# April 25, 2020
# Daily COVID-19 Literature Surveillance Summary


Jasmine Rah, BA, MS3[1*]
Erin Hartnett, BA, BS, MS4[2✣]
Emily V. Nelson, Ph.D[3*]
Samuel M. Philbrick, MD[4*]
Thamanna Nishath, MSPH, MS2[1•]
Jackson Schmidt, BA, MS3[1•]
Zainab Khan, BS, MS4[2•]
Brennan Enright, BS, MS1[2•]
Will Smith, MD, Paramedic, FAEMS[1,5#]

All contributors acknowledged on the final page.



Contributor Affiliations:
[1] University of Washington School of Medicine
[2] University of Arizona College of Medicine Phoenix
[3] Bernhard Nocht Institute for Tropical Medicine
[4] United States Air Force
[5] Wilderness and Emergency Medicine Consulting LLC.

Editor in Chief[*], Senior Editor[✣], Contributors[•], Editors[‘], Advisor [#]

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# Coming soon:


## COVID-19 Daily Literature Surveillance

COVID19LST

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


## The Swab

Jasmine Rah

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

# April 25th, 2020
# Executive Summary

**Climate**

- A cross sectional study of over 400 healthcare workers found that despite being hcp they actually had poor knowledge of the transmission, age, and profession that associated with poor perception of COVID-19 overall???
- We have Ongoing concerns for the health and safety of asylum seekers, undocumenterd migrants and those experiencing sex and gender disparities
- Literature is also beginning to quantify the amount of questionable information floating around inn social media regarding the pandemic.

**Epidemiology**

- A recent Lancet article proposesweekly, universal COVID-19 testing to ascertain a more accurate measure of prevalence and incidence so that policy can be guided by data.
- Increasing evidence support warmer climates inhibiting COVID-19 transmission
    - Many expect the northern hemisphere to experience reduced incidence while the southern hemisphere sees an increase in disease.
- Based on data from a Chinese study on complications in COVID-19 patients, 45% of the US population meets the criteria for being at increased risk for complications.
- There has been an unfortunate uptick in the number of accidental poisonings from household cleaning products
- Symptoms and clinical presentation
    - Serial CT scans in 112 patients found that COVID-19 lung findings begin peripherally and move centrally as the disease progresses.
    - A case series including 6 cases of COVID-19-associated upper GI bleeding found effective management and resolution of symptoms with conservative treatment with proton pump inhibitor, blood transfusion as needed, and frequent monitoring.

**Understanding the Pathology**

- Literature continues to point to
    - High incidence of venous thromboembolic events in patients with severe COVID-19
    - Obesity as a risk factor for severe infection
- In other news
    - A retrospective study found LDL to be a potential predictor of COVID-19 prognosis
    - A cross-sectional study found high prevalence of malnutrition in the elderly COVID-19 patients
- One cohort study of 54 patients found the unique pattern of immune dysregulation in severe COVID-19 to be characterized by IL-6-mediated low HLA-DR expression and lymphopenia, associated with sustained cytokine production and hyper-inflammation.
    - Such studies are growing the data we have on immunopathological mechanism of SARS-CoV-2

**Transmission & Prevention**

- widespread mask use among the general public is recommended for source control in all settings and N95 respirators to be used in settings where aerosolization of the virus is possible.

**Management**

- A case series of 362 patients found no difference in severity of the disease, complications, and risk of death in those who were taking ACEIs/ARBs compared with those who were not
    - Yet, research is still inconclusive and practitioners to wait until there is conclusive evidence before changing medication regimens
- Guidelines and recommendations for managing COVID-19 patients
    - Pain management
    - Critical care in resource-limited settings
    - Anesthesia scenario for emergency cesarean sections
    - Safer methods of intubation and extubation
    - Managing pregnancy and pediatric patients

- Amid rising concern over coagulation events in COVID-19 patients, the National Institute for Public Health of the Netherlands now recommends low-molecular weight heparin, baseline chest CT, and serial D-dimer measurements in all COVID-19 patients.

**Adjusting Practice during COVID-19**

- Strategies for managing cancer patients are presented
    - withholding chemotherapy and radiation in COVID-19 positive patients
    - relocating cancer teams away from COVID-19 treatment hospitals
    - and adapting treatment regimens to reduce patient visits.
    - But this remains controversial
- G6PD deficiency may be associated with increased COVID-19 morbidity
    - Ex vivo study showed G6PD deficient cells to be more vulnerable to COVID-19 infection.
    - A case of hemolytic crisis in a G6PD deficient after being treated with hydroxychloroquine

**R&D: Diagnosis & Treatments**

- Italian protocols for donation and collection of convalescent plasma in Italy

**Mental Health & Resilience**

- A cross-sectional web-based survey study of over 7,000 people in China found younger people reported a significantly higher prevalence of generalized anxiety disorder and depressive symptoms than older people during social distanncing
    - And, relative to other occupational groups, healthcare workers were more likely to have poor sleep quality
    - 2 case studies of self harm in India also highlighted how information overload can lead to increase in psychological distress among the general population as well
- Mental health experts draw upon data from previous large-scale sociaetal disruptions to suggest that the United States may be on the brink of a suicide epidemic given the current state of economic upheaval, social isolation, and easy access to firearms.

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### Global

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- The reproductive number R0 of COVID-19 in Peru: An opportunity for effective changes.
- Preparedness and Rapid Implementation of External Quality Assessment Helped Quickly Increase COVID-19 Testing Capacity in the Republic of Korea.
- Changes in testing rates could mask the novel coronavirus disease (COVID-19) growth rate.
- Epidemic update of COVID-19 in Hubei Province compared with other regions in China.
- Population-Based Estimates of Chronic Conditions Affecting Risk for Complications from Coronavirus Disease, United States.
- Cleaning and Disinfectant Chemical Exposures and Temporal Associations with COVID-19 - National Poison Data System, United States, January 1, 2020-March 31, 2020.

### Symptoms and Clinical Presentation

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## Understanding the Pathology

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Public Masking: An Urgent Need to Revise Global Policies to Protect against Novel Coronavirus Disease (COVID-19).

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- Safer intubation and extubation of patients with COVID-19.
- Laboratory haemostasis monitoring in COVID-19.
- Diagnosis, Prevention, and Treatment of Thromboembolic Complications in COVID-19: Report of the National Institute for Public Health of the Netherlands
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Future-proofing cardiac rehabilitation: Transitioning services to telehealth during COVID-19.

Restructuring Electrophysiology During the COVID-19 Pandemic: A Practical Guide from a New York City Hospital Network.

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- Neurological Insights of COVID-19 Pandemic.
- Neuropsychiatric adverse events of chloroquine: a real-world pharmacovigilance study using the FDA Adverse Event Reporting System (FAERS) database.
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Pharmacologic Therapy for COVID-19 Infection.

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Self-harm and COVID-19 Pandemic: An emerging concern - A report of 2 cases from India.

Challenges and Priorities in Responding to COVID-19 in Inpatient Psychiatry.

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The emergence of SARS, MERS and novel SARS-2 coronaviruses in the 21st century.

Scientific research progress of COVID-19/ SARS-CoV-2 in the first five months.

2019 Novel coronavirus (COVID-19) overview.

Covid-19: Simulation models for epidemics.

## Acknowledgements

# 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

# Climate

## Novel Coronavirus (COVID-19) Knowledge and Perceptions: A Survey of Healthcare Workers

Bhagavathula, Akshaya; Aldhaleei, Wafa Ali; Rahmani, Jamal Rahmani; Mahabadi, Mohammadjavad Ashrafi; Bandari, Deepak Kumar
JMIR Public Health Surveill
2020 Apr 19; PMID: 32320381
Level of Evidence: 4 - Cross Sectional Study
Type of Article: Research
**BLUF:** In a survey about COVID-19 delivered using social media, with 529 participants -453 of whom were healthcare workers (HCW), the authors found that HCWs had poor knowledge of transmission. Age and profession were associated with poor perception of COVID-19 overall.

**Abstract:**
Background: During the first week of March, the surge of coronavirus disease 2019 (COVID-19) cases reached over 100 countries with more than 100,000 cases. Healthcare authorities have already initiated awareness and preparedness activities beyond borders. A poor understanding of the disease among healthcare workers (HCWs) may result in delayed treatment and the rapid spread of infection.
Objective: This study aimed to investigate the knowledge and perceptions of HCWs about COVID-19.
Methods: A cross-sectional, web-based study was conducted among HCWs about COVID-19 during the first week of March 2020. A 23-item survey instrument was developed and distributed randomly to HCWs using social media; it required 5 minutes to complete. A chi-square test was used to investigate the level of association among variables at the significance level of $p<0.05$.
Results: Of 529 participants, a total of 453 HCWs completed the survey (response rate: 85.6%); 51.6% were males, 32.1% were aged 25-34 years, and most were doctors (30.2%) and medical students (29.6%). Regarding COVID-19, most of the participants used social media to obtain information (61%), and a significant proportion of HCWs had poor knowledge of its transmission (61%) and symptom onset (63.6%) and showed positive perceptions of COVID-19. Factors such as age and profession were associated with inadequate knowledge and poor perception of COVID-19.
Conclusions: As the global threat of COVID-19 continues to emerge, it is critical to improve the knowledge and perceptions of HCWs. Educational interventions are urgently needed to reach HCWs beyond borders, and further studies are warranted.

## The COVID-19 Pandemic: A Global Natural Experiment.

Thomson B.
Circulation.
2020 Apr 23; PMID: 32324429
Level of Evidence: 5 - Expert opinion
Type of Article: Editorial
**BLUF:** Natural experiments provide a unique opportunity to view the consequences of unprecedented circumstances on the health of many people. The authors urge researchers to be rigorous in studying the global response to the COVID-19 pandemic in order to improve patient health and mitigate harmful consequences.

**Summary: Natural experiments are shifts in exposure outside of researchers' control that can be studied for inferred causal effects.** The author discusses three other natural

experiments: the effects of greatly increased alcohol use in Russia after the collapse of the Soviet Union, the effects of decreased dietary intake and increased exercise in the economic depression in Cuba in the 1990s, and the effects of widespread famine in China during the time of the Great Leap Forward. **The widespread effects of COVID-19 are still broadly unknown, and the consequences of social distancing, economic challenges, and lingering effects of the virus itself will need to be studied in order to improve patient health now and long after the pandemic is over.**

## Imaging Publications in the COVID-19 Pandemic: Applying New Research Results to Clinical Practice.

Eng J, Bluemke DA.
Radiology.
2020 Apr 23; PMID: 32324100
Level of Evidence: 5- Expert opinion
Type of Article: Special Report
**Summary:** Thoughtful application of clinical epidemiology principles is necessary in order to evaluate emerging evidence as the clinical context continues to evolve. To understand the specificity, sensitivity, positive predictive value, and negative predictive value of tests used to diagnose COVID-19, it is important to consider the prevalence of the disease in the study population.

## COVID-19: Immense necessity and challenges in meeting the needs of minorities, especially asylum seekers and undocumented migrants

Bhopal, R S
Public Health
2020 Apr 15; PMID: 32325326
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter
**Summarizing Excerpt:** "In desperate times, we need to consider every possible solution. One that needs urgent consideration is to give temporary citizenship rights to every person in the country together with safeguards that by coming forwards people can expect confidentiality, respectful treatment and no detriment to their asylum and residency claims in the long term. We need everyone involved in the war against the pandemic—that includes asylum seekers and undocumented migrants. This is a radical proposal but what is better?"

## Information Technology-Based Tracing Strategy in Response to COVID-19 in South Korea-Privacy Controversies

Park, Sangchul; Choi, Gina Jeehyun; Ko, Haksoo
JAMA
2020 Apr 23; PMID: 32324202
Level of Evidence: 5 - Expert Opinion
Type of Article: Research
**Summarizing Excerpt:** "**Data sharing about infected individuals within the public sector and among medical professionals confers epidemiologic benefits.** In containing the spread of a highly infectious disease like COVID-19, an early response is critical. **The use of an integrated IT system helped epidemiology investigators save resources by automating the overall tracking processes."** Since the MERS epidemic in 2012, was already prepared with legislative changes that allowed for the controlled application of individuals' data.

## Twitter as a powerful tool for communication between pain physicians during COVID-19 pandemic.

Ghosh P, Schwartz G, Narouze S.
Reg Anesth Pain Med.
2020 Apr 21; PMID: 32321859
Level of Evidence: 6 - No Data Cited
Type of Article: Letter to the Editor

**Summary**: The author makes the case that the utilization of social media, especially Twitter, is steadily increasing across all medical specialties, and is now a very common way of disseminating novel research. The author refers to a simple tweet by @NarouzeMD and the resulting discussion on March 16, 2020 that lead to the official creation of the joint statement of ASRA and ESRA for recommendations on chronic pain practice which was published on March 27, 2020.

## An Infodemiological Study on Novel Coronavirus (COVID-19) in South Korea: Conversations and Medical News Frames on Twitter

Park HW, Park S, Chong M.Park HW
J Med Internet Res.
2020 April 22; PMID: 32325426
Level of Evidence: 3 Cross-sectional Study
Type of Article: Research

**BLUF:** Social media plays an important role during social disasters such as epidemics of infectious disease and this study investigates information transmission and news sharing regarding SARS-CoV-2 on Twitter in Korea. The study found social media to be the main modality of communication and education about SARS-CoV-2 and suggested public health officials utilize social media to help with their decision-making processes.

**Abstract**: Background**:** SARS-CoV-2 (severe acute respiratory coronavirus 2) was spreading rapidly in South Korea at the end of February 2020 following its initial outbreak in China, making Korea the new center of global attention. The role of social media amid the current SARS-CoV-2 pandemic has often been criticized, but little systematic research has been conducted on this issue. **Social media functions as a convenient source of information in pandemic situations.**
Objective**:** Few infodemiology studies have applied network analysis in conjunction with content analysis. This study investigates information transmission networks and news sharing behaviors regarding SARS-CoV-2 on Twitter in Korea. The real-time aggregation of social media data can serve as a starting point for designing strategic messages for health campaigns and establishing an effective communication system during this outbreak.
Methods**:** Korean SARS-CoV-2-related Twitter data were collected on February 29, 2020. Our final sample comprises 43,832 users and 78,233 relationships on Twitter. We generate four networks in terms of key issues regarding SARS-CoV-2 in Korea. This study comparatively investigates how SARS-CoV-2 -related issues have circulated on Twitter through network analysis. Next, we classify top news channels shared via tweets. Lastly, we conduct a content analysis of news frames used in the top shared sources.
Results**:** The network analysis suggests that the **spread of information was faster in the Coronavirus network than in the other networks** (Corona19, Shincheon, and Daegu). People who used the word "Coronavirus" communicated more frequently with each other. The spread of information was faster, and the **diameter value was lower than for those who used other terms**. Many of the news items highlighted the positive roles being played by individuals and groups, directing readers' attention to the crisis. Ethical issues such as deviant behavior among the population and an entertainment frame highlighting celebrity donations also often emerged. There was a

significant difference in the use of non-portal (n = 14) and portal news (n = 26) sites between the four network types (N = 40). The news frames used in top sources were similar across the networks (P= .89, CI = 0.004, 0.006). Tweets containing medically framed news articles (M = 7.571, SD = 1.988) were found to be more popular than tweets that included news articles adopting non-medical frames (M = 5.060, SD = 2.904; N = 40, P = .03, CI: 0.169, 4.852).
Conclusions**:** Most of the popular news on Twitter had non-medical frames. **Nevertheless, the spillover effect of the news articles that delivered medical information about COVID-19 was greater than that of news with non-medical frames.** While social media network analytics cannot replace the work of public health officials, monitoring public conversations and media news that propagates rapidly can assist public health professionals in their complex and fast-paced decision-making processes.

## Sex and Gender Disparities in the COVID-19 Pandemic.

Gausman J, Langer A.
J Womens Health (Larchmt)
2020 Apr 17; PMID: 32320331
Level of Evidence: 5 - Expert Opinion
Type of Article: Commentary

**Summary:** The authors of this article advise caution in interpreting data that suggests that women may have a lower mortality risk associated with COVID-19 than men. They encourage readers to have an expanded perspective on the factors that contribute to mortality risk, such as:

- Pregnant patients are often a vulnerable during public health emergencies
- Routine prenatal care visits may represent an increased exposure risk
- Pregnant patients are often not offered experimental treatments or vaccines
- Reduced social support during this time may also put pregnant and postpartum patients at risk of mental health problems
- Responses to the pandemic may put women at higher risk of unintended pregnancy and domestic violence
- Several states in the U.S. have restricted access to elective abortions
- Women's overrepresentation in certain healthcare professions may increase their exposure risk
- Women's overrepresentation in the informal employment sector could also increase exposure risk and limit access to healthcare

The authors conclude by urging application of a gender lens when developing policies to respond to the pandemic and urge the CDC to release sex disaggregated data on the pandemic.

## The post-lockdown period should be used to acquire effective therapies for future resurgence in SARS-Cov-2 infections.

Krause KL, Furneaux R, Benjes P, Brimble M, Davidson T, Denny W, Harris L, Hinkley S, Tyler P, Ussher JE, Ward V.Krause KL
N Z Med Journal
2020 April 24; PMID: 32325475
Level of Evidence: 5 Expert Opinion
Type of Article: Letter

**BLUF:** It will take at least 12-14 months to develop and test the SARS-CoV-2 vaccine, therefore the authors propose widespread use in New Zealand of convalescent sera and direct-acting anti-virals while waiting for the vaccine to be developed and emphasize the importance of government support.

**Abstract**: COVID-19 will be with us through the remainder of 2020 and almost certainly beyond. New Zealand needs a viable strategy to protect its populace until a vaccine is developed and in wide use. Until that time, it makes sense to protect the population by putting in place treatments that will be safe and effective, such as the use of **convalescent sera and the use of direct-acting anti-virals**. These treatments should be sourced externally or made locally, but **steps in this direction must now begin as the lockdown ends**. New Zealand has the scientists, the facilities and the will to make this happen, but the support of the government and the population will be needed if this plan is to succeed.

## Converting Home Spaces Into Food Gardens At the Time of Covid-19 Quarantine: All the Benefits of Plants in This Difficult and Unprecedented Period.

Sofo A, Sofo A.
Hum Ecol Interdiscip J.
2020 Apr 22. Doi; PMID: 32322132
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter
**BLUF:** Home gardens can bring numerous recreational, health, and economic benefits for people self-isolating during the COVID-19 pandemic, with the potential to impact environmental outcomes.

**Abstract:** People are facing uncertain and difficult times in the face of the Covid-19 pandemic. The benefits of plants (psychological, health, economic, productive) in this period of forced isolation can be of key importance. If many of us have to self-isolate in urban or suburban environments, we need something to do to keep our bodies and minds active and fed. In such a challenging scenario, a **vegetable garden in home spaces can bring recreational, health, economic and environmental benefits**. Regardless of the Covid-19 pandemic, there is untapped potential for this kind of garden to impact environmental outcomes, public awareness, and market trends. Home vegetable gardens could provide a **small-scale approach to the sustainable use of natural resources**, leading towards self-sufficiency, self-regulation, sustainability, and environmental protection

## Lifestyle behaviours during the COVID-19 - time to connect.

Balanzá-Martínez V, Atienza-Carbonell B, Kapczinski F, De Boni RB.Balanzá-Martínez V, et al.
Acta Psychiatr Scand
2020 Apr 23; PMID: 32324252
Level of Evidence: 5 - Expert Opinion
Type of Article: Editorial
**BLUF:** The author argues that the current lifestyle guidelines of “maintaining healthy nutritional status and engaging in physical exercise at home” are not entirely based on evidence based medicine. To address this, “observational studies of lifestyle behaviors” are needed for more effective public policies.

**Abstract:**Loneliness and social isolation are associated with poor mental and physical health and may increase the likelihood of common mental disorders (depressive and anxiety disorders), substance use, and cognitive decline1,2 . At this moment, people around the globe have been urged to self-isolate and refrain from social interaction due to the COVID-19 pandemic. **From public health and preventative care perspectives, there is a pressing need to provide individuals, communities and health agencies with information and interventions to maintain the healthiest possible lifestyle while in isolation.**

## Building trust while influencing online COVID-19 content in the social media world

Limaye RJ, Sauer M, Ali J, Bernstein J, Wahl B, et al.
Lancet Digit Health
2020 Apr 21. Doi; PMID: 32322814
Level of Evidence: 5 - No Evidence Provided
Type of Article: Commentary
**Summarizing excerpt: "**Because many are turning to social media for information and advice, the differentiation between individuals who are qualified to provide accurate information online and so-called armchair epidemiologists is increasingly difficult. Members of the lay public might try to identify the most seemingly qualified member of their close network as a trusted resource to vet information. These individuals might feel unequipped to respond effectively to misinformation that individuals are exposed to on social media."

## Pandemic Pandemonium: Pausing Clinical Research During the COVID-19 Outbreak.

Byrd JB, Bello N, Meyer MN.Byrd JB, et al.
Circulation.
2020 Apr 22; PMID: 32320272
Level of Evidence: 5 - Expert Opinion
Type of Article: Commentary
**Summary:**
The authors discussed the challenge of deciding which types of clinical research should or should not be paused during the COVID-19 crisis. Studies that risk participants becoming ill, and thus possibly more susceptible to COVID-19, **should be reassesed. Social distancing, allocation of personnel, and other measures to reduce risk of exposure may adversely affect the quality of clinical research.**

## Exercise in the time of COVID-19.

Fallon K.Fallon K.
Aust J Gen Pract.
2020 Apr 22; PMID: 32321207
Level of Evidence: 5 - Expert Opinion
Type of Article: Commentary
**Summarizing excerpt:** "The COVID-19 pandemic has restricted the physical activity of the population, but maintaining exercise could reduce the risk of contracting the infection itself and mitigate the effects of quarantine."

