflammatory response by inhibiting JAK and blocks virus entering into host cells through inhibiting AAK1	Being tested in clinical trials
MSCs	Cell therapy	MSCs have regenerative and immunomodulatory properties and protect lungs against ARDS	Proven efficacy in completed clinical trials
iNO	Vasodilator	iNO possesses capability of potent and selective pulmonary vasodilation and antimicrobial activity	Being tested in clinical trials
LHQW	TCM	LHQW is used for prevention and treatment for infuenza, and has previously been used for SARS outbreak	Being tested in clinical trials
Xuebijing injection	TCM	Xuebijing serving as endotoxin antagonist, anti-inflammatory agent and anti-coagulant is used for sepsis	Being tested in clinical trials
IFNs	Immunoenhancer	IFNs inhibit viral RNA transcription, protein translation and post translational modififfication, thus suppress virus replication	Being tested in clinical trials
IVIG	Immunoenhancer	IVIG provides passive immunity and anti-inflammatory effects	Being tested in clinical trials
NK cell therapy	Immunoenhancer	NK cells can elicit rapid and robust protective effects in defense against viral infections through direct cytotoxicity and immunomodulatory capability	Being tested in clinical trials
Corticosteroids	Corticosteroids	Corticosteroids dampen proinflammatory cytokines and possess antifibrotic property	Still in controversy
Heparin	Anticoagulants	Heparin can reverse the hypercoagulability in severe cases of COVID-19	Proven efficacy in severe types of COVID-19
Vitamin C	Nutritional supportive care	Vitamin C boosts immunity by stimulating IFN production, supplying lymphocyte proliferation and enhancing neutrophil phagocytic capability	Being tested in clinical trials
Vitamin D	Nutritional supportive care	Vitamin D induces secretion of antimicrobial peptides and has immunomodulatory property	Being tested in clinical trials
Zinc	Nutritional supportive care	Zinc is necessary for the immune system and has anti-viral activities	Being tested in clinical trials
Ibuprofen	NSAIDs	Ibuprofen has been widely used to treat fever or pain	Still in controversy
mRNA-1273	Vaccine	mRNA-1273 contains mRNA that can encode S protein of SARS-CoV-2	Being tested in clinical trials
Ad5-nCoV	Vaccine	Ad5-nCoV uses replication-defective adenovirus type 5 as vector to load some gene fragments of SARS-CoV-2 on it to express SARS-CoV-2 S protein	Being tested in clinical trials
PittCoVacc	Vaccine	PittCoVacc utilizes microneedle array to deliver pieces of S-protein of SARS-CoV-2 into body	Prepared for phase I clinical trials
NVX-CoV2373	Vaccine	NVX-CoV2373 is a stable, prefusion protein developed through the advanced nanoparticle technology	Prepared for phase I clinical trials

Abbreviation: ARDS, acute respiratory distress syndrome; COVID-2019, corona virus disease 2019; HIV, human immunodeficiency virus; IFNs, interferons; IL-6, interleukin 6; iNO, inhaled nitric oxide; IVIG, intravenous gammaglobulin; LHQW, Lianhua Qingwen; mAb, monoclonal antibody; MSCs, mesenchymal stem cells; NK, natural killer cell; NSAIDs, non-steroidal anti-inflammatory drugs; rhACE2, recombinant human angiotensin-converting enzyme 2; SARS, severe acute respiratory syndrome; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; TCM, traditional Chinese medicine; VEGF, vascular endothelial growth factor.

The old but new: Can unfractioned *[sic]* heparin and low molecular weight heparins inhibit proteolytic activation and cellular internalization of SARS-CoV2 by inhibition of host cell proteases?

Belen-Apak FB, Sarialioglu F.Belen-Apak FB, et al.
Med Hypotheses.
2020 Apr 20; PMID: 32335456
Level of Evidence: 5 - Mechanism Based Reasoning
Type of Article: Commentary

BLUF: The authors suggest **unfractionated heparin or LMWH may be effective against COVID-19 based on in-vitro studies.** They recommend their use with judicious clinical judgement as well as further in-vitro and clinical study.