## The Potential Health Care Costs And Resource Use Associated With COVID-19 In The United States

Bartsch SM, Ferguson MC, McKinnell JA, O'Shea KJ, Wedlock PT, Siegmund SS, Lee BY
Health Aff (Millwood)
2020 Apr 23; PMID: 32324428
Level of Evidence: 5 – Mechanism-based Reasoning
Type of Article: Research

**BLUF:** This study tracks the **potential healthcare costs** incurred by the US population under **different rates of SARS-CoV-2 infection** (80%, 50%, 20% of the population). The authors use a Monte Carlo simulation model outfitted with data associated with **frequency and cost of disease manifestations of COVID-19**, and they substitute healthcare cost data for diseases with similar treatment regimens in cases where the data are unavailable. The authors conclude that direct medical costs under a **20% infection rate would result in $163.3 billion cost**, whereas if **80%** were infected, the costs would jump to **$654.0 billion**, not accounting for cost of follow-up care, and they acknowledge that their **model likely underestimates healthcare cost burden**. They conclude with a brief commentary of the lack of excess hospital capacity to deal with a surge in infections, and that other strategies (namely the development of herd immunity) may cost more.

**Abstract:**
With the coronavirus disease 2019 (COVID-19) pandemic, one of the major concerns is the burden COVID-19 will impose on the United States (U.S.) health care system. We developed a **Monte Carlo simulation model representing the U.S. population** and what can happen to each person who gets infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV2). We **estimate resource use and direct medical costs per infection and at the national level**, with various "attack rates" (infection rates) to understand the potential economic benefits of reducing the burden of the disease. A **single symptomatic COVID-19 infection** would cost a median of **$3,045 in direct medical costs** incurred only during the course of the infection. Eighty percent of the U.S. population getting infected could result in a median of 44.6 million hospitalizations, 10.7 million ICU admissions, 6.5 million ventilators used, and 249.5 million hospital bed days, costing $654.0 billion in direct costs over the course of the pandemic. If **20% were to become infected**, there would be a median of **11.2 million hospitalizations**, 62.3 million hospital bed days, and **1.6 million ventilators used, costing $163.4 billion**.

## The Change to Pass/Fail Scoring for Step 1 in the Context of COVID-19: Implications for the Transition to Residency Process.

Whelan AJ.
Acad Med.
2020 Apr 21; PMID: 32324640
Level of Evidence: 5 - Expert Opinion
Type of Article: Invited Commentary
**BLUF: The chief medical education officer at AAMC argues that the switch to pass/fail scoring for Step 1 does not remove the need for additional reforms in the transition from undergraduate medical education to graduate medical education.** COVID-19 is disrupting medical education - positive aspects should be embraced and negative aspects managed.

**Abstract:**
In this Invited Commentary, the author considers the February 2020 announcement that scoring on the United States Medical Licensing Examination (USMLE) Step 1 will change to pass/fail no sooner than January 2022 and its effects on the transition to residency process in the context of both the recommendations of the Invitational Conference on USMLE Scoring (InCUS) held in March 2019 and the disruptions caused by the COVID-19 pandemic in the spring of 2020. The author suggests that the medical education community must embrace any positive changes that come about as a result of the pandemic while continuing to systematically review the strengths and areas for improvement in the current transition to residency process. In its recommendations, InCUS provided a thoughtful set of action priorities and an effective process to work together, which can inform and guide the work ahead. The COVID-19 pandemic is dominating the educational and clinical environments and is now

the biggest disruptor in all aspects of life, not just medical education. It is the responsibility of leaders in medical education to have a vision for and then implement an improved continuum of education that maintains the core values of the field and fits the health care delivery needs of today and the future.

## Déjà vu: stimulating open drug discovery for SARS-CoV-2.

Ekins S, Mottin M, Ramos PRPS, Sousa BKP, Neves BJ, Foil DH, Zorn KM, Braga RC, Coffee M, Southan C, Puhl AC, Andrade CH
Drug Discov Today
2020 Apr 19; PMID: 32320852
Level of Evidence: 5- Expert opinion
Type of Article: Review

**BLUF:** The authors provide a detailed account of drug discovery methods from previous pandemics and the current state of drug discovery research in this pandemic.

**"Highlights**

- We describe our prior efforts in open drug discovery for Ebola and Zika virus.
- We summarize the current literature for severe acute respiratory syndrome coronavirus (SARS-CoV-2).
- We detail computational repurposing efforts and results for SARS-CoV-2.
- To be prepared for future outbreaks we argue we need novel broad-spectrum antivirals.
- Limitations of these efforts include funding for experimental validation, and this lags behind the computational work."

**Abstract:**
In the past decade we have seen two major Ebola virus outbreaks in Africa, the Zika virus in Brazil and the Americas and the current pandemic of coronavirus disease (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). There is a strong sense of déjà vu because there are still no effective treatments. In the COVID-19 pandemic, despite being a new virus, there are already drugs suggested as active in in vitro assays that are being repurposed in clinical trials. Promising SARS-CoV-2 viral targets and computational approaches are described and discussed. Here, we propose, based on open antiviral drug discovery approaches for previous outbreaks, that there could still be gaps in our approach to drug discovery.

## Answering the right questions for policymakers on COVID-19.

Graeden E, Carlson C, Katz R.Graeden E, et al.
Lancet Glob Health.
2020 Apr 20; PMID: 32325018
Level of Evidence: 6 - No data cited
Type of Article: Commentary

**Summary:** The authors present **a list of urgent questions** they believe can be answered with available data. Questions fall into the following themes: **clinical presentation and testing**, **treatment**, **non-pharmaceutical interventions**, **public health response**, and **compound hazards and hazard planning**. They urge the "officials and experts in the USA" to focus on answering these questions.

## The most eagerly awaited summer of the Anthropocene: A perspective of SARS-CoV-2 decay and seasonal change.

Kumar M, Kuroda K, Dhangar K, et al.
Groundw Sustain Dev.

2020 Apr 22; PMID: 32322654
Level of Evidence:
Type of Article: Perspective
**BLUF:** Earth science, environmental and civil engineers are hopeful that summer will reduce COVID-19 transmission.
**Abstract:**
To date, the world perhaps has never waited for the summer so impatiently in the entire Anthropocene, owing to the debate whether increasing temperature and humidity will decrease the environmental endurance of SARS-CoV-2. We present the perspective on the seasonal change on SARS-CoV-2 decay and COVID-19 spread. **Our arguments are based on: i) structural similarity of coronavirus with several enteric viruses, and its vulnerability; ii) reports related to decay of those similar transmissible gastroenteritis viruses (TGEV) like norovirus and iii) improvement in the human immunity during summer with respect to winter**. We present reasons why we can be optimistic about the slowdown of corona in the upcoming summer.

## SARS-CoV-2 pandemic expanding in sub-Saharan Africa: Considerations for COVID-19 in people living with HIV.

Drain PK, Garrett N
EClinicalMedicine
2020 Apr 22; PMID: 32322805; No Abstract
Level of Evidence: 5 - Expert Opinion
Type of Article: Commentary
**Summary:** After the SARS-CoV-2 pandemic reached sub-Saharan Africa, concerns regarding COVID-19 cases in high HIV prevalence communities rapidly increased, especially in patients living with HIV who are unaware of their diagnosis or not yet receiving antiretroviral therapy. With no proven therapeutic options for COVID-19, the WHO recommends a “Test, Test, Test” strategy in response to the COVID-19 pandemic, including several common HIV medications like Lopinavir and Ritonavir. There is now concern that COVID-19 will severely divert limited health care resources, which may increase HIV and TB mortality.

# Epidemiology

## Global

### Modelling the COVID-19 Epidemic and Implementation of Population-Wide Interventions in Italy.

Giulia Giordano, Franco Blanchini, Raffaele Bruno, Patrizio Colaneri, Alessandro Di Filippo, et al.
Nat Med.
2020 Apr 22; PMID: 32322102
Level of Evidence: Predictive modeling
Type of Article: Letter

**BLUF:** The authors propose a model that shows that if lockdown is weakened, there will be a sudden increase in spread of disease causing prolongation of the current crisis and an increase in mortality (0.12% in the first 350 days). If there were population-wide testing and contact tracing, the peak would be reached sooner, and 0.43% of the population would contract the virus (0.33% diagnosed, 0.05% dying). Hence, current adopted lockdown measures are vital to contain the epidemic and cannot be relieved.

**Abstract:** In Italy, 128,948 confirmed cases and 15,887 deaths of people who tested positive for SARS-CoV-2 were registered as of 5 April 2020. Ending the global SARS-CoV-2 pandemic requires implementation of multiple population-wide strategies, including social distancing, testing and contact tracing. We propose a **new model** that predicts the course of the epidemic to help plan an effective control strategy. The model considers eight stages of infection: susceptible (S), infected (I), diagnosed (D), ailing (A), recognized (R), threatened (T), healed (H) and extinct (E), collectively termed SIDARTHE. Our SIDARTHE model discriminates between infected individuals depending on whether they have been diagnosed and on the severity of their symptoms. The distinction between diagnosed and non-diagnosed individuals is important because the former are typically isolated and hence less likely to spread the infection. This delineation also helps to explain misperceptions of the case fatality rate and of the epidemic spread. We compare simulation results with real data on the COVID-19 epidemic in Italy, and we model possible scenarios of implementation of countermeasures. Our results demonstrate that **restrictive social-distancing measures will need to be combined with widespread testing and contact tracing to end the ongoing COVID-19 pandemic.**

### Potential Impact of Climate on Novel Corona Virus (COVID-19) Epidemic.

Monami M, Silverii A, Mannucci E.
J Occup Environ Med
2020 Apr 22; PMID: 32324703
Level of Evidence: Regression model based on population data
Type of Article: Letter

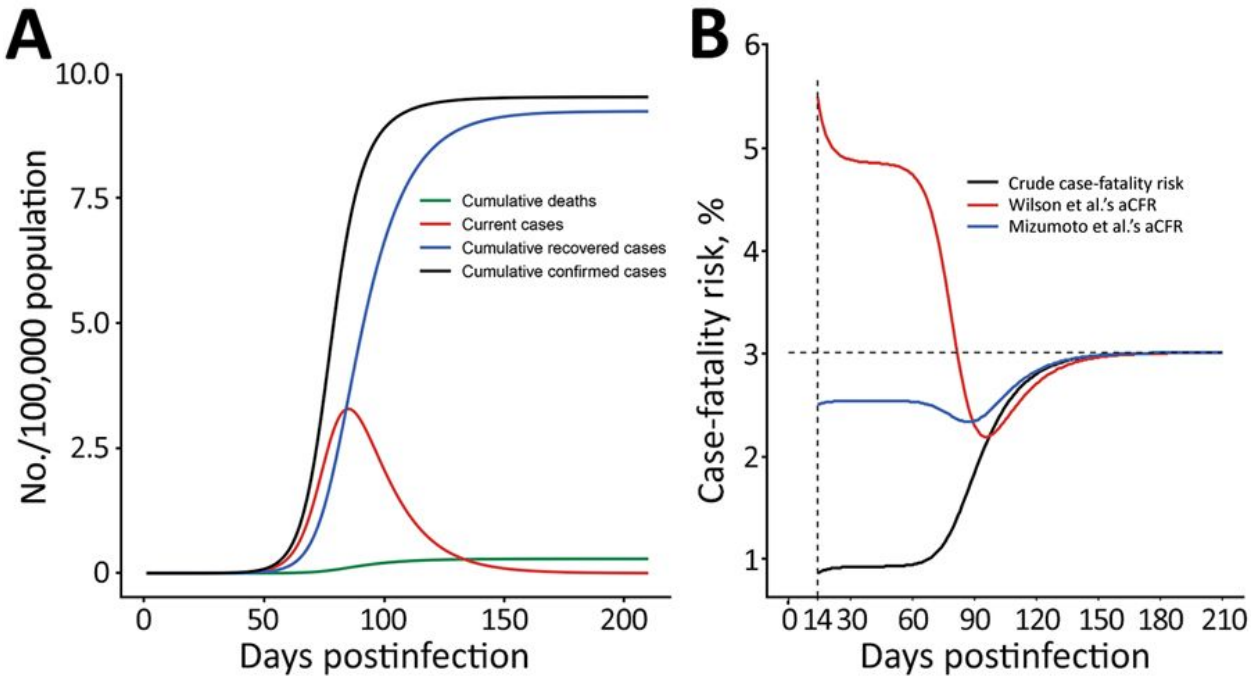
**Summarizing excerpt:** "In a linear regression model weighted for population size, the number of cases per million inhabitants, excluding China's People Republic, showed a significant inverse correlation (R=0.23, p=0.001) with average temperatures in February." This indicates a possible impact of **warmer climates inhibiting COVID-19 transmission** and suggests that "a **spontaneous slowdown of the epidemic could be expected in the Northern hemisphere** in the next weeks, whereas **risks could be increased in the Southern hemisphere**." Notably, differences in the kinetics may be attributable to the "biological characteristics of the virus strains or the host population," especially with the high number of undetected, oligosymptomatic cases and differences in screening and testing policies.

## Estimation of Coronavirus Disease Case-Fatality Risk in Real Time.

Ge Y, Sun S. Ge Y, et al.
Emerg Infect Dis.
2020 Apr 21; PMID: 32315282
Level of Evidence: 4 - Quantitative Research
Type of Article: Research Letter

**BLUF:** A simulation test on 3 case fatality risk (CFR) methods. Their simulated calculation of CFR of 3% , closest to the Mizumoto et al's adjusted case-fatality risk (aCFR) method. They therefore recommended aCFR model for real time estimations during early stages of an epidemic.

**Abstract:** We ran a simulation comparing 3 methods [crude case-fatality risk, adjusted case-fatality risk (aCFR) per Wilson et al.'s method, and aCFR per Mizumoto et al.'s method] to calculate case-fatality risk for coronavirus disease using parameters described in previous studies. Case-fatality risk calculated from these methods all are biased at the early stage of the epidemic. When comparing real-time case-fatality risk, the current trajectory of the epidemic should be considered.



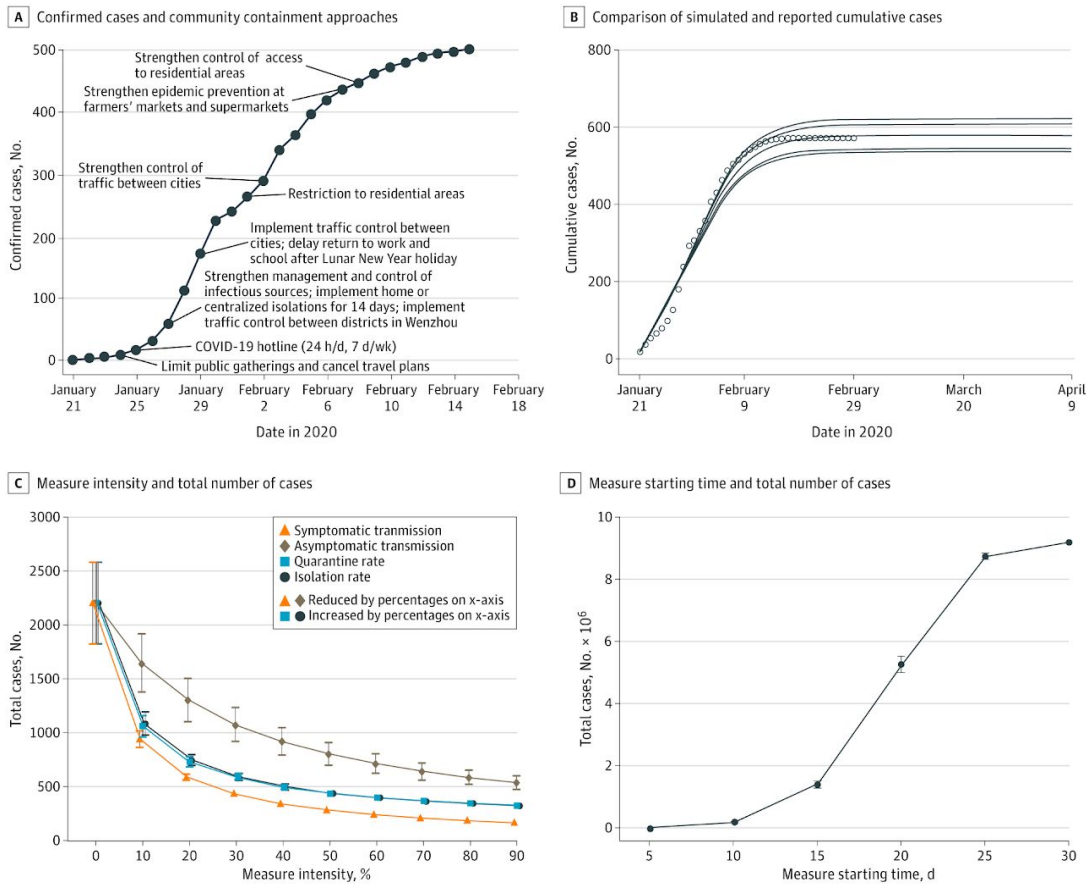

## Epidemiological Assessment of Imported Coronavirus Disease 2019 (COVID-19) Cases in the Most Affected City Outside of Hubei Province, Wenzhou, China.

Han Y, Liu Y, Zhou L, Chen E, Liu P, Pan X, Lu Y.Han Y, et al.
JAMA Netw Open.
2020 Apr 1; PMID: 32324236
Level of Evidence: 4 - Case Series
Type of Article: Research

**BLUF:** Researchers built a predictive epidemic model of COVID-19 spread in Wenzhou, China that closely mirrored actual reported cases. Simulated predictions of future cases, revealed the importance of immediately quarantining asymptomatic individuals in order to reduce transmission.

**Summary Excerpt:**
Intro: "To stop the spread of COVID-19 in Wenzhou, multiple community containment approaches were implemented beginning January 24, 2020, including quarantine, isolation, traffic control, and social distancing… As of February 15, 2020, there were 502 confirmed cases of COVID-19 but no deaths reported in Wenzhou…"
Methods: "The susceptible-asymptomatic-symptomatic-quarantined-isolated-removed model was used to simulate the dynamics of the COVID-19 epidemic [in Wenzhou]"
Results: "Comparison of simulated and reported cumulative cases revealed that our model mimicked the actual spread well [(see Figure below)]… Our simulation showed that the intensity and starting time of control and prevention measures had major impacts on the spread of COVID-19… **The total mean (SEM) cumulative number of cases 6 months later would decrease to 440 (16) if the quarantine of infected individuals from the general population before they develop clinical symptoms (ie, asymptomatic individuals) was increased by 50% from the baseline. In contrast, the mean (SEM) number of cumulative cases would increase to 15 576 (1554) if measures were delayed for 5 days after the first diagnosed case.** These findings suggest that quarantine of asymptomatic individuals is as important as isolation (hospitalization) of infected individuals with symptoms."

**Abstract:** A novel coronavirus (COVID-19) pandemic threatens the world. Here, we first studied the dynamics profile of SARS-CoV-2 from **56 recovered COVID-19 patients**. We found **virus shedding** was up to **6 weeks after onset of symptoms**. Prolonged observation period is necessary for older patients.



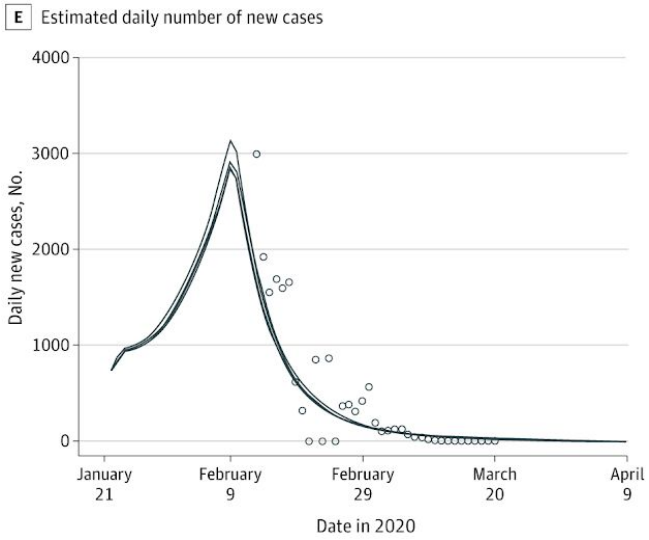



**Figure Legend:** Dynamics of the Spread of Coronavirus Disease 2019 (COVID-19) A, Confirmed cases and community containment approaches taken at different time points in Wenzhou. B, Comparison of simulated (lines) and reported (circles) cumulative cases in Wenzhou. Simulated cases were replicated with 5 different models. C, Measure intensity and total number of cases. In each scenario, 1 measure was changed to 0% to 90% of its baseline value on January 21, 2020, whereas the other 3 parameters remained unchanged. The consequence of changing measure intensity was evaluated by total number of cases 6 months later. D, Measure starting time and total number of cases. The consequence of delayed measure implementation was evaluated by total number of cases 6 months later. E, Estimated daily number of new cases in Wuhan. Simulated cases were replicated with 5 different models and are shown with lines; actual reported cases are shown with circles.

## The reproductive number $R_0$ of COVID-19 in Peru: An opportunity for effective changes.

Torres-Roman JS, Kobiak IC, Valcarcel B, Diaz-Velez C, La Vecchia C.Torres-Roman JS
Travel Med Infect Dis.
202 April 20; PMID: 32325120
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter

**BLUF:** As cases of COVID-19 increases in Peru and the Lima province, a mandated State of Emergency action was implemented to decrease the spread of COVID-19. However, limiting factors such as testing delays, high false positives rates, and low compliance to quarantine regulations may contribute to the likelihood of increased spread of COVID-19 in Peru and the Lima province.

**Summary**: On March 6, 2020 Peru reported its first case of COVID-19 from a man with recent travel history to Europe. As time went on, the number of cases increased leading to the Peruvian president to declare a State of Emergency on March 15, 2020. With the transmission of COVID-19 being of person-to-person contact, the need to determine the likelihood of spreading the disease became an important goal for the people of Peru and the Lima province. They estimated reproductive number **(R0)** during the outbreak in **Peru and Lima** province **was 2.97** and with the mandated State of Emergency, it was an opportunity to decrease the R0. However with testing delays, human errors that caused a high false positive rate, and low quarantine compliance may have pointed Peru and the Lima province towards a sustained or increased R0 in the population. This as a result will increase the likelihood of the spread of COVID-19 in Peru and Lima province.

## Changes in testing rates could mask the novel coronavirus disease (COVID-19) growth rate.

Omori, Ryosuke; Mizumoto, Kenji; Chowell, Gerardo

International Journal of Infectious Diseases
2020 Apr 19; PMID: 32320809
Level of Evidence: 5 - Mechanism-Based Reasoning
Type of Article: Short communication
**BLUF:** Analysis of daily series of COVID-19 reported laboratory confirmed cases was done using linear and nonlinear growth models to show that epidemic curves of reported cases might not always coincide with true growth rates; a possible explanation for this is the limited diagnostic testing capacity present early-on in the epidemic.

**Abstract:** Since the novel coronavirus disease (COVID-19) emerged in December 2019 in China, it has rapidly propagated to around the world, leading to one of the most significant pandemic events of recent history. Deriving reliable estimates of the COVID-19 epidemic growth rate is quite important to guide the timing and intensity of intervention strategies. Indeed, many studies have quantified the epidemic growth rate using time-series of reported cases during the early phase of the outbreak to estimate the basic reproduction number, R0. Using daily time series of COVID-19 incidence, we illustrate how **epidemic curves of reported cases may not always reflect the true epidemic growth rate due to changes in testing rates**, which could be **influenced by limited diagnostic testing capacity during the early epidemic phase**.

## Population-Based Estimates of Chronic Conditions Affecting Risk for Complications from Coronavirus Disease, United States.

Adams ML, Katz DL, Grandpre J.Adams ML, et al.
Emerg Infect Dis.
2020 Apr 23; PMID: 32324118
Level of Evidence: Predictive modeling
Type of Article: Data analysis
**Summary:** Data from a **Chinese study on complications in COVID-19 patients** was used to **extrapolate estimated risk in a select US population** of adults based on prevalence of chronic disease as reported in the 2017 BRFSS survey. **Based on their analysis 45.4% of the US population may be at a disproportionately increased risk of COVID-19 complications** compared to their healthy counterparts.

**Abstract:**
We **estimated that 45.4% of US adults are at increased risk for complications from coronavirus disease because of cardiovascular disease, diabetes, respiratory disease, hypertension, or cancer.** Rates increased by age, from 19.8% for persons 18–29 years of age to 80.7% for persons ≥80 years of age, and varied by state, race/ethnicity, health insurance status, and employment. **Data for China indicate that 81% of coronavirus disease (COVID-19) patients had mild cases, 14% had severe cases, and 5% had critical cases** (*1*,*2*). The overall case-fatality rate (CFR) in China was 3.8% (*3*), but **CFRs were higher for adults with chronic conditions of cardiovascular disease (CVD; CFR 13.2%), diabetes (9.2%), chronic respiratory disease (8.0%), hypertension (8.4%), and cancer (7.6%), compared with 1.4% for patients with none of these conditions** (*3*). Our objective for this study was to use population-based US data to estimate the fraction of adults in the community who might be at increased risk for complications from COVID-19 because they reported any of the chronic conditions with a high CFR in China.

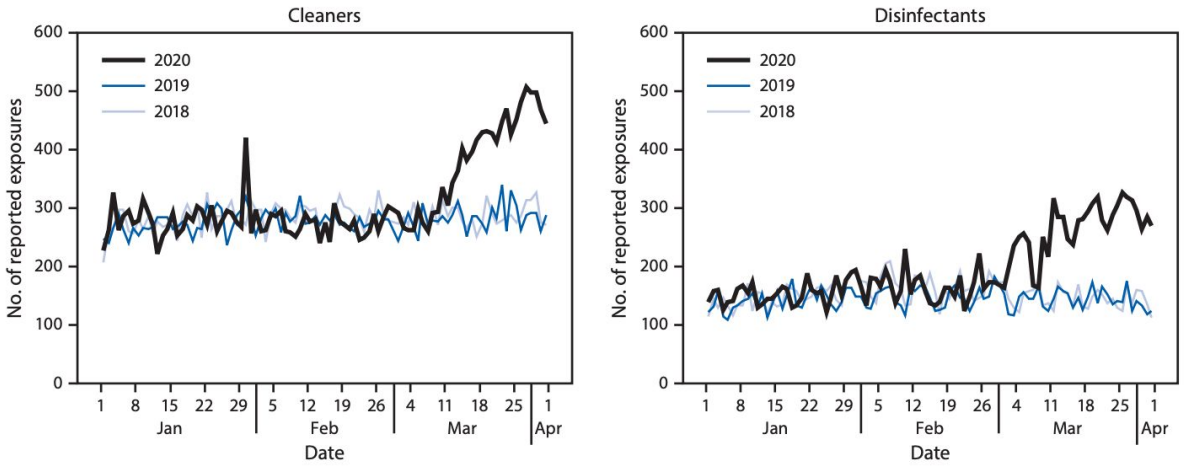
## Cleaning and Disinfectant Chemical Exposures and Temporal Associations with COVID-19 - National Poison Data System, United States, January 1, 2020-March 31, 2020.

Chang A, Schnall AH, Law R, Bronstein AC, Marraffa JM, Spiller HA, Hays HL, Funk AR, Mercurio-Zappala M, Calello DP, Aleguas A, Borys DJ, Boehmer T, Svendsen E.Chang A, et al.
MMWR Morb Mortal Wkly Rep.
2020 Apr 24; .PMID: 32324720
Level of Evidence: 4-Retrospective Study
Article Type: Research

**BLUF:** The authors report an increase in cleaner and disinfectant exposure calls (by 20.4% and 16.4%, respectively) to the national poison data system during the COVID-19 pandemic. Two vignettes -- a child consuming hand sanitizer and an adult inhaling disinfectant chemicals -- are illustrated to exemplify the current type of incidents that are being called into poison centers.

**Abstract:** On January 19, 2020, the state of Washington reported the first U.S. laboratory-confirmed case of coronavirus disease 2019 (COVID-19) caused by infection with SARS-CoV-2 (1). As of April 19, a total of 720,630 COVID-19 cases and 37,202 associated deaths* had been reported to CDC from all 50 states, the District of Columbia, and four U.S. territories (2). CDC recommends, with precautions, the proper cleaning and disinfection of high-touch surfaces to help mitigate the transmission of SARS-CoV-2 (3). **To assess whether there might be a possible association between COVID-19 cleaning recommendations from public health agencies and the media and the number of chemical exposures reported to the National Poison Data System (NPDS), CDC and the American Association of Poison Control Centers surveillance team compared the number of exposures reported for the period January-March 2020 with the number of reports during the same 3-month period in 2018 and 2019.** Fifty-five poison centers in the United States provide free, 24-hour professional advice and medical management information regarding exposures to poisons, chemicals, drugs, and medications. Call data from poison centers are uploaded in near real-time to NPDS. **During January-March 2020, poison centers received 45,550 exposure calls related to cleaners (28,158) and disinfectants (17,392), representing overall increases of 20.4% and 16.4% from January-March 2019 (37,822) and January-March 2018 (39,122), respectively.** Although NPDS data do not provide information showing a definite link between exposures and COVID-19 cleaning efforts, there appears to be a clear temporal association with increased use of these products.

**FIGURE. Number of daily exposures to cleaners and disinfectants reported to U.S. poison centers — United States, January–March 2018, 2019, and 2020*,†**




* Excluding February 29, 2020.
† Increase in exposures to cleaners on January 29, 2020, came from an unintentional exposure to a cleaning agent within a school.

TABLE. Number and percentage of exposures to cleaners and disinfectants reported to U.S. poison centers, by selected characteristics — United States, January–March 2018, 2019, and 2020

| | No. (%) | | | | | |
|---|---|---|---|---|---|---|
| | Cleaners | | | Disinfectants | | |
| Characteristic | 2018 | 2019 | 2020 | 2018 | 2019 | 2020 |
| **Total** | **25,583 (100.0)** | **25,021 (100.0)** | **28,158 (100.0)** | **13,539 (100.0)** | **12,801 (100.0)** | **17,392 (100.0)** |
| **Age group (yrs)** | | | | | | |
| 0–5 | 10,926 (42.7) | 10,207 (40.8) | 10,039 (35.7) | 7,588 (56.0) | 6,802 (53.1) | 8,158 (46.9) |
| 6–19 | 2,655 (10.4) | 2,464 (9.8) | 2,516 (8.9) | 1,803 (13.3) | 1,694 (13.2) | 2,358 (13.6) |
| 20–59 | 8,072 (31.6) | 8,203 (32.8) | 9,970 (35.4) | 2,659 (19.6) | 2,791 (21.8) | 4,056 (23.3) |
| ≥60 | 1,848 (7.2) | 1,936 (7.7) | 2,356 (8.4) | 929 (6.9) | 848 (6.6) | 1,455 (8.4) |
| Unknown | 2,082 (8.1) | 2,211 (8.8) | 3,277 (11.6) | 560 (4.1) | 666 (5.2) | 1,365 (7.8) |
| **Exposure route*** | | | | | | |
| Ingestion | 16,384 (64.0) | 15,710 (62.8) | 16,535 (58.7) | 11,714 (86.5) | 10,797 (84.3) | 13,993 (80.5) |
| Inhalation | 4,747 (18.6) | 4,713 (18.8) | 6,379 (22.7) | 540 (4.0) | 569 (4.4) | 1,188 (6.8) |
| Dermal | 4,349 (17.0) | 4,271 (17.1) | 4,785 (17.0) | 1,085 (8.0) | 1,078 (8.4) | 1,695 (9.7) |
| Ocular | 3,355 (13.1) | 3,407 (13.6) | 3,802 (13.5) | 984 (7.3) | 1,067 (8.3) | 1,533 (8.8) |
| Other/Unknown | 182 (0.7) | 169 (0.7) | 166 (0.6) | 89 (0.7) | 95 (0.7) | 147 (0.8) |

* Exposure might have more than one route.

# Symptoms and Clinical Presentation

## Acute-onset smell and taste disorders in the context of Covid-19: a pilot multicenter PCR-based case-control study.

Beltrán-Corbellini Á, Chico-García JL, Martínez-Poles J et al.
Eur J Neurol.
2020 Apr 22.; PMID: 32320508
Level of Evidence: 4 - Case Control
Type of Article: Research

**Summary**: 79 COVID-19 cases and 40 control cases were evaluated for smell or taste disorders (STD). **New-onset STD were significantly more frequent among cases (31, 39.2%) than in the control group (5, 12.5 %), adjusted OR 21.4 (2.77-165.4, p=0.003).** Among Covid-19 patients who presented STD, 22 (70.9%) recalled an acute onset and was an initial manifestation in 11 (35.5%). Twenty-five (80.6%) presented smell disorders (mostly anosmia, 14, 45.2%), and 28 (90.3%) taste disorders (mostly ageusia, 14, 45.2%). Findings suggest smell and taste disorders may help aid in COVID-19 diagnosis.

## Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area.

Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW; and the Northwell COVID-19 Research Consortium, Barnaby DP, Becker LB, Chelico JD, Cohen SL, Cookingham J, Coppa K, Diefenbach MA, Dominello AJ, Duer-Hefele J, Falzon L, Gitlin J, Hajizadeh N, Harvin TG, Hirschwerk DA, Kim EJ, Kozel ZM, Marrast LM, Mogavero JN, Osorio GA, Qiu M, Zanos TP.
JAMA
2020 Apr 22, PMID: 32320003
Level of Evidence: 4 - Case Series
Article Type: Research

**BLUF:** The authors determined there were a significant amount of COVID-19 patients with preexisting hypertension and diabetes. Many of the patients were on an ACEi or ARB which resulted

in an increase of ACE2 mRNA making authors conclude that prescription of these medications in confirmed COVID-19 patients may produce adverse effects.

**Abstract:**
Importance: There is limited information describing the presenting characteristics and outcomes of US patients requiring hospitalization for coronavirus disease 2019 (COVID-19).
Objective: To describe the clinical characteristics and outcomes of patients with COVID-19 hospitalized in a US health care system.
Design, Setting, and Participants: Case series of patients with COVID-19 admitted to 12 hospitals in New York City, Long Island, and Westchester County, New York, within the Northwell Health system. The study included all sequentially hospitalized patients between March 1, 2020, and April 4, 2020, inclusive of these dates.
Exposures: Confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection by positive result on polymerase chain reaction testing of a nasopharyngeal sample among patients requiring admission.
Main Outcomes and Measures: Clinical outcomes during hospitalization, such as invasive mechanical ventilation, kidney replacement therapy, and death. Demographics, baseline comorbidities, presenting vital signs, and test results were also collected.
Results: A total of 5700 patients were included (median age, 63 years [interquartile range {IQR}, 52-75; range, 0-107 years]; 39.7% female). The most common comorbidities were hypertension (3026; 56.6%), obesity (1737; 41.7%), and diabetes (1808; 33.8%). At triage, 30.7% of patients were febrile, 17.3% had a respiratory rate greater than 24 breaths/minute, and 27.8% received supplemental oxygen. The rate of respiratory virus co-infection was 2.1%. Outcomes were assessed for 2634 patients who were discharged or had died at the study end point. During hospitalization, 373 patients (14.2%) (median age, 68 years [IQR, 56-78]; 33.5% female) were treated in the intensive care unit care, 320 (12.2%) received invasive mechanical ventilation, 81 (3.2%) were treated with kidney replacement therapy, and 553 (21%) died. Mortality for those requiring mechanical ventilation was 88.1%. The median postdischarge follow-up time was 4.4 days (IQR, 2.2-9.3). A total of 45 patients (2.2%) were readmitted during the study period. The median time to readmission was 3 days (IQR, 1.0-4.5) for readmitted patients. Among the 3066 patients who remained hospitalized at the final study follow-up date (median age, 65 years [IQR, 54-75]), the median follow-up at time of censoring was 4.5 days (IQR, 2.4-8.1).
Conclusions and Relevance: This case series provides characteristics and early outcomes of sequentially hospitalized patients with confirmed COVID-19 in the New York City area.

## Acute Pulmonary Embolism in COVID-19 Patients on CT Angiography and Relationship to D-Dimer Levels.

Leonard-Lorant I, Delabranche X, Severac F, Helms J, Pauzet C, Collange O, Schneider F, Labani A, Bilbault P, Moliere S, Leyendecker P, Roy C, Ohana M.
Radiology
2020 Apr 23; PMID: 32324102
Level of Evidence: 4 - Case series
Type of Article: Research
**BLUF:** Thirty-two of 106 (30%, [95%CI 22-40%]) patients with COVID-19 infection were positive for acute pulmonary emboli on pulmonary CT angiograms at a tertiary referral center.

**Summary:**
The purpose of this report is to describe the rate of pulmonary embolism in patients classified as COVID-19 infection and who underwent chest CT at a tertiary referral center. "During this period, it was recorded that 1696 patients had CT for suspicion or follow-up of COVID-19 infection. Dedicated pulmonary CT angiograms were performed in 135/1696 (8%) patients, 25 additional patients had pulmonary arterial phase images included in the chest/ abdomen/ pelvic CT scan (total, 160 patients). Of these 160 patients, 106 patients were classified as COVID-19 infection (97 patients by RT-PCR and 9 patients with positive CT and negative RT-PCR test). The reason for CT angiography in these patients was suspicion of pulmonary embolus in 67/106 (63%) patients and other CT indication in 39/106 (37%) patients." Overall, the study indicated that **of the 106 pulmonary CT angiograms performed for COVID-19 patients over a one-month period in a tertiary care center; 32/106 (30%) of patients had acute pulmonary embolism. In this patient population, the D-dimer threshold of 2660 µg/L detected all patients with pulmonary embolism on chest CT.** It was predicted that the high values of d-dimer could be related to a higher activation of blood coagulation in COVID-19 patients secondary to a systemic inflammatory response syndrome or as a direct consequence of the SARS-CoV-2. These results indicate potential for pulmonary embolism associated with COVID-19 infection and may serve to inform the medical community of this serious complication.

## Chest CT findings of COVID-19 pneumonia by duration of symptoms.

Ding X, Xu J, Zhou J, Long Q.
Eur J Radiol
2020 Apr 18; PMID: 32325282
Level of Evidence: 4 - Case Series
Type of Article: Full Length Article
**BLUF:** This retrospective study included 112 patients with confirmed COVID-19 pneumonia and classified thin-section CT images according to time after initial onset of symptoms. The authors found that the distribution of pneumonia in most patients was peripheral and became more central with disease progression, most lesions were bilateral, and the most frequent CT findings were ground glass opacities, crazy-paving pattern, consolidation, and linear opacities. The CT abnormalities were found to last greater than 28 days after disease onset in the majority of patients.

**Abstract:**
Purpose: To evaluate lung abnormalities on thin-section computed tomographic (CT) scans in patients with COVID-19 and correlate findings to duration of symptoms.
Methods: In total, **348 CT scans in 112 patients were classified according to the time after the onset of the initial symptoms**, namely stage-1 (0–4 days); stage-2 (5–9 days); stage-3 (10–14 days); stage-4 (15–21 days); stage-5 (22–28 days); and stage-6 (>28 days). Each lung lobe was evaluated for extent affected by ground-glass opacities (GGO), crazy-paving pattern and consolidation, in five categories of percentual severity. Summation of scores from all five lung lobes provided the total CT score (maximal CT score, 25).
Results: **The predominant patterns of lung abnormalities were GGOs, crazy-paving pattern, consolidation and linear opacities**. **The frequency of crazy-paving pattern, consolidation and linear opacities peaked at stage-3 (62.7 %), stage-4 (75.0 %) and stage-5 (83.1 %), respectively, and decreased thereafter**. Total CT scores increased from stage-1 to stage-2 (2.8 ± 3.1, vs. 6.5 ± 4.6, respectively, $P < 0.01$), and thereafter remained high. **The lower lobes were more inclined to be involved with higher CT scores except for stage-1. At stage-6 98.1 % of CT scans still showed abnormalities (CT score 7.5 ± 4.1).**

Conclusion: Thin-section CT could provide semi-quantitative analysis of pulmonary damage severity. This disease changed rapidly at the early stage, then tended to be stable and lasted for a long time.

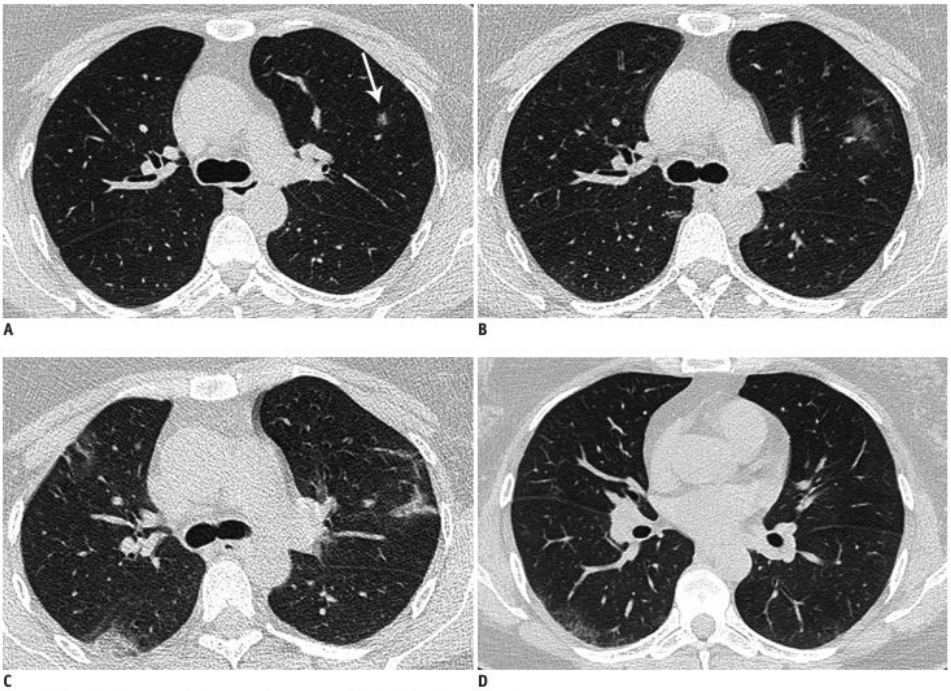



**Fig. 1. Chest CT images of 44-year-old woman with COVID-19 pneumonia.**
Day 2, baseline CT image **(A)** shows solitary sub-centimeter ground-glass nodule 8 mm in size (arrow) in left upper lobe. Day 7 follow-up CT image **(B)** shows initial nodule enlarged with ground-glass opacities. Day 9 follow-up CT image **(C)** shows initial nodule presenting with absorption change and typical radiological manifestation of COVID-19 infection began to appear in whole lung. Day 27 latest follow-up CT image **(D)** shows most of lesions are absorbed and some residues still exist in peripheral lung. COVID-19 = coronavirus disease 2019

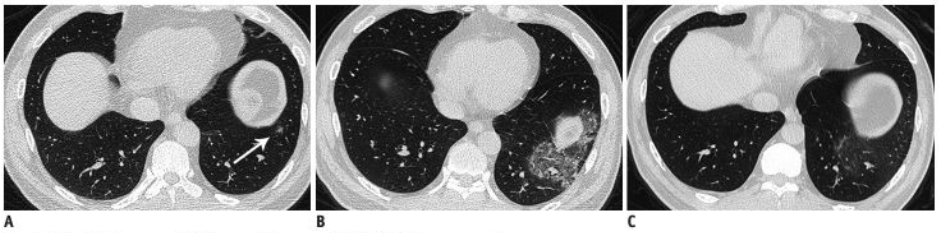



**Fig. 2. Chest CT images of 51-year-old man with COVID-19 pneumonia.**
**A.** Baseline chest CT image (7 days before onset of symptoms) shows solitary ill-defined ground-glass nodule 7 mm in size (arrow) in left lower lobe. Day 2, patient presented with fever and chest pain day earlier; follow-up CT image **(B)** shows confluent crazy-paving pattern and consolidation opacities appear in same location. Day 15 follow-up CT image **(C)** shows area of lesion has become smaller and density has begun to decrease.