Abstract: ...The pathogenic infectivity of the virus requires the S1 subunit of the spike (S) protein to bind the host cell receptor, angiontensin [sic] converting enzyme (ACE2). While the binding to host cell receptor is the first step of infection, the entrance of the virus into the cell needs the cleavage of S1–S2 subunits to expose S2 for fusion to cell membrane via host proteases including cathepsins, cell surface transmembrane protease/serine (TMPRSS) proteases, furin, trypsin and factor Xa. Previous in vitro studies have shown that factor Xa inhibition can decrease viral infectivity. We suppose that host cell proteases including furin (as expressed highly in lungs), factor Xa and cathepsin are possible targets to decrease viral burden, therefore unfractioned *[sic]* heparin and low molecular weight heparin-LMWH (specifically dalteparin and tinzaparin for their anti inflammatory action) can be potential inhibitors of multiple endoproteases involved in virus infectivity. Our hypothesis needs to be tested in in vitro and clinical studies, however as we are in an urgent situation as the burden of SARS-CoV2 is increasing all around the world, we recommend the usage of unfractioned heparin or LMWH in intensive care unit (ICU) and non-ICU hospitalized patients with the risk–benefit judgement of the clinician. Whether our hypothesis is clinically applicable and successful in decreasing viral infection will be evaluated for further studies.

Enhancing immunity in viral infections, with special emphasis on COVID-19: A review.

Jayawardena R, Sooriyaarachchi P, Chourdakis M, Jeewandara C, Ranasinghe P
Diabetes Metab Syndr.
2020 Apr 16; PMID: 32334392
Level of Evidence: 1 - systematic review
Type of Article: Review

BLUF: The authors performed a **systematic review for nutrition-based interventions for viral diseases other than COVID-19.** Vitamins A and D supplementation showed potential benefits for patients already deficient; selenium and zinc showed immune-modulatory effects in viral respiratory infections, and nutraceuticals and probiotics may have a role in enhancing immune function with implications for use in COVID-19 patients .

Abstract:
Background and aims: Balanced nutrition which can help in maintaining immunity is essential for prevention and management of viral infections. While data regarding nutrition in coronavirus infection (COVID-19) are not available, in this review, we aimed to evaluate evidence from previous clinical trials that studied nutrition-based interventions for viral diseases (with special emphasis on respiratory infections), and summarise our observations.
Methods: A systematic search strategy was employed using keywords to search the literature in 3 key medical databases: PubMed®, Web of Science® and SciVerse Scopus®. Studies were considered eligible if they were controlled trials in humans, measuring immunological parameters, on viral and respiratory infections. Clinical trials on vitamins, minerals, nutraceuticals and probiotics were included.
Results: A total of 640 records were identified initially and 22 studies were included from other sources. After excluding duplicates and articles that did not meet the inclusion criteria, 43 studies were obtained (vitamins: 13; minerals: 8; nutraceuticals: 18 and probiotics: 4). Among vitamins, A and D showed a potential benefit, especially in deficient populations. Among trace elements, selenium and zinc have also shown favourable immune-modulatory effects in viral respiratory infections. Several nutraceuticals and probiotics may also have some role in enhancing immune functions. Micronutrients may be beneficial in nutritionally depleted elderly population.
Conclusions: We summaries possible benefits of some vitamins, trace elements, nutraceuticals and probiotics in viral infections. Nutrition principles based on these data could be useful in possible prevention and management of COVID-19.

Shedding Light on the Effect of Natural Anti-Herpesvirus Alkaloids on SARS-CoV-2: A Treatment Option for COVID-19.

Hassan STS.
Viruses.
2020 Apr 23; PMID: 32340120
Level of Evidence: Level 5 - Mechanism based reasoning
Article Type: Editorial

BLUF: This author reports on a recent study of two natural alkaloid type compounds (homoharringtonine and emetine) with known antiviral properties that were observed to inhibit SARS-CoV-2 replication (with EC50 values of 2.55µM and 0.46µM).