## Small Solitary Ground-Glass Nodule on CT as an Initial Manifestation of Coronavirus Disease 2019 (COVID-19) Pneumonia.

Xia T, Li J, Gao J, Xu X
Korean J Radiol
2020 Apr 6; PMID: 32323499
Level of Evidence: 4 - Case Series
Type of Article: Research

**BLUF**: Radiologist in Wuhan, China report three cases of atypical COVID-19 CT presentation with a shared similarity of a solitary subcentimeter ground-glass nodule that eventually progressed, suggesting that this solitary nodule indicates an initial stage of COVID-19.

**Abstract**: The 2019 novel coronavirus (2019-nCoV) outbreak in Wuhan, Hubei Province, China in 2019 led to large numbers of people being infected and developing atypical pneumonia (coronavirus disease 2019, COVID-19). Typical imaging manifestations of patients infected with 2019-nCoV has been reported, but we encountered an **atypical radiological manifestation** on baseline computed

tomography (CT) images in three patients from Wuhan, China infected with the 2019-nCoV. Surprisingly, the **only similar CT finding was a solitary sub-centimeter ground-glass nodule adjacent to bronchovascular bundles**, which could be easily overlooked. In addition, the follow-up images in these patients showed how COVID-19 pneumonia evolved from these small nodules. The radiologic manifestation of the three cases will expand contemporary understanding of COVID-19.

## Spontaneous Pneumomediastinum: A Probable Unusual Complication of Coronavirus Disease 2019 (COVID-19) Pneumonia.

Wang J, Su X, Zhang T, Zheng C.
Korean J Radiol.
2020 May; PMID: 32323507
Level of Evidence: 4 – Case Study
Type of Article: Letter to the Editor

**Summary**: The authors present the case of a previously healthy 36 year-old female with COVID-19 who was found to have pneumatosis extending from the mediastinal pericardium to the bilateral cervical soft tissue space. The patient was considered to have spontaneous pneumomediastinum because no other sources of mediastinal air could be identified. Despite combined antiviral drugs, anti-inflammatory drugs, and supportive care, the patient died from respiratory failure and ARDS.

## Pulmonary, Cerebral, and Renal Thromboembolic Disease Associated with COVID-19 Infection.

Lushina N, Kuo JS, Shaikh HA.
Radiology
2020 Apr 23; PMID: 32324099
Level of Evidence: 4 - Case Report
Type of Article: Research

**BLUF:** This case report demonstrates a poor outcome in an 84-year-old male patient with multifocal thromboembolic disease in the setting of COVID-19.

**Summarizing Excerpt:**
"This case illustrates severe coagulopathy in a patient with COVID-19 pneumonia. Possible explanations of his multifocal thromboembolic disease involving the pulmonary, cerebral, and renal circulations include coagulopathy due to COVID-19 versus cardioembolic etiology in the setting of atrial fibrillation. Given that the patient had no known hypercoagulable conditions and no prior history of atrial fibrillation, the latter etiology was felt to be less likely. There are emerging global reports of coagulopathy in the setting of COVID-19, including pulmonary emboli, cerebral infarcts, and limb ischemia. A recent publication identified antiphospholipid antibodies in a COVID-19 patient with significant coagulopathy. It has also been proposed that coagulopathy may portend a poor prognosis in COVID-19 patients and may require early intervention. Our case supports the growing body of data by demonstrating a poor outcome in a patient with multifocal thromboembolic disease in the setting of COVID-19."

## Explanation for COVID-19 infection neurological damage and reactivations.

Roe K
Transbound Emerg Dis
2020 Apr 22; PMID: 32320129

Level of Evidence: 5 - Expert Opinion
Type of Article: Letter
**BLUF**: An author in California examines high rates of neurological symptoms (36.4%) and viral reactivation (9%) of COVID-19 infections, and compares SARS-CoV-2 to the similarly bat-derived, enveloped Nipah virus, suggesting that COVID-19 may be a greater public health challenge than expected.

**Summarizing Excerpts**: "A new pathogenic virus, COVID-19, appeared in 2019, in Wuhan, China, typically causing fever, cough, diarrhea and fatigue and significant mortality (Mao, 2020). From mid-January to mid-February in 2020, **214 patients** with both non-severe and severe COVID-19 infections **confirmed by nucleic acid tests**, were examined by a panel of neurologists. **Seventy-eight patients (36.4%) displayed neurological symptoms**, including **central nervous system symptoms** of dizziness, headache, impaired consciousness, acute cerebrovascular disease with either ischemic stroke or cerebral hemorrhage, ataxia, seizures; **peripheral nervous system symptoms** of taste impairment, smell impairment, vision impairment, and nerve pain; and **skeletal muscle injury** (Mao, 2020). The **reactivation of previous COVID-19 infections** after recent previously negative test results has also been **reported in about 9% of a small study of patients** (55 total patients with 5 reactivations, but the time window of reactivation observation was only 17 days long, and more reactivations could likely have been seen over a longer time period), and this and other disturbing reports of COVID-19 reactivation will likely be unwelcome and met with skepticism (Ye, 2020). The patients, **aged 27 to 42 years old**, who had reactivation of COVID-19 did **not have any underlying diseases**, such as diabetes, chronic hypertension, or cardiovascular disease; and **reactivations occurred regardless of any antiviral therapy received, without any discovery of any clinical characteristics to enable the prediction of future viral reactivation** (Ye, 2020)."

### An Atypical Presentation of Novel Coronavirus Disease 2019 (COVID-19).
Singhania N, Bansal S, Singhania G.Singhania N, et al.
Am J Med.
2020 Apr 19; PMID: 32320693
Level of Evidence: 4 - Case Report
Type of Article: Research
**Summary**: Altered mental status in an elderly patient can be an atypical presentation of COVID-19. Absence of fever and cough does not exclude COVID-19. Negative procalcitonin, lymphopenia, and ground-glass densities on chest CT scan directs differential towards COVID-19.

# Pediatrics
### Covid-19 and Neonatal Resuscitation
Halliday HL, Speer CP
Neonatology.
2020 Apr 23; PMID: 32325458
Level of Evidence: 5 – Expert Opinion
Type of Article: Editorial
**BLUF:** There is little evidence of vertical transmission of COVID -19 from mother to baby in newborns. Authors present a Chinese case series of four babies who were infected, possibly through nosocomial transmission and that they have recovered.

**Abstract:** In this issue of Neonatology, we publish two papers with suggestions for neonatal resuscitation when the mother is suspected of having COVID-19 infection. These papers come from

Italy where the COVID-19 pandemic has resulted in many thousands of deaths and from Hong Kong where, in contrast, only 4 lives to date have been lost to the infection. These differences in outcomes between Europe and Asia will need to be explored in future research studies taking into account demographic factors as well as government and medical responses. There is **uncertainty about whether the COVID-19 virus can be transmitted vertically from mother to newborn infant** either in utero or at birth. Although **vertical transmission seems unlikely**, there have been reports of early neonatal infection. Zhu et al. reported some adverse outcomes in 10 babies born to mothers with COVID-19 infection. These **adverse outcomes included fetal distress, premature labor, respiratory distress, thrombocytopenia and abnormal liver function**, but the neonates themselves tested negative for the virus. It is likely that vertical transmission of the virus did not occur, and the neonatal complications were related to preterm delivery. Zhang et al. in a very recent report could only find 4 infected newborns in China and they presented aged between 30 h and 17 days after birth suggesting nosocomial infection. These babies had mild or no illness, none needed intensive care, and all seemed to have recovered. Three of the infants had been separated from their mother right after birth and were not breastfed.

## COVID-19 – a mild disease in children

Devulapalli, Chandra S.
2020, March 24; PMID: 32321222
Tidsskr Nor Laegeforen
Level of Evidence: 5- Expert Opinion
Type of Article: Opinion

**Summary**: Data has shown that in past coronavirus outbreaks, such as SARS in 2003 and MERS in 2012 and 2016, the virus occurs less frequently and has a milder presentation in the pediatric population. Of the COVID-19 pandemic, the author emphasizes that we can expect similar statistics, with “practically no risk of a fatal outcome” in children.

# Understanding the Pathology

## Biomechanics

### G6PD deficiency in COVID-19 pandemic: "A ghost in the ghost".

Al-Abdi S, Al-Aamri M.
Hematol Oncol Stem Cell Ther
2020 Apr 18; PMID: 32325028
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter to Editor

**Summary:** The authors cite an *ex vivo* study that has shown **G6PD-deficient cells to be more vulnerable to COVID-19 infection** than normal cells. If the use of hydroxychloroquine to treat COVID-19 proves effective it could provide a challenge for patients with G6PD deficiency as it can cause severe hemolysis in these patients. For this reason the authors believe it is important to take additional precautions to prevent COVID-19 from reaching G6PD deficient patients.

### Spontaneous Pneumomediastinum: A Probable Unusual Complication of Coronavirus Disease 2019 (COVID-19) Pneumonia.

Wang J, Su X, Zhang T, Zheng C.
Korean J Radiol.
2020 May; PMID: 32323507
Level of Evidence: 4 – Case Study
Type of Article: Letter to the Editor

**Summary**: The authors present the case of a previously healthy 36 year-old female with COVID-19 who was found to have pneumatosis extending from the mediastinal pericardium to the bilateral cervical soft tissue space. The patient was considered to have spontaneous pneumomediastinum because no other sources of mediastinal air could be identified. Despite combined antiviral drugs, anti-inflammatory drugs, and supportive care, the patient died from respiratory failure and ARDS.

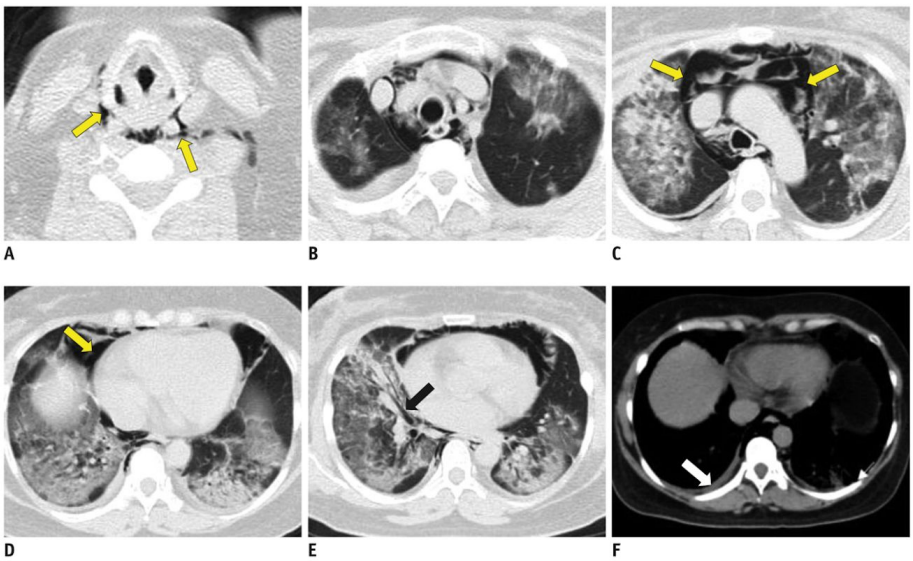



**Fig. 1. Chest CT of 36-year-old woman with COVID-19 pneumonia obtained 12 days after onset of symptoms.**
**A-D.** Pneumatosis extends from mediastinal pericardium to bilateral cervical soft tissue space (yellow arrows; **A**, **C**, **D**). **B-E.** Images show multifocal diffuse bilateral ground-glass opacities and consolidation with air bronchogram in middle lobe of right lung (black arrow; **E**). **F.** There are small pleural effusion and reactive thickening of pleura (white arrow).

## Endothelial cell infection and endotheliitis in COVID-19

Varga Z, Flammer AJ, Steiger P, Haberecker M, Andermatt R, Zinkernagel AS, Mehra MR, Schuepbach RA, Ruschitzka F, Moch H

Lancet

April 20,2020; PMID: 32325026

Level of Evidence: 4 - Case Study

Type of Article: Letter

**Summary:** The authors evaluate endothelial cell involvement in post-mortem biopsies of COVID-19 patients (see figure below). They found evidence of endothelial and inflammatory cell death, in addition to the presence of intracellular viral elements and accumulation of inflammatory markers. Their findings suggest that viral involvement and host inflammatory response are a direct cause of multiorgan endotheliitis. They wonder if anti-inflammatory drugs, ACE inhibitors and statins would stabilise the endothelium and reduce viral replication.

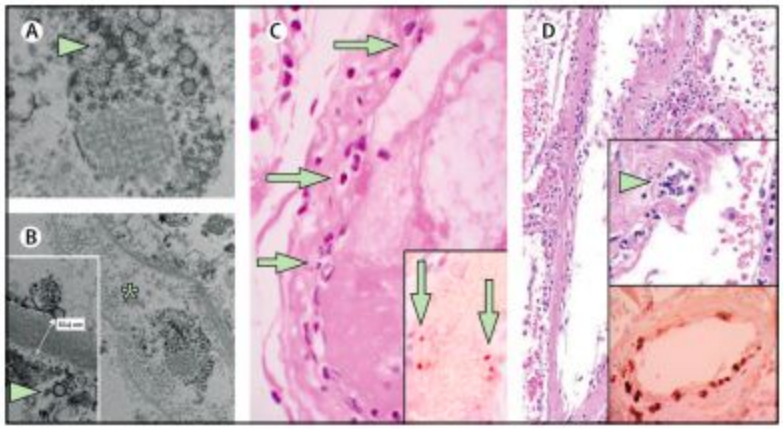



**Figure: Pathology of endothelial cell dysfunction in COVID-19** (A, B) Electron microscopy of kidney tissue shows viral inclusion bodies in a peritubular space and viral particles in endothelial cells of the glomerular capillary loops. Aggregates of viral particles (arrow) appear with dense circular surface and lucid centre. The asterisk in panel B marks peritubular space consistent with capillary containing viral particles. The inset in panel B shows the glomerular basement membrane with endothelial cell and a viral particle (arrow; about 150 nm in diameter). (C) Small bowel resection specimen of patient 3, stained with haematoxylin and eosin. Arrows point to dominant mononuclear cell infiltrates within the intima along the lumen of many vessels. The inset of panel C shows an immunohistochemical staining of caspase 3 in small bowel specimens from serial section of tissue described in panel D. Staining patterns were consistent with apoptosis of endothelial cells and mononuclear cells observed in the haematoxylin-eosin-stained sections, indicating that apoptosis is induced in a substantial proportion of these cells. (D) Post-mortem lung specimen stained with haematoxylin and eosin showed thickened lung septa, including a large arterial vessel with mononuclear and neutrophilic infiltration (arrow in upper inset). The lower inset shows an immunohistochemical staining of caspase 3 on the same lung specimen; these staining patterns were consistent with apoptosis of endothelial cells and mononuclear cells observed in the haematoxylin-eosinstained sections. COVID-19=coronavirus disease 2019.

## Emerging SARS-CoV-2 mutation hot spots include a novel RNA-dependent-RNA polymerase variant

Pachetti M,, Marini B, Benedetti F, Giudici F,, Mauro E, Storici P, Masciovecchio C, Angeletti S, Ciccozzi M, Gallo RC, Zella D,, Ippodrino R.

J Transl Med

2020 Apr 22; PMID: 32321524

Level of Evidence: 5- Mechanism-based reasoning

Type of Article: Research

**BLUF:** The authors compare the SARS-CoV-2 reference sequence first published in January 2020, with 220 sequenced SARS-CoV-2 genomes from patient isolates randomly chosen from the FISAID database, to characterize viral mutations. They examine mutation hotspots in 4 different geographic areas (Asia, Oceania, Europe and North America) over time. They identify what they determine to be mutation hotspots within the viral genome but do not indicate the role these mutations play in terms of viral pathogenesis or disease outcome.

**Abstract**:
**BACKGROUND:** SARS-CoV-2 is a RNA coronavirus responsible for the pandemic of the Severe Acute Respiratory Syndrome (COVID-19). RNA viruses are characterized by a high mutation rate, up to a million times higher than that of their hosts. Virus mutagenic capability depends upon several factors, including the fidelity of viral enzymes that replicate nucleic acids, as SARS-CoV-2 RNA dependent RNA polymerase (RdRp). Mutation rate drives viral evolution and genome variability, thereby enabling viruses to escape host immunity and to develop drug resistance. **METHODS: We analyzed 220 genomic sequences from the GISAID database derived from patients infected by SARS-CoV-2 worldwide from December 2019 to mid-March 2020**. SARS-CoV-2 reference genome was obtained from the GenBank database. Genomes alignment was performed using Clustal Omega. Mann-Whitney and Fisher-Exact tests were used to assess statistical significance.**RESULTS:We characterized 8 novel recurrent mutations of SARS-CoV-2,** located at positions 1397, 2891, 14408, 17746, 17857, 18060, 23403 and 28881. Mutations in 2891, 3036, 14408, 23403 and 28881 positions are predominantly observed in Europe, whereas those located at positions 17746, 17857 and 18060 are exclusively present in North America. We noticed for the first time a silent mutation in RdRp gene in England (UK) on February 9th, 2020 while a different mutation in RdRp changing its amino acid composition emerged on February 20th, 2020 in Italy (Lombardy). Viruses with RdRp mutation have a median of 3 point mutations [range: 2-5], otherwise they have a median of 1 mutation [range: 0-3] (p value < 0.001). **CONCLUSIONS:** These findings suggest that the virus is evolving and European, North American and Asian strains might coexist, each of them characterized by a different mutation pattern. The contribution of the mutated RdRp to this phenomenon needs to be investigated. To date, several drugs targeting RdRp enzymes are being employed for SARS-CoV-2 infection treatment. Some of them have a predicted binding moiety in a SARS-CoV-2 RdRp hydrophobic cleft, which is adjacent to the 14408 mutation we identified. Consequently, it is important to study and characterize SARS-CoV-2 RdRp mutation in order to assess possible drug-resistance viral phenotypes. It is also important to recognize whether the presence of some mutations might correlate with different SARS-CoV-2 mortality rates.

## Obesity a Risk Factor for Severe COVID-19 Infection: Multiple Potential Mechanisms.

Sattar N, McInnes IB, McMurray JJV.Sattar N, et al.
Circulation
2020 Apr 22.; 2020.PMID: 32320270
Level of Evidence: 5 - Expert opinion
Type of Article: Letter
**Summary:** The authors suggest that obesity or excess ectopic fat deposition may be a unifying risk factor for severe COVID-19 infection. Obesity leads to reduced protective cardiorespiratory reserve as well as potentiating the immune dysregulation that appears to mediate the progression to critical illness and organ failure in a proportion of COVID-19 patients. Whether obesity is an independent risk factor for susceptibility to infection requires further research.

## COVID-19 pathophysiology: A review.

Yuki K, Fujiogi M, Koutsogiannaki S.Yuki K, et al.
Clin Immunol.
2020 Apr 20; PMID: 32325252
Level of Evidence: 4-Review
Article Type: Research
**BLUF:** Reports from China and the US show that children experience a lower rate of infection with COVID19 and are less symptomatic as well. The authors postulate that this is due to 1) different

expression of ACE2 between adults and children, 2) qualitatively different response to the SARS-CoV-2, 3) simultaneous presence of other viruses in the mucosa lungs and airways in young children limiting the growth of SARS-CoV-2 virus.