Abstract: The whole world is currently facing an unseen enemy, called coronavirus disease 2019 (COVID-19), which is causing a global pandemic. This disease is caused by a novel single-stranded enveloped RNA virus, known as the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2). Although huge efforts are being made to produce effective therapies to combat this disease, it continues to be one of the greatest challenges in medicine. There is no doubt that herpesviruses are one of the most important viruses that infect humans and animals, and infections induced by these pathogens have developed into a great threat to public health. **According to the currently available evidence, the correlation between herpesviruses and coronaviruses is limited to the induced complications following the infections.** For instance, the inflammation that is induced at the sites of infection could tie these viruses to each other in a relationship. Another example, bovine herpesvirus 1, which is an important pathogen of cattle, can cause a severe respiratory infection; the same way in which SARS-CoV-2 affects humans. Considering the current circumstances related to the COVID-19 crisis, **this editorial paper, which belongs to the Special Issue "Recent Advances in Herpesviruses Research: What's in the Pipeline?" aims to draw attention to some natural anti-herpesvirus alkaloid compounds, which have recently been proven to have excellent inhibitory efficacy against SARS-CoV-2 replication.** Thus, this special focus is an attempt to hunt down various treatment options to combat COVID-19 based on repurposing drugs that are known to have multiple antiviral properties, including against herpesvirus.

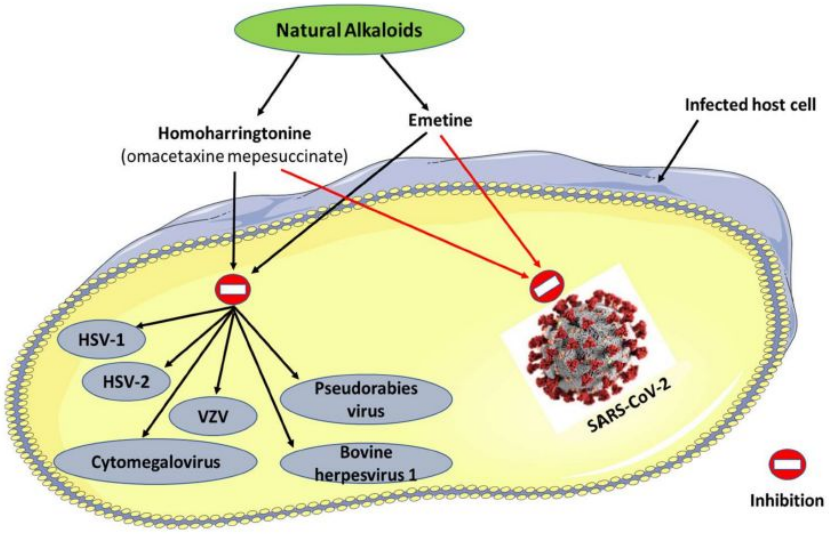


Figure 1. Natural alkaloids with dual anti-infective properties against SARS-CoV-2 and various types of herpesvirus. HSV: herpes simplex virus; VZV: varicella-zoster virus; SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus-2.

Dapsone and doxycycline could be potential treatment modalities for COVID-19.
Farouk A, Salman S
Medical Hypotheses
2020, April 22; PMID: 32339778
Level of Evidence: 5- Expert Opinion
Type of Article: Letter to the Editor
Summarizing Excerpt: "Given that cytokine storm and lung fibrosis sequalae are the devesting *[sic]* outcomes in COVID-19, we suggest that emerging clinical trials should assess the efficacy of dapsone, and/or doxycycline in improving pulmonary affection and the mortality outcome in COVID-19."