**Abstract:** In December 2019, a novel coronavirus, now named as SARS-CoV-2, caused a series of acute atypical respiratory diseases in Wuhan, Hubei Province, China. The disease caused by this virus was termed COVID-19. The virus is transmittable between humans and has caused pandemic worldwide. The number of death tolls continues to rise and a large number of countries have been forced to do social distancing and lockdown. Lack of targeted therapy continues to be a problem. Epidemiological studies showed that elder patients were more susceptible to severe diseases, while children tend to have milder symptoms. **Here we reviewed the current knowledge about this disease and considered the potential explanation of the different symptomatology between children and adults.**

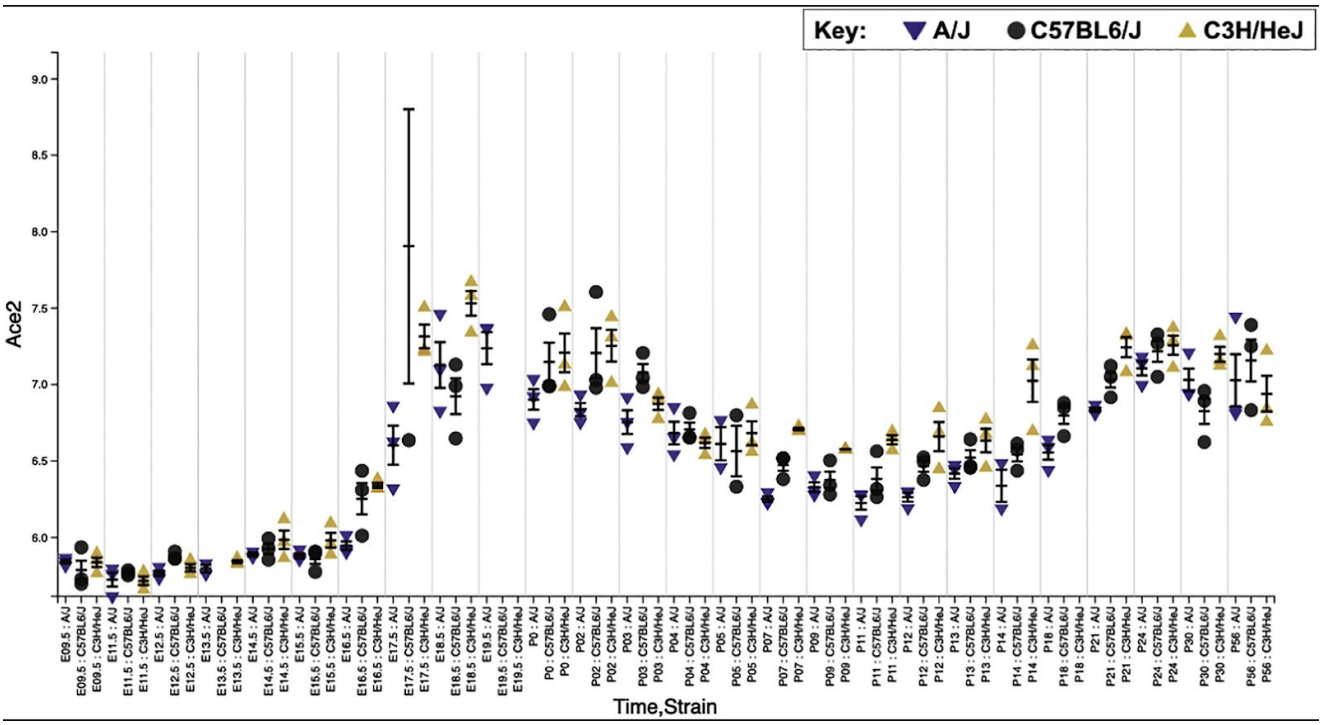



**Fig. 2. Age-dependent ACE2 expression profiles in the mouse lung:** the expression of ACE2 was examined. This data was obtained from microarray experiments of three mice strains A/J mice, C57BL/6J mice and C3H/HeJ mice at different ages. X axis showed age and mouse strain, and y axis showed ACE2 expression level.

# Immune response

## The laboratory tests and host immunity of COVID-19 patients with different severity of illness.

Wang F, Hou H, Luo Y, Tang G, Wu S, Huang M, Liu W, Zhu Y, Lin Q, Mao L, Fang M, Zhang H, Sun Z.

JCI Insight

2020 Apr 23; PMID: 32324595

Level of Evidence: 4 - Case series

Type of Article: Research

**BLUF:** A case series analyzing the host immunity of 65 SARS-CoV-2 positive patients in Wuhan, China with different severities of disease found that extremely severe disease was associated with

hyperfunctioning CD4+ and CD8+ T cells and increased levels of their associated cytokines. Elevated inflammatory biomarker serum levels suggest that COVID-19 involves an inflammatory response. The authors hypothesize that host immunity in severe COVID-19 infection is characterized by a consumptive state of antigen presenting cells, inconsistent number and function of T cells, and activated negative immune regulation.

**Abstract:**
Background: The Coronavirus Disease-2019 (COVID-19), infected by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has caused a severe outbreak in China. The host immunity of COVID-19 patients is unknown.
Methods: The routine laboratory tests and host immunity in COVID-19 patients with different severity of illness were compared after patient admission.
Results: A total of 65 SARS-CoV-2-positive patients were classified as mild (n=30), severe (n=20), and extremely severe (n=15) illness. Many routine laboratory tests such as ferritin, lactate dehydrogenase and D-dimer were increased in severe and extremely severe patients. The absolute numbers of CD4+ T cells, CD8+ T cells and B cells were all gradually decreased with increased severity of illness. The activation markers such as HLA-DR and CD45RO expressed on CD4+ and CD8+ T cells were increased in severe and extremely severe patients compared with mild patients. The co-stimulatory molecule CD28 had opposite results. The percentage of natural regulatory T cells was decreased in extremely severe patients. The percentage of IFN-γ producing CD8+ T cells was increased in both severe and extremely severe patients compared with mild patients. The percentage of IFN-γ producing CD4+ T cells was increased in extremely severe patients. The IL-2R, IL-6, and IL-10 were all increased in extremely severe patients. The activation of DC and B cells was decreased in extremely severe patients.
Conclusions: The **number and function of T cells are inconsistent in COVID-19 patients**. The **hyperfunction of CD4+ and CD8+ T cells is associated with the pathogenesis of extremely severe SARS-CoV-2 infection**.

## Complex Immune Dysregulation in COVID-19 Patients with Severe Respiratory Failure.

Giamarellos-Bourboulis, Evangelos J; Netea, Mihai G; Rovina, Nikoletta; Akinosoglou, Karolina; Antoniadou, Anastasia; Antonakos, Nikolaos; Damoraki, Georgia; Gkavogianni, Theologia; Adami, Maria-Evangelia; Katsaounou, Paraskevi; Ntaganou, Maria; Kyriakopoulou, Magdalini; Dimopoulos, George; Koutsodimitropoulos, Ioannis; Velissaris, Dimitrios; Koufargyris, Panagiotis; Karageorgos, Athanassios; Katrini, Konstantina; Lekakis, Vasileios; Lupse, Mihaela; Kotsaki, Antigone; Renieris, George; Theodoulou, Danai; Panou, Vassiliki; Koukaki, Evangelia; Koulouris, Nikolaos; Gogos, Charalambos; Koutsoukou, Antonia
Cell Host & Microbe
2020 Apr 17; PMID: 32320677
Level of Evidence: 3 - Cohort Study
Type of Article: Research
**BLUF:** In this cohort study of 54 COVID-19 patients, 28 of whom had severe respiratory failure (SRF), it was found that all patients with SRF caused by SARS-CoV-2 have a unique pattern of immune dysregulation when compared with that of bacterial sepsis and the 2009 H1N1 influenza. This pattern is characterized by IL-6 mediated low HLA-DR expression and severe lymphopenia.

**Abstract:** Proper management of COVID-19 mandates better understanding of disease pathogenesis. The sudden clinical deterioration 7-8 days after initial symptom onset suggests that severe respiratory failure (SRF) in COVID-19 is driven by a unique pattern of immune dysfunction. We studied immune

responses of 54 COVID-19 patients, 28 of whom had SRF. All patients with SRF displayed either macrophage activation syndrome (MAS) or very low human leukocyte antigen D related (HLA-DR) expression accompanied by profound depletion of CD4 lymphocytes, CD19 lymphocytes, and natural killer (NK) cells. Tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6) production by circulating monocytes was sustained, a pattern distinct from bacterial sepsis or influenza. SARS-CoV-2 patient plasma inhibited HLA-DR expression, and this was partially restored by the IL-6 blocker Tocilizumab; off-label Tocilizumab treatment of patients was accompanied by increase in circulating lymphocytes. Thus, the unique pattern of immune dysregulation in severe COVID-19 is characterized by IL-6-mediated low HLA-DR expression and lymphopenia, associated with sustained cytokine production and hyper-inflammation.

## Increased expression of CD8 marker on T-cells in COVID-19 patients.

Ganji A, Farahani I, Khansarinejad B, Ghazavi A, Mosayebi G.
Blood Cells Mol Dis
2020 Apr 13; PMID: 32325421
Level of Evidence: 5- Mechanism-based reasoningType of Article: Short Communication

**BLUF:** The authors analyze peripheral blood samples of 25 RT-PCR confirmed COVID-19 patients and 25 healthy matched controls to try and very broadly identify differences in the lymphocyte (T cell) compartment. Their results indicate lower overall levels of circulating lymphocytes in COVID19 compared to healthy controls, and they observe an upregulation of CD8 molecules on CD8+ T cells in the blood of their COVID-19 positive patients.

**Abstract**:
BACKGROUND: Cell-mediated immunity including T-cells (T helper and cytotoxic) plays an essential role in efficient antiviral responses against coronavirus disease-2019 (COVID-19). Therefore, in this study, w**e evaluated the ratio and expression of CD4 and CD8 markers in COVID-19 patients to clarify the immune characterizations of CD4 and CD8 T-cells in COVID-19 patient**s.
METHODS: Peripheral blood samples of 25 COVID-19 patients and 25 normal individuals with similar age and sex as the control group were collected. White blood cells, platelets, and lymphocytes were counted and CD4 and CD8 T lymphocytes were evaluated by flow cytometry.
RESULTS: The number of white blood cells, lymphocytes, and platelets were reduced significantly in COVID-19 patients ($P < 0.05$). The difference in CD4:CD8 ratio, CD4 T-cell frequency, CD8 T-cell frequency, and CD4 mean fluorescence intensity (MFI) was not significant between COVID-19 patients and healthy individuals ($P > 0.05$); however, the CD8 MFI increased significantly in COVID-19 infected patients ($P < 0.05$).
CONCLUSION: Although, there is no significant difference in the ratio of CD4 to CD8 between two groups, the expression level of CD8 in COVID-19 patients was significantly higher than the normal individuals. This result suggested that the cellular immune responses triggered by COVID-19 infection were developed through overexpression of CD8 and hyperactivation of cytotoxic T lymphocytes.

## Does high cardiorespiratory fitness confer some protection against pro-inflammatory responses after infection by SARS-CoV-2?

Zbinden-Foncea H, Francaux M, Deldicque L, Hawley JA.Zbinden-Foncea H
Obesity (Silver Spring)
202 April 23; PMID: 32324968
Level of Evidence: 6 No Data Cited
Type of Article: Review

**BLUF:** The article suggests that healthy lifestyles and high levels of cardiorespiratory fitness are likely to be immuno-protective in patients who contract SARS-CoV-2; however, this correlation has yet to be established.

**Abstract**:Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) originated in China in late 2019 and has since spread rapidly to every continent in the world. This pandemic continues to cause widespread personal suffering, along with severe pressure on medical and health care providers. The symtoms of SARS-CoV-2 and the subsequent **prognosis is worsened in individuals who have pre-exisiting comorbidities prior to infection by the virus**. Individuals with **obesity/overweight, insulin resistance and diabetes typically have chronic low-grade inflammation** characterized by **increased levels of several pro-inflammatory cytokines and the inflammasome**: this state predisposes to greater risk for infection along with more adverse outcomes. Here we consider whether a high level of cardiorespiratory fitness induced by prior exercise training may confer some innate immune-protection against Covid-19 by attenuating the "cytokine storm syndrome" often experienced by "at risk" individuals.

# Transmission & Prevention

## Developments in Transmission & Prevention

### Profile of RT-PCR for SARS-CoV-2: A Preliminary Study From 56 COVID-19 Patients

Xiao, Ai Tang; Tong, Yi Xin; Zhang, Sheng
Clinical Infectious Disease
2020 Apr 19; PMID: 32306036
Level of Evidence: 4 - Case series
Type of Article: Research

**BLUF:** The dynamic profiles of SARS-CoV-2 from 56 recovered COVID-19 patients were studied via routine SARS-CoV-2 RT-PCR assays; the majority of patients had positive results within 3 weeks of onset of symptoms with all results of RT-PCR becoming negative by week 6. It was found that SARS-CoV viral replication has a relatively long period in infected patients and is specifically prolonged in older patients and patients with comorbidities.

### Aerosol or droplet: critical definitions in the COVID-19 era.

Kohanski MA, Palmer JN, Cohen NA.
International Forum of Allergy and Rhinology
2020 Apr 23; PMID: 32323923
Level of Evidence: 5 - Expert opinion
Type of Article: Correspondence

**Summary**: This article discusses a weakness in Workman *et al.* study "Endonasal Instrumentation and Aerosolization Risk in the Era of COVID-19: Simulation, Literature Review, and Proposed Mitigation Strategies" by pointing out that atomizer used to simulate aerosol generation in the study did not account for the fact that the particles could cling to other larger particles. These aggregates were found to be much larger than the target range of 30-100μ in diameter. The author of the correspondence points out that in order for SARS-CoV2 to make it to the type II airway pneumocytes deep in the lungs (diameter 1-10 microns), the size of the respiratory droplet is important and should not be overlooked.

## Prevention in the community

### Coronavirus Disease Outbreak in Call Center, South Korea.

Park SY, Kim YM, Yi S, Lee S, Na BJ, Kim CB, Kim JI, Kim HS, Kim YB, Park Y, Huh IS, Kim HK, Yoon HJ, Jang H, Kim K, Chang Y, Kim I, Lee H, Gwack J, Kim SS, Kim M, Kweon S, Choe YJ, Park O, Park YJ, Jeong EK.
Emerg Infect Dis
2020 Apr 23; PMID: 32324530
Level of Evidence: 3 - Cross sectional of non-random sample
Type of Article: Research

**BLUF:** The authors of this epidemiological investigation of 1,143 individuals who visited or worked at a building in South Korea concluded that SARS-CoV-2 is exceptionally contagious. Transmission in crowded office settings may be prevented with targeted prevention strategies such as extensive testing. When restricting analysis to the 216 employees who worked in a South Korean call center located within a larger building, the attack rate was 43.5% and the household secondary attack rate was 16.2% among symptomatic case-patients.

**Abstract:**
We describe the epidemiology of a coronavirus disease (COVID-19) outbreak in a call center in South Korea. We obtained information on demographic characteristics by using standardized epidemiologic investigation forms. We performed descriptive analyses and reported the results as frequencies and proportions for categoric variables. **Of 1,143 persons who were tested for COVID-19, a total of 97** (8.5%, 95% CI 7.0%-10.3%) **had confirmed cases**. Of these, **94 were working in an 11th-floor call center** with 216 employees, translating to an **attack rate of 43.5%** (95% CI 36.9%-50.4%). The **household secondary attack rate among symptomatic case-patients was 16.2%** (95% CI 11.6%- 22.0%). Of the 97 persons with confirmed COVID-19, only 4 (1.9%) remained asymptomatic within 14 days of quarantine, and none of their household contacts acquired secondary infections. **Extensive contact tracing, testing all contacts, and early quarantine blocked further transmission and might be effective for containing rapid outbreaks in crowded work settings.**

## Universal weekly testing as the UK COVID-19 lockdown exit strategy.

Peto J, Alwan NA, Godfrey KM, Burgess RA, Hunter DJ, Riboli E, Romer P; 27 signatories.
Lancet
2020 Apr 20; PMID: 32325027
Level of Evidence: 6 - No data cited
Type of Article: Correspondence
**Summary:** The authors recommend a feasibility study to evaluate a strategy of weekly SARS-CoV-2 antigen testing of the entire population in one or two cities with 200,000 - 300,000 people with strict household quarantine after a positive test. The rate that infections rise or fall would then be compared with the rest of the UK and could be used to influence policy instead of relying on models.

## Response to Letters to the Editor About the Safe Handling of Containers of Expressed Human Milk in All Settings During the SARS-CoV-2 (COVID-19) Pandemic.

Marinelli KA, Lawrence RM.
J Hum Lact
2020 Apr 23; PMID: 32324443
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter
**Summary:** This response to concerns about an article published in early April by these authors indicates that they stand by the conclusions of the original article. They also note that:

- The article was written to provide preliminary guidance despite the unknowns that still exist around COVID-19 and not intended to make any suggestions that would limit the success of breastfeeding efforts.
- Breast milk is unlikely to be a common source of COVID-19 transmission, but the practices they recommended could still help to protect milk bank and hospital workers.
- No studies to date have found SAR-COV-2 in breast milk.
- Several organizations, including WHO, CDC, and UNICEF have recommended hand hygiene and mask wearing for breastfeeding COVID-19 patients and disinfection of containers for expressed milk - the author's original article provides specific instructions for container cleaning that are absent from these organization's guidelines.
- The potential for asymptomatic infections provides a rationale for a cautious approach that assumes the virus could be spread by more than just airborne and respiratory droplet routes. The authors also note that evidence is emerging that SARS-CoV-2 can survive on surfaces for extended periods of time, making fomite transmission a possibility.

- The concentration of bleach they recommended for disinfection of containers was based on virology research on concentrations effective against SARS-CoV-2 and other coronaviruses and is in line with FDA and CDC recommendations on safe use of bleach.

## Concerns Regarding the Article Entitled 'Safe Handling of Containers of Expressed Human Milk in all Settings During the SARS-CoV-2 (COVID-19)'.

Mitchell KB, Weinstein SR.
J Pharm Pharm Sci
2020 Apr 23; PMID: 32324442
Level of Evidence: 6 - No Data Cited
Type of Article: Letter

**Summary:** This letter is a response to an article published in early April with recommendations for breastmilk handling during COVID-19. Concerns expressed in this article include:

- Limited evidence that breastmilk can be contaminated with SARS-CoV-2 and a lack of rationale for implementing different approaches to cleaning donor milk containers;
- Limited evidence that COVID-19 can be spread by fomites;
- The recommendations in the original article do not reflect those of the CDC, WHO, or Human Milk Banking Association of North America (HMBANA);
- The original article could cause unnecessary alarm and result in increased use of formula over breastfeeding or donor milk.

## Use of Disinfectant Wipes to Sanitize Milk's Containers of Human Milk Bank During COVID-19 Pandemic.

Rose DU, Reposi MP, Amadio P, Auriti C, Dall'Oglio I, Corsetti T, Dotta A, Salvatori G.
J Hum Lact
2020 Apr 23, PMID: 32324441
Level of Evidence: 5 - Expert Opinion
Article Type: Letter

**Summary:** Authors express their recommendations for breast milk donors with suspected COVID-19 be tested before continuing to donate. It is also recommended to clean containers with a disinfecting wipe as this is less costly and an effective method to avoid contamination of multiple containers.

## The Practice of Wearing Surgical Masks during the COVID-19 Pandemic.

Chiang CH, Chiang CH, Chiang CH, Chen YC.
Emerg Infect Dis.
2020 Apr 23; PMID: 32324531
Level of Evidence: Level 5 - Expert opinion
Type of Article: Letter to the Editor

**BLUF:** The authors argue that due to the limitations of the studies included in a recent meta-analysis and the epidemiologic data of COVID-19 incidence in Taiwan vs Singapore, the wearing of surgical masks by the general public may still have substantial results in reducing transmission of COVID-19 and should be encouraged.

## Use of facemasks to limit COVID-19 transmission.

Garcia LP.
Epidemiol Serv Saude.
2020 Apr 22; PMID: 32321003

Level of Evidence: 6 – No data
Type of Article: Correspondence
**BLUF:** Although its protective effect is relatively uncertain, **many countries are recommending the use of facemasks by all people during the COVID-19 pandemic**; evidence is needed to determine the strength of this preventive strategy.

**Summary:**
Nonpharmaceutical interventions, including hand hygiene, social distancing, and prohibiting access to schools, universities, and public transport have proven effective in restricting transmission of respiratory infections. In response to the COVID-19 pandemic, China instituted rigorous preventive measures that included the massive use of facemasks, even by asymptomatic people. In contrast, use of facemasks by asymptomatic people is not recommended by the WHO, due to a lack of evidence as to their effectiveness in reducing transmission, among other reasons. Recent reports have demonstrated some evidence that hand hygiene, facemask use, and case isolation together provided the highest level of protection against respiratory viruses. Experts are advocating for facemask use amongst asymptomatic people, particularly in lieu of the documented COVID-19 transmission rates via asymptomatic carriers. China, Hong Kong, Japan, Thailand, South Korea, and Brazil, among others, have since used diverse types of facemasks against COVID-19. **The recommendation for massive use of facemasks amongst asymptomatic people must be accompanied by education to avoid stigma, as well as clear guidance on their correct use.**

### Public Masking: An Urgent Need to Revise Global Policies to Protect against Novel Coronavirus Disease (COVID-19).

Keshtkar-Jahromi M, Sulkowski M, Holakouie-Naieni K.
Am J Trop Med Hyg
2020 Apr 22; PMID: 32323645;
Level of Evidence: 5 - Descriptive Study
Type of Article: Editorial
**Summary Excerpt:** "In summary, laboratory data support both surgical and cloth masks, but real-world efficacy of cloth masks needs further evaluation. Cloth masks are affordable globally and might be the only option in some areas with limited resources. Based on our current level of evidence, we highly recommend mass masking around the world during the pandemic. Whereas surgical masks are the preferred recommendation for the general public, cloth masks should be considered as a substitute if supplies are limited or surgical masks are not available."

## Prevention in the hospital

### COVID-19 in cardiac arrest and infection risk to rescuers: a systematic review.

Couper K, Taylor-Phillips S, Grove A, Freeman K, Osokogu O, Court R, Mehrabian A, Morley PT, Nolan JP, Soar J, Perkins GD.Couper K
Resuscitation
2020 April 20; PMID: 32325096
Level of Evidence: 1 - Systematic Review
Type of Article: Research
**BLUF:** This aim of this review was to investigate available evidence related to aerosol generation, infection transmission and protection afforded by PPE in rescuers who are performing key interventions such as chest compression, defibrillation and CPR. The results revealed uncertainty in

aerosol generation from chest compression or defibrillation that leads to transmission of COVID-19 to rescuers.