SARS-CoV-2 and COVID-19: What are our options? Where should we focus our attention on to find new drugs and strategies?
Magro G
Travel Med Infect Dis
2020 Apr 22; PMID: 32334088
Level of Evidence: 5-Mechanism based reasoning
Type of Article: Letter
Summary excerpt: "We write this letter to focus everybody's attention on the possible and viable strategies to find new drugs and therapeutic compounds. In doing so we describe the virus cycle of infection, showing for each phase a possible compound of therapeutic use."
Possible therapeutic compounds for viral cycle:

- Adhesion and Viral Entry: TMPRSS2 Inhibitor camostat mesylate
- Endocytosis: AAK1 inhibitor/hydroxychloroquine
- Replication: Remdesivir
- Protein Protease: Lopinavir/Ritonavir
- Cytokine Storm: Tocilizumab/other IL-6 inhibitors
- Free circulation: Human 47D11 antibody

Mental Health & Resilience Needs

COVID-19's Impact on Healthcare Workforce

Mental health problems faced by healthcare workers due to the COVID-19 pandemic-A review.
Spoorthy MS.Spoorthy MS.
Asian J Psychiatr.
2020 Apr 22; PMID: 32339895
Level of Evidence: Level 2- Systematic review
Article Type: Research
Summarizing excerpt: " The current review was done to conduct systematic appraisal of studies conducted on Mental health problems faced by healthcare workers due to the COVID-19 pandemic. Review of all 6 articles showed that several socio-demographic variables like **gender, profession, age, place of work, department of work and certain psychological variables like poor social support, self-efficacy were found to be associated with increased reporting of stress, anxiety, depressive symptoms, insomnia in healthcare workers**. There is increasing evidence which suggests that COVID-19 can be an independent risk factor for stress in HCW."

Protecting the psychological well-being of healthcare providers affected by the COVID-19 outbreak: Implications for the psychological rescue work of international community.
Hu X, Huang W
Nurs Health Sci.
2020 Apr 26; PMID: 32335991
Level of Evidence: 5 - Expert Opinion
Type of Article: Commentary
BLUF: The article outlines recommendations for the psychological support of healthcare workers during the COVID-19 pandemic based on the author's experience. These include providing healthcare workers with 1) transparent and clear communication, 2) adequate PPE, 3) regular screening for psychological distress, and 4) tailored psychological support. The authors conclude their experience may serve as a reference point for the international community.

Summarizing statement: "Overall, healthcare workers, and in particular those providing care for patients with confirmed or suspected COVID-19, are, as a group, the most vulnerable to mental health disorders. However, to date, the mental wellbeing of healthcare workers affected by the COVID-19 outbreak has not drawn enough attention worldwide. The mental wellbeing of healthcare workers should be a fundamental goal and critical aspect of public health and safety. **Therefore, promptly establishing and implementing a long-term psychological relief mechanism that integrates psychological assessment, treatment, support, training, and services for healthcare workers should be one of the most crucial and pressing missions within the health emergency response to the COVID-19 outbreak**. As COVID-19 is an uneven epidemic at the global level, countries and communities have different contexts and require a tailored response, our experience can only be seen as a reference for the international community, and not as a complete solution."

Impact on Public Mental Health

Comparison of Prevalence and Associated Factors of Anxiety and Depression Among People Affected by versus People Unaffected by Quarantine During the COVID-19 Epidemic in Southwestern China.
Lei L, Huang X, Zhang S, Yang J, Yang L, Xu M.Lei L, et al.
Med Sci Monit.
2020 Apr 26; PMID: 32335579
Level of Evidence: 4 - Cross sectional study
Type of Article: Research
Summary: A cross sectional study conducted in Southwestern China in early February 2020 performed an online questionnaire receiving n = 1593 participants placed in groups of 'affected' and 'unaffected' (whether they or someone they knew had been quarantined) and examined the prevalence of anxiety and depression and their associated factors. The results showed prevalence of anxiety and depression was approximately 8.3% and 14.6%, and the 'affected' group was significantly higher than the unaffected groups. Concluding that more economic and medical support is needed by the government to improve the general population's mental state.