**Abstract**:
Background**:** There may be a risk of COVID-19 transmission to rescuers delivering treatment for cardiac arrest. The aim of this review was to identify the potential risk of transmission associated with key interventions (chest compressions, defibrillation, cardiopulmonary resuscitation) to inform international treatment recommendations.
Methods**:** We undertook a systematic review comprising three questions: 1) aerosol generation associated with key interventions; 2) risk of airborne infection transmission associated with key interventions; and 3) the effect of different personal protective equipment strategies. We searched MEDLINE, Embase, Cochrane Central Register of Controlled Trials, and the World Health Organisation COVID-19 database on 24th March 2020. Eligibility criteria were developed individually for each question. We assessed risk of bias for individual studies, and used the GRADE process to assess evidence certainty by outcome.
Results**:** We included eleven studies: two cohort studies, one case control study, five case reports, and three manikin randomised controlled trials. **We did not find any direct evidence that chest compressions or defibrillation either are or are not associated with aerosol generation or transmission of infection.** Data from manikin studies indicates that donning of personal protective equipment delays treatment delivery. **Studies provided only indirect evidence**, with no study describing patients with COVID-19. Evidence certainty was low or very low for all outcomes.
Conclusion**:** It is uncertain whether chest compressions or defibrillation cause aerosol generation or transmission of COVID-19 to rescuers. There is very limited evidence and a rapid need for further studies. Review registration: PROSPERO CRD42020175594.

## Electrostatic Charged Nanofiber Filter for Filtering Airborne Novel Coronavirus (COVID-19) and Nano-aerosols.

Woon Fong Leung W, Sun Q
Sep Purif Technol
2020 Apr 22; PMID: 32322159
Level of Evidence: 5 - Mechanistic
Type of Article: Research, Transmission & Prevention
**BLUF:** Studies have shown that COVID-19 has a mean size of 100 nm, but can range anywhere from 60-140 nm. However, the CDC's National Institute for Occupational Safety and Health (NIOSH) has standardized N95 and N98 filters at 300 nm. As such, there are no filter standards tailored for capturing these 100 nm nano-aerosols to-date. This study addresses the nanofiber filter technology and has developed four optimized filters with an efficiency over 90% in capturing a target set at 100 nm.

**Abstract:**
The World Health Organization declared the novel coronavirus (COVID-19) outbreak as a pandemic on March 12, 2020. Within 3-1/2 months since outbreak in December 2019, over 1.3 million people have been infected across 206 countries with over 70,000 deaths. **COVID-19 has a size of 60-140nm with mean size of the nano-aerosols, 100nm.** The virus can be airborne by attaching to human secretion (fine particles, nasal/saliva droplets) of infected person or suspended fine particulates in air. While NIOSH has standardized N95 and N98 at 300nm, **to-date there is no filter standards, nor special filter technologies, tailored for capturing airborne viruses and 100nm nano-aerosols.** The latter also are present in high number concentration in atmospheric pollutants. This study addresses developing novel charged PVDF nanofiber filter

technology to effectively capture the deadly airborne coronavirus with **our target set at 100nm (nano-aerosol), and not 300nm**. The virus and its attached particle were simulated by sodium chloride aerosols, 50-500nm, generated from sub-micron aerosol generator. PVDF nanofibers were produced with fiber diameters 84, 191, 349 and 525nm with excellent morphology. The fibers were subsequently charged by corona discharge. The amounts of charged fibers in a filter were increased to achieve high efficiency of 90% for the virus filter but the electrical interference between neighbouring fibers resulted in progressively marginal increase in efficiency and concurrently much higher pressure drop across the filter. The quality factor which measured the efficiency-to-pressure-drop kept decreasing. By redistributing the fibers in the filter into several modules, each separated by a permeable scrim material, the electrical interference was reduced, if not fully mitigated. Also, the additional scrim materials introduced macropores into the filter that further reduced the airflow resistance. With this approach, the quality factor can maintain relatively constant with increasing fiber amounts to achieve high filter efficiency. The optimal amounts of fiber in each module depended on the diameter of fibers in the module. Small fiber diameter that has already high performance required small amount of fibers per module. In contrast, large diameter fiber required more amounts of fiber per module to compensate for the poorer performance without incurring higher pressure drop. This approach was applied to **develop four new nanofiber filters tailored for capturing 100nm airborne COVID-19 to achieve over 90% efficiency with pressure drop below 30Pa (3.1mm water).** One filter developed meeting the 90% efficiency has ultralow pressure drop of only 18Pa (1.9mm water) while another filter meeting the 30Pa limit has high efficiency reaching 94%. **These optimized filters based on rigorous engineering approach provide the badly needed technology for protecting the general public from the deadly airborne COVID-19 and other viruses, and nano-aerosols from air pollution which lead to chronic diseases.**

## Prevention of nosociomial *(sic)* Covid-19: another challenge of the pandemic.

Van Praet, Jens T; Claeys, Bram; Coene, Ann-Sofie; Flore, Kateligne; Reynders, Marijke
Infection Control & Hospital Epidemiology
2020 Apr 23; PMID: 32321612
Level of Evidence: 4 - Case series
Type of Article: Letter to the Editor

**Summary:** The authors in this letter describe a **case series of patients at their tertiary-care hospital in Belgium** in which they observed an increase in probable nosocomial COVID-19 cases from 0 to 31 in a four-week time period; **71% of these cases were observed in geriatric wards**. Further studies are required to identify the most effective preventive approach in wards with high rates of nosocomial transmission.

## Respiratory Protection Considerations for Healthcare Workers During the COVID-19 Pandemic.

Friese CR, Veenema TG, Johnson JS, Jayaraman S, Chang JC, Clever LH
Health Secur
2020 Apr 22; PMID: 32320327
Level of Evidence: 5-Expert opinion
Type of Article: Guideline

**BLUF:** Members of the 2018 National Academy of Medicine Study Committee on the Use of Elastomeric Respirators in Health Care offer their recommendations on how to protect healthcare workers during this pandemic through careful use, decontamination and re-use, and increased production of PPE as well as how to better prepare for future pandemics through increased infrastructure and data tracking of PPE supply and healthcare worker infections.

**Abstract:**
The COVID-19 pandemic has resulted in a surge of patients that exceeds available human and physical resources in many settings, triggering the implementation of crisis standards of care. High-quality respiratory protection is essential to reduce exposure among healthcare workers, yet dire shortages of personal protective equipment in the United States threaten the health and safety of this essential workforce. In the context of rapidly changing conditions and incomplete data, this article outlines 3 important strategies to improve healthcare workers' respiratory protection. At a minimum, healthcare workers delivering care to patients with confirmed or suspected COVID-19 should wear N95 respirators and full-face shields. Several mechanisms exist to boost and protect the supply of N95 respirators, including rigorous decontamination protocols, invoking the Defense Production Act, expanded use of reusable elastomeric respirators, and repurposing industrial N95 respirators. Finally, homemade facial coverings do not protect healthcare workers and should be avoided. These strategies, coupled with longer-term strategies of investments in protective equipment research, infrastructure, and data systems, provide a framework to protect healthcare workers immediately and enhance preparedness efforts for future pandemics.

## Aerosolization of COVID-19 and Contamination Risks During Respiratory Treatments.

Benge CD, Barwise JA.
Fed Pract.
2020 Apr; PMID: 32322146
Level of Evidence: 5 – Expert Opinion
Type of Article: Recommendations
**BLUF**: Aerosolized medications that are frequently administered to acutely ill patients increase the risk of COVID-19 transmission, particularly to health care workers. The authors provide the following recommendations to protect HCWs.

**Summary:**
- Deprescribe nebulized therapies on medical wards and ICUs as an infection control measure.
- Avoid initiation of nebulized unproven therapies (n-acetylcysteine, hypertonic saline)
- Use alternative bronchodilator formulations as appropriate before prescribed nebulized agents
- Limit nebulized drug utilization on patients who are on mechanical ventilation and will receive nebulized therapies via a closed system or to patients housed in negative pressure rooms.
- Add a safety net to the drug-ordering process by restricting new orders for nebulized therapies to the prior authorization process
- Add a safety net to environmental service practices. Nursing staff should track patients who received ≥ 1 nebulizations via open or closed systems so that staff wear suitable PPE.

## Protective shields for ophthalmic equipment to minimise droplet transmission of COVID-19.

Wong DHT, Mak ST, Yip NKF, Li KKW.
Graefes Arch Clin Exp Ophthalmol.
2020 Apr 22; PMID: 32322964
Level of Evidence: 5 - Expert opinion
Type of Article: Letter

**Summary:** The authors of this letter describe the material and dimensions of protective shields that they have created and applied to their slit lamps to prevent spread of COVID-19 during close-contact ophthalmologic exams (see figure below). The efficacy of this product was not discussed.

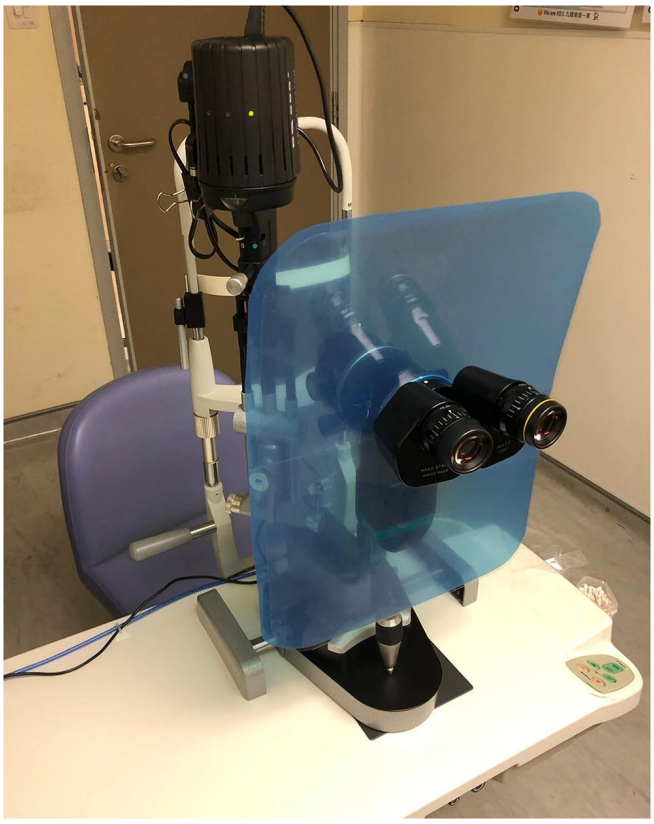


Figure: Protective shield with rounded corners on a tower slit lamp. Typical dimensions of a custom made slit lamp shield. A central cut-out circular area (ranging from 2 to 3 in., size depends on the actual calibre of the slit lamp) is created with scissors on a plastic sheet of desired thickness of A3 size, i.e. approximately 16 by 12 in. (Height × Width)

# Management

## General

### Coronavirus disease 19 (Covid-19) and non-steroidal anti-inflammatory drugs (NSAID).

Giollo A, Adami G, Gatti D, Idolazzi L, Rossini M
Ann Rheum Dis
2020 Apr 22; PMID: 32321720
Level of Evidence: 5- Expert opinion
Type of Article: Letter

**Summary:** Due to the current confusion around the risks and benefits of NSAID use in patients with COVID-19 the authors make 2 recommendations: 1) **clinical studies should actively report the use of NSAIDs** in their patients, 2) patients already on regularly prescribed NSAIDs for their chronic inflammatory arthritis **should continue their medications as prescribed**. The second recommendation comes from the known benefit of NSAIDs in improving arthritis symptoms and the known increased risk of infection associated with uncontrolled inflammation.

### Risks of ACE inhibitor and ARB usage in COVID-19: evaluating the evidence.

Sriram, Krishna; Insel, Paul A
Clinical Pharmacology & Therapeutics
2020 Apr 22; PMID: 32320478
Level of Evidence: 1 - Systematic review of cohort studies
Type of Article: Mini-review

**BLUF:** A literature review of studies in experimental animals (n=12) and human subjects (n=12) was completed. The 12 studies in humans did not show a strong association between ACE2 protein expression and the use of ARBs or ACEIs, implying that ACEIs/ARBs are unlikely to increase the risk of developing COVID-19, suggesting that patients being treated with these medications will likely suffer little consequence.

**Abstract:** Concerns have been raised regarding the safety of Angiotensin Converting Enzyme Inhibitors (ACEIs) and Angiotensin Receptor Blockers (ARBs) in patients with COVID-19, based on the hypothesis that such medications may raise expression of ACE2, the receptor for SARS-CoV-2. We conducted a literature review of studies (n=12) in experimental animals and human subjects (n=12) and **evaluated the evidence regarding the impact of administration of ACEIs and ARBs on ACE2 expression**. We prioritized studies that assessed ACE2 protein expression data, measured directly or inferred from ACE2 activity assays. The findings in animals are inconsistent with respect to an increase in ACE2 expression in response to treatment with ACEIs or ARBs. Control/sham animals show little to no effect in the plurality of studies. Those studies that report increases in ACE2 expression tend to involve acute injury models and/or higher doses of ACEIs or ARBS than are typically administered to patients. Data from human studies overwhelmingly **imply that administration of ACEIs/ARBs does not increase ACE2 expression**. Available evidence, in particular, data from human studies, does not support the hypothesis that ACEI/ARB use increases ACE2 expression and the risk of complications from COVID-19. We conclude that **patients being treated with ACEIs and ARBs should continue their use for approved indications**.

| Source | Details of Study | Effect of ACEI / ARB on ACE2 |
|---|---|---|
| Mizuiri et al., [32] | Urinary ACE2 protein levels were measured in 190 patients with chronic kidney disease and 36 healthy subjects. | No significant difference in urinary ACE2 was observed in response to treatment with ACEI and ARB |
| Furuhashi et al., [33] | Urinary ACE2 protein concentration was assayed in 617 subjects, including 101 subjects who did not use any medication and 100 hypertensives treated with various drugs. | Enalapril, losartan, valsartan, candesartan, valsartan and telmisartan had no effect. Olmesartan increased urinary ACE2. |
| Liang et al., [34] | Urinary ACE2 protein concentration was assessed in 132 Type-2 Diabetic patients and 34 healthy volunteers. | Patients with hypertension had a ~40% decrease in urinary ACE2 if treated with inhibitors of renin-angiotensin signaling, compared to hypertensive patients not taking such medications. |
| Mariana et al., [35] | Urinary ACE2 protein levels were measured via ELISA in 75 patients with Type-2 diabetes | Use of ARBs or ACEIs had no effect on urinary ACE2 levels |
| Epelman et al., [36] | Plasma ACE2 activity was assayed from 228 patients with heart failure. | No association was found between ACEI/ARB use and ACE2 levels. |
| Soro-Paavonen et al., [37] | Serum ACE2 activity was measured in 859 patients with Type-1 Diabetes and 99 healthy control subjects. | ACE2 was increased ~10 to 20% (higher in women) in diabetics using ACEIs. No association was found between ARB usage and ACE2 levels. |
| Ortiz-Perez et al.[38] | Serum ACE2 activity was assayed in 95 patients with ST-elevation myocardial infarction and 22 control subjects. | No association was found between ACEI use and ACE2 levels. ARB usage was not discussed. |
| Anguiano et al.,[39] | Plasma ACE2 activity was measured in n = 568 control subjects, n = 1458 with stage 3-5 chronic kidney disease and n = 546 patients on dialysis. Multivariate regression analysis was performed to identify which factors influenced ACE2. | ACEI use had no effect on ACE2 in any group. ARB use did not predict ACE2 activity in control or stage 3-5 patients; in patients on dialysis ARB use had a small effect raising ACE2 activity. |
| Uri et al., [40] | Serum ACE2 activity was assayed in 141 healthy subjects, 239 hypertensive patients, and 188 patients with heart failure of different types. | Logistic regression analysis showed that ACEI and ARB usage had no association with ACE2 levels |
| Walters et al., [41] | Plasma ACE2 activity was assessed in 25 control subjects and 88 patients with atrial fibrillation. | No association was found between ACE2 levels and ACEI/ARB use. |
| Ramchand et al., [42] | Plasma ACE2 activity was measured in 79 patients with obstructive coronary artery disease. | ACE2 levels had no association with use of ACEIs or ARBs |

## Association of Renin-Angiotensin System Inhibitors With Severity or Risk of Death in Patients With Hypertension Hospitalized for Coronavirus Disease 2019 (COVID-19) Infection in Wuhan, China.

Li J, Wang X, Chen J, Zhang H, Deng A.Li J, et al.
JAMA Cardiol.
2020 Apr 23; PMID: 32324209
Level of Evidence: 3 - cohort study
Type of Article: Research

**Summary Excerpt:** "In this single-center case series involving 362 patients with hypertension hospitalized with COVID-19 infection, **there was no difference in severity of the disease, complications, and risk of death in those who were taking ACEIs/ARBs compared with those not treated with these medications.**"

**Abstract:**

Importance: Data are lacking whether patients with hypertension who are taking angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) have increased severity or risk of mortality during hospitalization for coronavirus disease 2019 (COVID-19).
Objective: To investigate the association between ACEIs/ARBs and severity of illness and mortality in patients with hypertension hospitalized for COVID-19 infection.
Design, Setting, and Participants: Retrospective, single-center case series of the 1178 hospitalized patients with COVID-19 infections at the Central Hospital of Wuhan, China, from January 15 to March 15, 2020.
Main Outcomes and Measures: COVID-19 was confirmed by real-time reverse transcription–polymerase chain reaction and epidemiologic, clinical, radiologic, laboratory, and drug therapy data were analyzed in all patients. The percentage of patients with hypertension taking ACEIs/ARBs was compared between those with severe vs nonsevere illness and between survivors vs nonsurvivors.
Results: Of the 1178 patients with COVID-19, the median age was 55.5 years (interquartile range, 38-67 years) and 545 (46.3%) were men. The overall in-hospital mortality was 11.0%. There were 362 patients with hypertension (30.7% of the total group; median age, 66.0 years [interquartile range, 59-73 years]; 189 [52.2%] were men), of whom 115 (31.8%) were taking ACEI/ARBs. The in-hospital mortality in the patients with hypertension was 21.3%. **The percentage of patients with hypertension taking ACEIs/ARBs did not differ between those with severe and nonsevere infections (32.9% vs 30.7%; P = .65) nor did it differ between nonsurvivors and survivors (27.3% vs 33.0%; P = .34).** Similar findings were observed when data were analyzed for patients taking ACEIs and those taking ARBs.
Conclusions and Relevance: This study provides clinical data on the association between ACEIs/ARBs and outcomes in patients with hypertension hospitalized with COVID-19 infections, suggesting that ACEIs/ARBs are not associated with the severity or mortality of COVID-19 in such patients. These data support current guidelines and societal recommendations for treating hypertension during the COVID-19 pandemic.

## Low-density lipoprotein is a potential predictor of poor prognosis in patients with coronavirus disease 2019

Fan, Junli; Wang, Hui; Ye, Guangming; Cao, Xiaoling; Xu, Xianqun; Tan, Wenbin; Zhang, Yongxi
Metabolism
2020 Apr 19; PMID: 32320740
Level of Evidence: 4 - Retrospective Analysis
Type of Article: Research
**BLUF:** In a sample size of 17 surviving and 4 non-surviving COVID-19 positive patients, researchers analyzed serum low-density lipoprotein (LDL) levels during infection. LDL levels were found to be inversely correlated with disease progression (p = .006).

**Abstract:**
Background: The pandemic of coronavirus disease 2019 (COVID-19) has become a global threat to public health. The lipid pathophysiology in COVID-19 is unknown.
Methods: In this retrospective longitudinal study, we monitored the serum lipids in 17 surviving and 4 non-surviving COVID-19 cases prior to their viral infections and duration the entire disease courses.

Results: I**n surviving cases, the low-density lipoprotein (LDL) levels decreased significantly on admission as compared with the levels before infection; the LDL levels remained constantly low during the disease progression and resumed to the original levels when patients recovered** (pre-infection: 3.5 (3.0-4.4); on admission: 2.8 (2.3-3.1), p < .01; progression: 2.5 (2.3-3.0); discharge: 3.6 (2.7-4.1); median (IQR), in mmol/L). In non-surviving patients, LDL levels showed an irreversible and continuous decrease until death (1.1 (0.9-1.2), p = .02 versus the levels on admission). The ratio changes of LDL levels inversely correlated with ratio changes of high-sensitivity C-reactive protein levels. **Logistic regression analysis showed increasing odds of lowered LDL levels associated with disease progression** (odds ratio: 4.48, 95% IC: 1.55-12.92, p = .006) and in-hospital death (odds ratio: 21.72, 95% IC: 1.40-337.54, p = .028).
Conclusions: LDL levels inversely correlated to disease severities, which could be a predictor for disease progress and poor prognosis.

## Prevalence of Malnutrition and Analysis of Related Factors in Elderly Patients With COVID-19 in Wuhan, China

Li, Tao; Zhang, Yalan; Gong, Cheng; Wang, Jing; Liu, Bao; Shi, Li; Duan, Jun
Eur J Clin Nutr
2020 Apr 22; PMID: 32322046
Level of Evidence: 4 – Cross Sectional study
Type of Article: Research
**BLUF**: A high prevalence of malnutrition in elderly patients with COVID-19 was seen in Wuhan, China. As a result, the authors believe that nutritional support should be strengthened for elderly patients with diabetes mellitus, low calf circumference, or low albumin.

**Abstract:**
Background/objectives: To evaluate the prevalence of malnutrition and its related factors in elderly patients with COVID-19 in Wuhan, China.
Subjects/methods: In a cross-sectional study, we evaluated the nutritional status of elderly inpatients with COVID-19 using the Mini Nutritional Assessment (MNA). Based on MNA scores, patients were divided into non-malnutrition group (MNA ≥ 24), the group with risk of malnutrition (MNA 17-23.5) and malnutrition group (MNA score < 17). Regression analysis was conducted to screen for risk factors for malnutrition.
Results: A total of 182 patients were included in the study, of which 27.5% were in the group with malnutrition risk and 52.7% were in the malnutrition group. There were statistical differences in the incidence of comorbid diabetes mellitus, body mass index (BMI), calf circumference, albumin, hemoglobin, and lymphocyte counts among the three groups. Further regression analysis suggested that combined diabetes, low calf circumference, and low albumin were independent risk factors for malnutrition.
Conclusions: The prevalence of malnutrition in elderly patients with COVID-19 was high, and nutritional support should be strengthened during treatment, especially for those with diabetes mellitus, low calf circumference, or low albumin.