Abstract:

BACKGROUND: At the end of 2019, the COVID-19 outbreak began in Wuhan, Hubei, China, and spread rapidly to the whole country within 1 month. This new epidemic caused a great mental reaction among the public. **This study aimed to assess and compare the prevalence and associated factors of anxiety and depression among the public affected by quarantine and those unaffected during the COVID-19 outbreak in southwestern China in early Feb. 2020**.
MATERIAL AND METHODS: Data were collected using the **self-rating anxiety scale (SAS) and the self-rating depression scale (SDS)** administered to **1593 respondents aged 18 years and above**. The respondents were grouped as 'affected group' and 'unaffected group' on the basis of whether they or their families/colleagues/classmates/neighbors had been quarantined.
RESULTS: **Among 1593 participants**, the **prevalence of anxiety and depression was approximately 8.3% and 14.6%**, respectively, and the **prevalence in the affected group (12.9%, 22.4%) was significantly higher than that in the unaffected group (6.7%, 11.9%)**. Lower average household income, lower education level, having a higher self-evaluated level of knowledge, being more worried about being infected, having no psychological support, greater property damage, and lower self-perceived health [conditions] were [significantly] associated with higher scores on the SAS and SDS. **People living in Chongqing had higher SAS and SDS scores than those living in Yunnan Province.**
CONCLUSIONS: **The prevalence of anxiety and depression of the affected group are higher than in the unaffected group during the COVID-19 outbreak in southwestern China in early Feb. 2020**. The government should focus more on providing economic and medical support to improve the general population's mental state.

Impact of COVID-19 pandemic on pre-existing mental health problems
Chatterjee SS, Barikar C M, Mukherjee A.Chatterjee SS, et al.
Asian J Psychiatr
2020 Apr 18; PMID: 32334407
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter
Summary: COVID-19 has had a sprawling impact on the mental health of people in India. The letter demonstrates how various psychiatric disorders could be exacerbated with renewed severity leading to PTSD, suicidal thoughts, or suicide attempts. Strategies to prevent these effects include: increased awareness of psychiatric emergencies in emergency services, policy changes to continue availability of healthcare services and essential drugs, e-dispensing rules should be relaxed with close monitoring, and telemedicine consults should be practiced.

The other side of COVID-19: Impact on obsessive compulsive disorder (OCD) and hoarding.
Banerjee DD
Psychiatry Res
2020 Apr 11; PMID: 32334276
Level of Evidence: 5 - Expert opinion
Type of Article: Letter
BLUF: Due to the lack of consistent healthcare follow-up due to the COVID-19 pandemic the burden of OCD has become worrisome. Furthermore, with panic and fear of the pandemic looming large, there is a lack of inhibitory control in this population. Thus, psychoeducation and awareness to healthcare workers is of utmost importance in order to circumvent possible surges of OCD cases.

Summary: Although not systematically analyzed, the number of OCD patients relapsing in India is increasing. With non-essential medical services being suspended there is a lack of follow-ups, prescription refills, and discontinuation of psychotherapy described anecdotally. Uncontrolled obsessions and compulsions can lead to dermatological conditions, chronic stress, insomnia and high risk for suicide. In addition to training healthcare workers to identify OC complaints, Dr. Banerjee emphasized the importance of explaining to this patient population the context and circumstances of washing and as well as minimizing any unnecessary hoarding.

Infection Prevention Partners Up With Psychology in a Danish Hospital Successfully Addressing Staffs Fear During the COVID-19 Pandemic
Olesen B, Gyrup HB, Troelstrup MW, Marloth T, Mølmer M
J Hosp Infect
2020 Apr 24; PMID: 32339619
Level of Evidence: 5 – Expert opinion
Type of Article: Letter to the Editor

Summary: This letter to the editor reported a novel approach addressing a COVID unit personnel's concerns, fears, and anxiety by bringing in a psychologist to practice an inductive change strategy (bottom-up approach) in collaboration with an infection prevention/control nurse. The goal of this intervention was to "release defense mechanisms blocking rational thinking and change of behavior" as well as psychoeducation in coping strategies towards fear and high levels of stress. The approach has been used in five sessions comprising 20 nurses and 15 physicians with an "overwhelmingly positive" response, chiefly that the participants were reassured of their ability to risk assess behavior when in close proximity to COVID-19 patients, and are more trusting of their knowledge of infection prevention and correct use of PPE.

Acknowledgements

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