# Acute care

## Critical Care

### Clinical ethics recommendations for the allocation of intensive care treatments in exceptional, resource-limited circumstances: the Italian perspective during the COVID-19 epidemic.

Vergano M, Bertolini G, Giannini A, Gristina GR, Livigni S, Mistraletti G, Riccioni L, Petrini F.
Crit Care
2020 Apr 22; PMID: 32321562
Level of Evidence: 5 - Expert Opinion
Type of Article: Editorial

**Summary:** This article summarizes the ethical recommendations made by the Italian Society of Anesthesia, Analgesia, Resuscitation, and Intensive Care (SIAARTI) in March. The recommendations include:

- **Allocation of ICU resources:** Criteria for admission of any patient admitted to the ICU need to be adapted according to resource availability.
- **Triage principles:** Should include evaluation of patient's age, comorbidities, and functional status and favor allocation of resources to those with a greater probability of survival and higher life expectancy. First come, first serve approaches are never advisable.
- **Advance healthcare directives:** Patients should be included in conversations about "ceilings of care" (e.g., withholding mechanical ventilation) and decisions need to be documented.
- **Decision-making process:** Decisions to withhold life-saving care need to be discussed among healthcare staff and shared with patients and/or proxies when possible.
- **Palliative care:** Appropriate palliative care should always be provided to hypoxemic patients.
- **ICU trials and proportionality of care:** Any admission to the ICU should be communicated as an "ICU trial," with daily re-evaluation of the effectiveness of the care being provided in the ICU and consideration of whether care should be withdrawn.
- **Networking and family care:** Consideration of risk of burnout and moral distress during this time necessitates networking between healthcare workers. The impact of restricted family and proxy visiting opportunities for patients near death also deserves consideration.

### Achieving a Popliteal Venous Access for RRT in Critically Ill COVID-19 Patient in Prone position.

Adams E, Mousa AY.Adams E, et al.
J Vasc Surg Cases Innov Tech
2020 Apr 22; PMID: 32322766
Level of Evidence: 4 - Case Report
Type of Article: Case Report

**BLUF:** Patients experiencing acute respiratory distress (ARDS) with acute renal failure makes renal replacement therapy (RRT) a challenge when a patient is placed in a prone position to maintain adequate oxygenation. This case report describes a micro-puncture technique to access the left popliteal vein via ultrasound to place a 50cm dialysis catheter as a possible alternative.

**Abstract:**This patient is a 67-year-old male who initially presented to our facility with acute respiratory failure secondary to COVID-19. Soon after arrival at our facility, the patient decompensated, developing severe ARDS requiring intubation and prone positioning to maintain adequate oxygenation. Over the next few days, the patient developed acute kidney injury with oliguria and severe volume overload. The vascular surgery service was consulted to obtain central venous

access for emergent CRRT. Upon our exam, the patient was sedated and paralyzed in a rotating prone-positioning bed. He could not be positioned supine without immediately becoming hypoxic and decompensating. A 50-cm Permcath was inserted via left popliteal vein. **This case report outlines a possible challenging scenario that may encounter vascular interventionist when dealing with COVID-19 patients with respiratory compromise in prone position**.

## Managing COVID-19 in Resource-Limited Settings: Critical Care Considerations.

Wen Ting Siow, Mei Fong Liew, Babu Raja Shrestha, Faisal Muchtar, Kay Choong See
Crit Care.
2020 Apr 22; PMID: 32321566
Level of Evidence: 5 - Expert opinion
Type of Article: Editorial

**Summary:** Siow et al. outline some strategies healthcare facilities can use in resource-limited scenarios. For instance **a shortage of isolation beds,** can be addressed by **transforming clinics into inpatient care units**. I**nsufficient ICU ventilators** can be managed by **splitting ventilators** and using pressure cycling rather than volume cycling. A **shortage of PPE** can be addressed by **using UV light decontamination and re-using surgical masks and goggles**.

# Emergency Medicine

## Early Self-Proning in Awake, Non-intubated Patients in the Emergency Department: A Single ED's Experience during the COVID-19 Pandemic.

Caputo ND, Strayer RJ, Levitan R
Acad Emerg Med; PMID: 32320506
Level of Evidence: 4-Cohort study without control
Type of Article: Research

**BLUF:** A cohort study of 50 COVID-19 (positive per RT-PCR) patients at a single New York emergency department arriving with SpO2<90 and treated with early proning demonstrated that after 5 minutes of proning SpO2 improved significantly above the improvement seen with supplemental oxygen alone (p<0.001). 24% of patients still went on to need endotracheal intubation within 24 hours. This study suggests a **possible benefit of early proning in relieving patient hypoxia, but further research is still needed to determine causality and effect on patient outcomes**.

**Abstract:**

Objective: Prolonged and unaddressed hypoxia can lead to poor patient outcomes. Proning has become a standard treatment in the management of patients with ARDS who have difficulty achieving adequate oxygen saturation. The purpose of this study was to describe the use of early proning of awake, non-intubated patients in the emergency department (ED) during the COVID-19 pandemic.
Methods: This pilot study was carried out in a single urban ED in New York City. We included patients suspected of having COVID19 with hypoxia on arrival. A standard pulse oximeter was used to measure $SpO_2$. $SpO_2$ measurements were recorded at triage and after five minutes of proning. Supplemental oxygenation methods included non-rebreather mask (NRB) and nasal cannula. We also characterized post-proning failure rates of intubation within the first 24 hours of arrival to the ED.
Results: Fifty patients were included. Overall, the median $SpO_2$ at triage was 80% (IQR 69 to 85). After application of supplemental oxygen was given to patients on room air it was 84% (IQR 75 to 90). After 5 minutes of proning was added $SpO_2$ improved to 94% (IQR 90 to 95). Comparison of the pre- to post-median by the Wilcoxon Rank-sum test yielded P=0.001. Thirteen patients (24%) failed to

improve or maintain their oxygen saturations and required endotracheal intubation within 24 hours of arrival to the ED.
Conclusion: Awake early self-proning in the emergency department demonstrated improved oxygen saturation in our COVID-19 positive patients. Further studies are needed to support causality and determine the effect of proning on disease severity and mortality.

## Changes to management of a non-pandemic illness during the COVID-19 pandemic: case study of invasive management of acute coronary syndrome.

Coffey S, Moynagh A, Green B, Edmond J, Wilkins GT, Pemberton J, Wilkins B, Williams MJ, Arnold B.
N Z Med J.
2020 Apr 24; PMID: 32325474
Level of Evidence: 5 - Expert opinion
Type of Article: Editorial
**BLUF:** Cardiologists affiliated with Dunedin School of Medicine put forth recommendations in managing ACS during COVID-19, with the goal of balancing likely consequent increase in cardiovascular complications of ACS against the risk of COVID-19 to patients and staff. These changes are summarized in the table below.

**Abstract:**
The coronavirus 2019 (COVID-19) pandemic requires significant changes to standard operating procedures for non-COVID-19 related illnesses. Balancing the benefit from standard evidence-based treatments with the risks posed by COVID-19 to patients, healthcare workers and to the population at large is difficult due to incomplete and rapidly changing information. In this article, we use management of acute coronary syndromes as a case study to show how these competing risks and benefits can be resolved, albeit incompletely. While the risks due to COVID-19 in patients with acute coronary syndromes is unclear, the benefits of standard management are well established in this condition. As an aid to decision making, we recommend systematic estimation of the risks and benefits for management of any condition where there is likely to be an increase in non-COVID-19 related mortality and morbidity due to changes in routine care.

**Table 2:** Summary of key changes to management of ACS in non-PCI capable hospitals due to pandemic.

| Routine standard of care | Pandemic standard of care |
|---|---|
| **STEMI** | |
| Pre-hospital or in-hospital thrombolysis with immediate transfer to PCI capable centre | Pre-hospital or in-hospital thrombolysis with local hospital medical management for low-risk STEMI |
| **NSTEACS** | |
| Routine transfer to PCI capable centre in majority of cases | Transfer to PCI capable centre only for patients with:<br>• Presence of >0.5mm ST deviation on admission ECG<br>• Two or more episodes of angina in last 24 hours<br>• Positive biomarker |

Abbreviations: ACS, acute coronary syndrome; ECG, electrocardiogram; PCI, percutaneous coronary intervention; NSTEACS, non-ST elevation acute coronary syndrome; STEMI, ST-elevation myocardial infarction.

## [Safer intubation and extubation of patients with COVID-19.]

Asenjo JF.Asenjo JF.
Can J Anaesth.
2020 Apr 22; PMID: 32323101
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter
**Summary**: This letter suggests an alternative method for intubation and extubation using various techniques and protective equipment, such as the plastic cover to serve as a barrier, in order to minimize provider's risk of COVID-19 infections via respiratory droplets (see Figure below).

**Figure.** A step-by-step description of a method for safer intubation/extubation in COVID-19 patients. An endotracheal tube (ETT) is prepared (A) with the black plunger-end of a 20-mL syringe serving as a cap through which a 14G needle (B) is used to make a hole to allow a stylet (C) to be placed during intubation. The intubation process keeps the black cap in place until the ETT cuff is inflated and the ETT is clamped after removing the stylet halfway while keeping the cap in place (D–F). The ETT is then reconnected through the anesthesia mask (G). Prior to extubation, a suction catheter is placed in the mouth (depicted in a simulation mannequin) in preparation for extubation (H). Before connecting to the ventilator circuit, the anesthesia mask with a clear plastic drape placed over it is positioned (I). The plastic drape provides protection from contaminating particles coming out of the mouth on extubation. After exubation (J), the sealing action of the mask around the mouth and the suction catheter inside the mask prevents further contamination risk. The patient is then extubated and hand-assisted with the mask while the nasal prongs are already providing oxygen in preparation for transfer (K). A surgical mask is placed on the patent prior to transfer (L).

## Laboratory haemostasis monitoring in COVID-19.

Thachil J, Tang N, Gando S, Falanga A, Levi M, Clark C, Iba T.
J Thromb Haemost
2020 Apr 23; PMID: 32324960
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter to the Editor

**Summary:** This response to the ISTH guidance document for coagulopathy in COVID-19 states the authors' belief that the use of available laboratory markers at admission and during hospitalization is necessary in the management of COVID-19 patients as there have been reports of high incidence of arterial and venous thromboembolism in COVID-19 patients. **The authors suggest that D-dimers, prothrombin time, and platelet count measurements might be clinically relevant in COVID-19 patients.**

## Diagnosis, Prevention, and Treatment of Thromboembolic Complications in COVID-19: Report of the National Institute for Public Health of the Netherlands

Oudkerk M, Büller HR, Kuijpers D, van Es N, Oudkerk SF, McLoud TC, Gommers D, van Dissel J, Cate HT, van Beek EJ
Radiology
2020 Apr 23; PMID: 32324101
Level of Evidence: 5 – Expert Opinion
Type of Article: Review

**BLUF:** This article **reviews findings of elevated D-dimers and coagulation events** in patients with **COVID-19**. In their review, the authors, a group of Dutch radiologists and vascular physicians, cite studies of **microvascular thrombosis** and correlations of elevated D-dimers with poor outcomes to hypothesize that **high D-dimer levels "reflect true thrombotic disease,"** though they acknowledge a lack of data on the prevalence of deep vein thrombosis or pulmonary embolism. They conclude with a **list of recommendations** for The National Institute for Public Health of the Netherlands:

- **Prophylactic low-molecular weight heparin** for all patients with COVID-19
- **Baseline Chest CT** for all patients admitted with suspected COVID-19
- **Serial D-dimer** measurements during hospital stay for risk stratification

**Abstract:**
A potential link between **mortality, D-dimer values and a prothrombotic syndrome** has been reported in patients with **COVID-19 infectio**n. The National Institute for Public Health of the Netherlands asked a group of Radiology and Vascular Medicine experts to provide guidance for the imaging workup and treatment of these important complications. This report **summarizes evidence for thromboembolic disease, potential diagnostic and preventive actions** as well as recommendations for patients with COVID-19 infection.

## Lupus anticoagulant is frequent in patients with Covid-19.

Harzallah I, Debilquis A, Drenou B.
J Thromb Haemost.
2020 Apr 23; PMID: 32324958
Level of Evidence: 4 – Case series
Type of Article: Letter to the Editor

**BLUF:** Anticoagulant therapy **may be important in the** early treatment of severe COVID-19 in patients with detectable levels of lupus anticoagulant, with or without antiphospholipid antibodies.

**Abstract:**
**Patients hospitalized for Covid-19 severe infection are more prone to excessive coagulation activation leading to thrombotic events.** Tang et al.1 discussed the importance of high D-dimer and Fibrin degradation product level to determine the patient prognostic and the risk of thrombosis. However they did not look at lupus anticoagulant (LAC). Zhang et al. described, three cases of thrombosis associated with antiphospholipid antibodies represented by anticardiolipin (aCL) and anti-β2-glycoprotein I (aβ2GPI)2. No lupus anticoagulant was detected in any of the patients.

## Surgical tracheostomies in Covid-19 patients: important considerations and the "5Ts" of safety.

Broderick D, Kyzas P, Sanders K, Sawyerr A, Katre C, Vassiliou L.Broderick D, et al.Br J Oral Maxillofac Surg.
2020 Apr 16;PMID: 32321662
Level of Evidence: 5 - Expert Opinion
Type of Article: Commentary
**BLUF:** Surgical tracheostomies in COVID-19 patients present as a high viral transmission risk for healthcare workers, but various steps can be taken to minimize this risk: deep suctioning of the chest and oral cavity prior to transfers; suctioning of the ET tube and oral cavity during the procedure; maintain closed circuit until tracheostomy tubing is in trachea.

**Abstract**:
The coronavirus disease (covid19) pandemic (caused by the SARS-CoV-2 virus) is the greatest healthcare challenge in a generation. Clinicians are modifying the way they approach day-to-day procedures. Safety and reduction of transmission risk is paramount. **Surgical tracheostomies in covid19 patients are aerosol generating procedures linked with a significant risk of viral contamination**. Here, we describe our local approach for these procedures, introducing the "5Ts" of safe tracheostomy practice: **Theatre set-up, Team Briefing, Transfer of patient, Tracheostomy Procedure, Team Doffing and De-brief**. We identify the critical steps of the procedure and explain how we overcome the risks associated with breaking the transfer circuit to attach the patient to the theatre ventilator. We explain our technique to **reduce secretion spillage when opening the trachea**. We emphasise the importance of **closed tracheal suctioning and mouth suctioning prior to patient transfer**. We highlight the importance of **maintaining a closed circuit throughout the procedure and describe tips on how to achieve this.** We summarise the steps of our protocol in an "easy to reproduce" way. Finally, we emphasise the importance of communication in a constantly changing environment and challenging circumstances.

## Tracheostomy in the COVID-19 pandemic.

Mattioli F, Fermi M, Ghirelli M, Molteni G, Sgarbi N, Bertellini E, Girardis M, Presutti L, Marudi A. Eur Arch Otorhinolaryngol.
2020 Apr 22. Doi; PMID: 32322959
Level of Evidence: 4 - Case Series
Type of Article: Research
**Summarizing Excerpt: "** In the context of prolonged [invasive mechanical ventilation] required in COVID-19 experience, tracheostomy should be suggested to avoid potential tracheal damages within 7 and 14 days."

**Abstract:**
Purpose: The role of tracheostomy in COVID-19-related ARDS is unknown. Nowadays, there is no clear indication regarding the timing of tracheostomy in these patients.
Methods: We describe our synergic experience between ENT and ICU Departments at University Hospital of Modena underlining some controversial aspects that would be worth discussing tracheostomies in these patients. During the last 2 weeks, we performed **28 tracheostomies on patients with ARDS due to COVID-19** infection who were treated with IMV.
Results: **No differences between percutaneous and surgical tracheostomy** in terms of timing and no case of team virus infection.
Conclusion: In our experience, tracheostomy should be performed only in selected patients within 7- and 14-day orotracheal intubation.

## Acute Pulmonary Embolism Associated with COVID-19 Pneumonia Detected by Pulmonary CT Angiography.

Grillet F, Behr J, Calame P, Aubry S, Delabrousse E.Grillet F, et al.Radiology.
2020 Apr 23; PMID: 32324103
Level of Evidence: 4 - Case Series
Type of Article: Research

**BLUF: In patients with confirmed or suspected COVID-19 and severe clinical features, pulmonary embolism was a common finding (23% with a 95%CI of 12-33%) and was associated with presence in a critical care unit.** This study indicates that preferential use of contrast enhanced CT may be warranted among patients with severe clinical features.

**Summary:** Retrospective study of 100 patients with confirmed or suspected COVID-19 and severe clinical features who underwent contrast enhanced CT scan revealed 23% had acute pulmonary embolism (PE) (95% CI, 15-33%). “Patients with pulmonary embolus were more frequently in the critical care unit than those without pulmonary embolus (17 (74%) vs 22 (29%) patients, p<.001), required mechanical ventilation more often (15 (65%) versus 19 (25%) patients, p<.001) and had longer delay from symptom onset to CT diagnosis of pulmonary embolus (12 ± 6 versus 8 ± 5 days, p<.001), respectively. In multivariable analysis, requirement for mechanical ventilation (OR = 3.8 IC95% [1.02 - 15], p=.049) remained associated with acute pulmonary embolus.” The authors to propose that contrast enhanced CT may be the preferred imaging modality among patients with severe clinical features.

# Internal Medicine

## Incidence of Adverse Drug Reactions in COVID-19 patients in China: an active monitoring study by Hospital Pharmacovigilance System.

Sun J, Deng X, Chen X, Huang J, Huang S, Li Y, Feng J, Liu J, He G
Clin Pharmacol Ther.
2020 Apr 23; PMID: 32324898
Level of Evidence: 3 -Retrospective cohort study
Type of Article: Research

**BLUF:** In this retrospective cohort study of 217 admitted COVID-19 patients at the Hospital of Changsha in China, the authors found that there was a 37.8% prevalence of adverse drug reactions during their hospital stay. Of the many drugs being used in the treatment of COVID-19, they found that a majority of these reactions (mainly GI, liver and lipid disorders) could be explained by Lopinavir/ritonavir (63.8%) and umifenovir (18.1%).

**Abstract:**
To evaluate the incidence, type and risk factors associated with adverse drug reactions (ADRs) among COVID-19 patients by Hospital Pharmacovigilance System (CHPS). A retrospective analysis was performed on 217 COVID-19 patients admitted to the First Hospital of Changsha in China, from January 17, 2020 to February 29, 2020. The active monitoring model in CHPS was used to detect ADR signals of hospital information system *(sic)*. The risk factors for the ADRs were classified using the WHO-UMC system. Univariate and multivariate logistic regression was carried out to analyze the risk factors of ADRs. Our results showed that the prevalence of ADRs was 37.8% in the patients, which was predominated by drug-induced gastrointestinal disorders and liver system disorders (23.0% vs. 13.8% ). The ADR could be explained by the use of lopinavir/ ritonavir and umifenovir by 63.8% and 18.1%, respectively. 96.8% of ADRs occurred within 14 days of hospitalization. Multivariable analysis showed that length of stay (OR: 2.02, [95% CI: 1.03-3.96], P=0.04), number of drugs used in hospital (OR: 3.17, [95%CI: 1.60-6.27], P=0.001) and underlying basic diseases (OR:2.07, [95%CI: 1.02-4.23], P = 0.04) were independent risk factor for ADRs in the patients. Together, the incidence of ADRs was significantly high during the treatment period. Moreover, the active monitoring of the CHPS system reflected ADRs during COVID-19 treatment in the real world, which provided reference for safe medication in clinic.

## Cardiology

### Switching to another antihypertensive effective drug when using ACEIs/ARBs to treat arterial hypertension during COVID-19.

Ciulla MM
European Heart Journal.
2020 Apr 23; PMID: 32324222
Level of Evidence: 5 - Opinion
Type of Article: Commentary
**Summary**: The article details the author's opinion that ACEI/ARB medications should be withdrawn in COVID-19 patients and replaced with other anti-hypertensive medications (calcium channel blockers) based on the correlation that found 52% of deceased patients were on an ACEI/ARB.

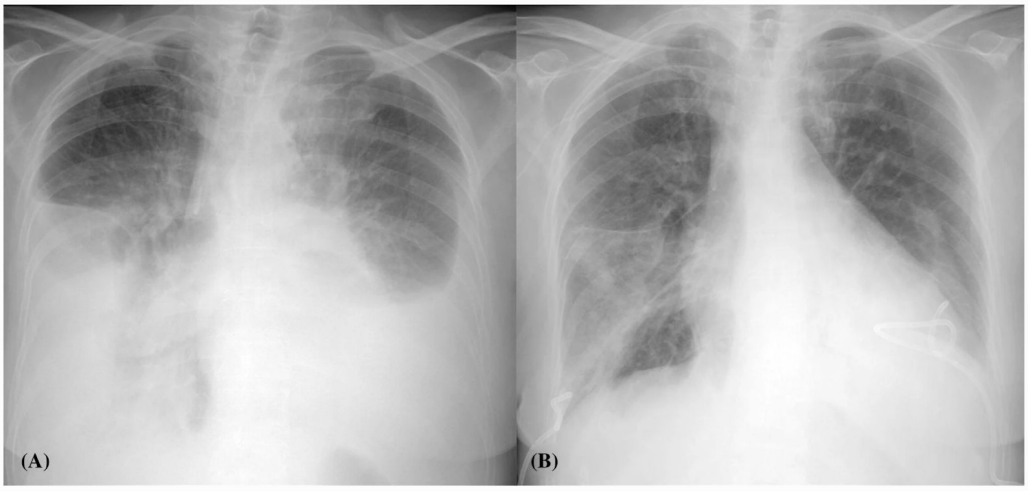
### An Anti-Oxidative Therapy for Ameliorating Cardiac Injuries of Critically Ill COVID-19-infected Patients.

Grant Christey, Janet Amey, Alaina Campbell, Alastair Smith
Int J Cardiol.
2020 Apr 6; PMID: 32321655
Level of Evidence: 5 - Expert opinion
Type of Article: Letter
**Summary:** Reactive oxygen species (ROS) is important to regulate an immunologic response to clear pathogens. However, excessive ROS can oxidize cellular proteins and not only destroy pathogen-infected cells, but also normal cells resulting in organ failure. Christey et al. propose that anti-oxidative therapy can alleviate cardiogenic casualties caused by COVID-19 related oxidative stress. Antioxidants can include Vitamin C and E and/or plant-derived molecules Curcumin and Baicalin.

## Radiology

### Contribution of Interventional Radiology to the Management of COVID-19 patient.

Monfardini L, Sallemi C, Gennaro N, Pedicini V, Bnà C
Cardiovasc Intervent Radiol
2020 Apr 22; PMID: 32322916; No Abstract
Level of Evidence: 4 - Case Report
Type of Article: Letter
**Summary:** Although COVID-19 infection does not usually lead to pleural effusions, it is a common finding in metastatic oncologic patients and may severely impact respiratory function. With ventilation being the first line treatment for patients with COVID-19, ultrasound-guided thoracic interventions like pleural drainage is recommended to improve oxygenation. Through these kinds of minimally invasive procedures, interventional radiology may play a key role in optimizing patient ventilation during this COVID-19 outbreak.




**A** Chest X-ray shows bilateral pleural effusion and diffuse interstitial thickening. **B** Chest X-ray performed 24 h after bilateral pleural drainages shows nearly complete resolution of the pleural effusions on both sides

# OBGYN

## A practice of anesthesia scenario design for emergency cesarean section in patients with COVID-19 infection based on the role of standard patient.

Kang Y, Deng L, Zhang D, Wang Y, Wang G, Mei L, Zhou G, Shu H.Kang Y, et al.
Biosci Trends.
2020 Apr 22; PMID: 32321903
Level of Evidence: 5 - Expert Opinion
Type of Article: Commentary

**BLUF:** A protocol has been developed to train and plan emergency response teams (ERT) responsible for anesthetizing COVID-19 patients during procedures. There is an anesthesia precaution checklist that includes Level 3 PPE for all team members and requires patients to wear surgical or N95 masks at all times.

**Abstract:**
The new coronavirus (COVID-19) has been characterized as a world pandemic by WHO since March 11, 2020. Although it is likely that COVID-19 **transmission is primarily via droplets and close contact, airborne transmission and fecal-oral route remains a possibility.** The medical staff working in the operating room, such as anesthesiologists, surgeons and nurses, are at **high risk of exposure to virus d**ue to closely contacting patients. The perioperative management is under great challenge while performing surgeries for patients suffering COVID-19, including emergency cesarean section, which is one of the most common surgeries under such circumstances. How to **prevent medical staff from cross-infection** is an issue of great concern. In this article, we **give a practice of anesthesia scenario design for emergency cesarean section in a supposed standard patient suffering COVID-19**, aimed to optimize the work flow and implement the protective details through simulation of a real operation scenario, which may be useful for training and clinical practice of anesthesia management for patients suffering COVID-19 or other fulminating infectious diseases.

## Management of the first patient with confirmed COVID-19 in pregnancy in India: From guidelines to frontlines.

Sharma KA, Kumari R, Kachhawa G, Chhabra A, Agarwal R, Sharma A, Bhatla N.
Int J Gynaecol Obstet
2020 Apr 23, PMID: 32324897
Level of Evidence: 4 - Case Report
Article Type: Research

**BLUF**: Pregnant females presenting with flu-like symptoms to labor and delivery should be considered a suspected case. The authors recommend preparing an isolated area for confirmed cases of COVID-19 pregnant women in order to lower the risk of spread.

**Abstract:**
As the COVID-19 pandemic continues to affect millions of people across continents, it follows that pregnancy and childbirth will also be affected. Data are emerging on the consequences of the infection on mother and baby. Many guidelines on pregnancy management during the pandemic have been released, but the actual journey to establishing an obstetric unit can be challenging. The present article describes the stepwise informed approach that was taken to rapidly establish a unit for suspected COVID-19 patients within existing resources, and the experience of delivering the first pregnant patient with confirmed COVID-19 in India.

## SARS-CoV-2 Infection in Pregnancy - a Review of the Current Literature and Possible Impact on Maternal and Neonatal Outcome.

Stumpfe FM, Titzmann A, Schneider MO, Stelzl P, Kehl S, Fasching PA, Beckmann MW, Ensser A.Stumpfe FM, et al.
Geburtshilfe Frauenheilkd.
2020 Apr; PMID: 32322107
Level of Evidence: Systematic Review-2
Article Type: Research

**BLUF:**. Review of management showed 1) therapeutic options are under review (remdesivir, hydroxychloroquine), 2) decisions to isolate pregnant women should be made generously, 3) COVID-19 and co-infection testing is advised, 4) empiric antibiotic treatment for secondary bacterial infections is indicated, 5) regular CTG exams, follow-up fetal growth checks, and Doppler and amniotic fluid exams should be performed.

**Abstract:** In December 2019, cases of pneumonia of unknown cause first started to appear in Wuhan in China; subsequently, a new coronavirus was soon identified as the cause of the illness, now known as Coronavirus Disease 2019 (COVID-19). Since then, infections have been confirmed worldwide in numerous countries, with the number of cases steadily rising. **The aim of the present review is to provide an overview of the new severe acute respiratory syndrome (SARS) coronavirus 2 (SARS-CoV-2) and, in particular, to deduce from it potential risks and complications for pregnant patients.** For this purpose, the available literature on cases of infection in pregnancy during the SARS epidemic of 2002/2003, the MERS (Middle East respiratory syndrome) epidemic ongoing since 2012, as well as recent publications on cases infected with SARS-CoV-2 in pregnancy are reviewed and reported. **Based on the literature available at the moment, it can be assumed that the clinical course of COVID-19 disease may be complicated by pregnancy which could be associated with a higher mortality rate. It may also be assumed at the moment that transmission from mother to child in utero is unlikely. Breastfeeding is possible once infection has been excluded or the disease declared cured.**

▶ **Table 5** Neonatal outcome of the known SARS-CoV cases from Wuhan ("Wuhan patient population") [34].

| | Case 1 | Case 2 | Case 3 | Case 4 | Case 5 | Case 6 | Case 7 | Case 8 | Case 9 | n (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| GA at delivery (weeks + days) | 37 + 2 | 38 + 3 | 36 + 0 | 36 + 2 | 38 + 1 | 36 + 3 | 36 + 2 | 38 + 0 | 39 + 4 | |
| Birth weight (g) | 2870 | 3730 | 3820 | 1880 | 2970 | 3040 | 2460 | 2800 | 3530 | |
| Low birth weight (< 2500 g) | no | no | no | yes | no | no | yes | no | no | 2 (22 %) |
| Premature delivery | no | no | yes | yes | no | yes | yes | no | no | 4 (44 %) |
| Apgar scores after 1/5 min | 8/9 | 9/10 | 9/10 | 8/9 | 9/10 | 9/10 | 9/10 | 9/10 | 8/10 | |
| Severe neonatal asphyxia | no | no | no | no | no | no | no | no | no | 0 |
| Neonatal death | no | no | no | no | no | no | no | no | no | 0 |
| IUFT | no | no | no | no | no | no | no | no | no | 0 |

GA: gestational age; g: gramm; min: minute; IUFT: intrauterine fetal death

# Pediatrics

## Late-Onset Neonatal Sepsis in a Patient with Covid-19.

Coronado Munoz A, Nawaratne U, McMann D, Ellsworth M, Meliones J, Boukas K
N Engl J Med

2020 Apr 22; PMID: 32320556
Level of Evidence: 4- Case report
Type of Article: Letter
**Summary excerpt:** The authors present a case report of a neonate initially suspected of sepsis who was diagnosed by nasal swab RT-PCR with COVID-19. "Although children are less likely than adults to have severe COVID-19, this case illustrates that it can occur and **can be successfully managed with standard PICU protocols**.[1] The one exception to the standard protocol was that **noninvasive mechanical ventilation was not attempted**, since COVID-19 was suspected."

## COVID-19 Diagnostic and Management Protocol for Pediatric Patients.

Carlotti APCP, Carvalho WB, Johnston C, Rodriguez IS, Delgado AF.Carlotti APCP, et al.
Clinics (Sao Paulo)
2020 Apr 17, PMID: 32321116
Level of Evidence: 5 - Expert Opinion
Article Type: Literature Review
**BLUF:** The authors provide numerous protocols for pediatric patients such as avoiding the use of aerosol bronchodilators if presenting with wheezing and providing fluids or vasoactive drugs for patients with cardiocirculatory dysfunction or shock.

**Abstract:**
This review aims to verify the main epidemiologic, clinical, laboratory-related, and therapeutic aspects of coronavirus disease 2019 (COVID-19) in critically ill pediatric patients. An extensive review of the medical literature on COVID-19 was performed, mainly focusing on the critical care of pediatric patients, considering expert opinions and recent reports related to this new disease. Experts from a large Brazilian public university analyzed all recently published material to produce a report aiming to standardize the care of critically ill children and adolescents. The report emphasizes on the clinical presentations of the disease and ventilatory support in pediatric patients with COVID-19. It establishes a flowchart to guide health practitioners on triaging critical cases. COVID-19 is essentially an unknown clinical condition for the majority of pediatric intensive care professionals. Guidelines developed by experts can help all practitioners standardize their attitudes and improve the treatment of COVID-19.

## Chloroquine dosing recommendations for pediatric COVID-19 supported by modeling and simulation

Verscheijden LFM, van der Zanden TM, van Bussel LPM, de Hoop-Sommen M, Russel FGM, Johnson TN, de Wildt SN.
Clinical Pharmacology and Therapeutics
2020 Apr 22; PMID: 32320477
Level of Evidence: 5 - Mechanism based reasoning
Type of Article: Research
**BLUF**: This article details the appropriate age-adjusted chloroquinolone doses for COVID-19 patients across the pediatric age range as determined by "Physiologically-based pharmacokinetic (PBPK) modeling." The dosing information can be found in Table 1 below.

**Abstract**: As chloroquine (CHQ) is part of the Dutch Centre for Infectious Disease Control COVID-19 experimental treatment guideline, pediatric dosing guidelines are needed. Recent pediatric data suggest that existing WHO dosing guidelines for children with malaria are suboptimal. The aim of our study was to establish best-evidence to inform pediatric CHQ doses for children infected with COVID-19. A previously developed physiologically-based pharmacokinetic (PBPK) model for CHQ

was used to simulate exposure in adults and children and verified against published pharmacokinetic data. The COVID-19 recommended adult dosage regimen of 44mg/kg total was tested in adults and children to evaluate the extent of variation in exposure. Based on differences in $AUC_{0\text{-}70h}$ the optimal CHQ dose was determined in children of different ages compared to adults. Revised doses were re-introduced into the model to verify that overall CHQ exposure in each age band was within 5% of the predicted adult value. Simulations showed differences in drug exposure in children of different ages and adults when the same body-weight based dose is given. As such, we propose the following total cumulative doses: 35 mg/kg (CHQ base) for children 0-1 month, 47 mg/kg for 1-6 months, 55 mg/kg for 6 months-12 years and 44 mg/kg for adolescents and adults, not to exceed 3300 mg in any patient. Our study supports age-adjusted CHQ dosing in children with COVID-19 in order to avoid suboptimal or toxic doses. The knowledge-driven, model-informed dose selection paradigm can serve as a science-based alternative to recommend pediatric dosing when pediatric clinical trial data is absent.

**Table 1. Age adjusted pediatric dose recommendation**

| Age group | AUC ratio ($AUC_{adult}$/ $AUC_{pediatric}$) | New age adjusted dose (mg/kg) | AUC after new pediatric dose (SEM) mg/L.h | Final age-adjusted dose advice (mg/kg) |
|---|---|---|---|---|
| Adults and children >12 years | NA | 44 (day 1: 8mg/kg, followed by 4mg/kg after 12 h. day 2-5: 4mg/kg twice daily) | 76.6 (1.1) | 44 mg/kg* (day 1: 8mg/kg, followed by 4mg/kg after 12 h. day 2-5: 4mg/kg twice daily). (max dose: 3300mg) |
| Pediatric 5 – 12 years | 1.33 | 58.5 (day 1: 10mg/kg, followed by 5mg/kg after 12 h. day 2-5: 5.4mg/kg twice daily) | 76.4 (0.8) | 55 mg/kg (day 1: 10mg/kg, followed by 5mg/kg after 12 h. day 2-5: 5mg/kg twice daily) (max dose: 3300 mg) |
| Pediatric 6 months – 5 years | 1.29 | 56.8 (day 1: 10mg/kg, followed by 5mg/kg after 12 h. day 2-5: 5.2mg/kg twice daily) | 76.1 (0.8) | 55 mg/kg (day 1: 10mg/kg, followed by 5mg/kg after 12 h. day 2-5: 5mg/kg twice daily) |
| Pediatric 1 month – 6 months | 1.01 | 44.4 (day 1: 10mg/kg, followed by 5mg/kg after 12 h. day 2-5: 3.7mg/kg twice daily) | 76.9 (0.8) | 47 mg/kg (day 1: 10mg/kg, followed by 5mg/kg after 12 h. day 2-5: 4mg/kg twice daily) |
| Pediatric 0 – 1 month | 0.80 | 35.2 (day 1: 10mg/kg, followed by 5mg/kg after 12 h. day 2-5: 2.5mg/kg twice daily) | 77.3 (1.1) | 35 mg/kg (day 1: 10mg/kg, followed by 5mg/kg after 12 h. day 2-5: 2.5mg/kg twice daily) |

NA = Not applicable, * adults receive a dose for an average (75kg) individual irrespective of body weight (44mg/kg x 75kg = 3300mg total dose)

# Adjusting Practice during COVID-19

## Telemedicine During The COVID-19 in Italy: A Missed Opportunity?

Omboni S.
Telemed J E Health.
2020 Apr 22; PMID: 32324109
Level of Evidence: 5 - Opinion
Type of Article: Opinion

**BLUF:** The article discusses how Italy's slow move towards the use of telemedicine in the COVID-19 pandemic left the country unprepared to take care of patients with longstanding chronic conditions. They conclude by stating that telemedicine "should be considered as a proactive approach to secure continuity of care to patients suffering from chronic diseases, for which care cannot be postponed during national emergencies."

**Abstract:**
In the time of COVID-19 epidemic, Italy was found unprepared to manage lockdown patients with chronic diseases, due to limited availability and diffusion of large-scale telemedicine solutions. **The scattered distribution and heterogeneity of available tools, the lack of integration with the electronic health record of the national health system, the poor interconnection between telemedicine services operating at different levels, the lack of a real multidisciplinary approach to the patient's management, the heavy privacy regulations, and lack of clear guidelines, together with the lack of reimbursement, all hinder the implementation of effective telemedicine solutions** for long-term patients' management. This COVID-19 epidemic should help promote better use and a larger integration of telemedicine services in the armamentarium of health care services. Telemedicine must no longer be considered as an option or add-on to react to an emergency.

# Acute Care

## Emergency Medicine

### Dynamic adaptation to COVID-19 in a Singapore paediatric emergency department.

Tan RMR, Ong GY, Chong SL, Ganapathy S, Tyebally A, Lee KP.
Emerg Med J.
2020 Apr 22; PMID: 32321705
Level of Evidence: 5 – Expert Opinion
Type of Article: Perspective

**Summary:** The authors share the reassessment of workflow processes in a tertiary pediatric emergency department to help manage COVID-19. Interventions include:

- Segregation of ED into physically separate areas stratified by risk of COVID-19 infection
- Reorganization of medical manpower into modular teams
- Management of unwell accompanying adult caregivers
- Progressive introduction of outpatient COVID-19 testing for enhanced

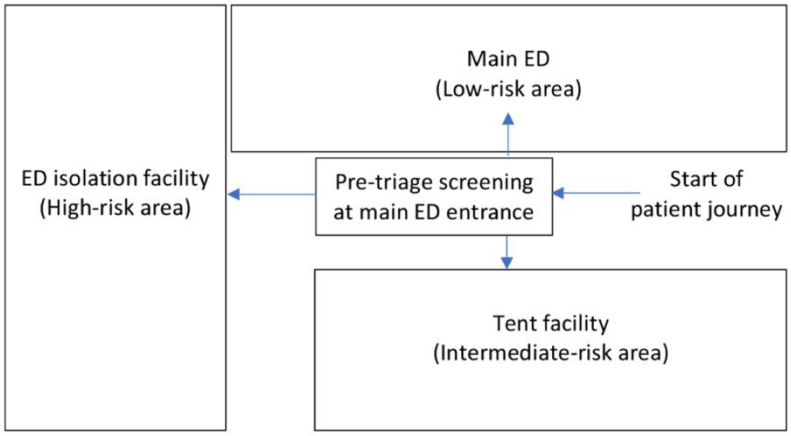



**Figure 1** Initial layout of high-risk, intermediate-risk and low-risk areas of the emergency department (ED). The intermediate-risk and low-risk areas were later switched due to space constraints and patient numbers.

## Variation in volumes and characteristics of trauma patients admitted to a level one trauma centre during national level 4 lockdown for COVID-19 in New Zealand.

Christey G, Amey J, Campbell A, Smith A.
N Z Med J.
2020 Apr 24; PMID: 32325471
Level of Evidence: 3 – Local, non-random sample
Type of Article: Research

**BLUF:** In spite of a national lockdown, **trauma of all age groups and severities still occur, albeit at a reduced volume.** Until resources are restricted, it remains important for hospitals to provide full services.

**Abstract:**

Aim: The aims of this study were to describe the variation in volumes and types of injuries admitted to a level one trauma centre in New Zealand over two 14-day periods before and during the national level 4 lockdown for COVID-19; and highlight communities at risk of preventable injury that may impact negatively on hospital resources.

Method: A retrospective, descriptive study of prospectively collected data in the Midland Trauma Registry in New Zealand.

Results: Overall there was a **reduction of 43% in all injury-related admissions** with significant reductions seen in major injury (50% reduction), males (50% reduction) and children aged 0-14 years (48% reduction). Results for ethnicity and persons aged over 14 years were within 3% deviation of this overall 43% reduction. **Injuries at home, particularly falls, predominate.**

Conclusion: **Despite the significant reduction in admissions during level 4 lockdown, hospitals should continue to provide full services until resource limitations are unavoidable.** Immediate messaging is recommended to reduce rates of injury on the farm and at home, specifically falls prevention. Ongoing attention of road users to road safety is essential to reduce the incidence of preventable major injury. These immediate measures can potentially reduce unnecessary pressure on hospital beds and resources during the pandemic.

# Internal Medicine

## Anaesthesiology

### Pain Management During the COVID-19 Pandemic in China: Lessons Learned.

Song, Xue-Jun; Xiong, Dong-Lin; Wang, Zhe-Yin; Yang, Dong; Zhou, Ling; Li, Rong-Chun
Pain Medicine
2020 Apr 23; PMID: 32321173
Level of Evidence: 4 - Case Reports
Type of Article: Research

**BLUF:** These are the recommendations and lessons learned by a pain management clinic in China during the COVID-19 pandemic, as summarized below. Two case studies of pain medicine patients are also described.

**Summary:**

**Strategies that were helpful for pain management:**

- Pain clinic patients were triaged into different levels of care based on pain level and exposure to COVID-19, and managed either inpatient or outpatient based on that.
    - Inpatient treatment: necessary pain treatments were minimized and recovered patients discharged with telemedicine.
    - Outpatient treatment: telemedicine and if needed, patient home-visits were utilized.

**Lessons learned/Recommendations:**

- Keep information transparent and up-to-date as well as take action quickly and firmly.
- Usage of quarantine and adequate personal protective equipment.
- Usage of telemedicine Support.
- Pain management in patients with and without COVID-19
    - Need to consider strategies to encourage patients to seek outpatient care.
    - Pain may be related to COVID-19 as an earlyas early symptom or may be a manifestation of a non-COVID-19 related process.

## Cardiology

### Priority plan for invasive cardiac electrophysiology procedures during the coronavirus disease 2019 (COVID-19) pandemic

Norman C Wang, Norman C; Jain, Sandeep K; Estes 3rd, N A Mark; Barrington, William W; Bazaz, Raveen; Bhonsale, Aditya; Kancharla, Krishna; Shalaby, Alaa A; Voigt, Andrew H; Saba, Samir
J Cardiovasc Electrophysiol
2020 Apr 23; PMID: 32323382
Level of Evidence: 5 - Mechanism-Based Reasoning
Type of Article: Guidelines

**Summarizing Excerpt:** "**The priority plan for invasive cardiac electrophysiology procedures presented here is a flexible yet organized method to facilitate triage during the COVID-19 pandemic.** Procedure priority should be decided proactively and with social distancing in mind. Uncertainty or disagreement should be adjudicated by a formal institution-specific process. This simplified approach could also aid in preparations for emergencies that may strain medical resources in the future and in other countries."

## Switching antihypertensive therapy in times of COVID-19: why we should wait for the evidence.

Kuster GM, Osswald S.
Eur Heart J.
2020 Apr 23; PMID: 32324223
Level of Evidence: 5 - Expert Opinion
Type of Article: Comment

**Summary:** This commentary is made in response to a number of research articles that are pushing for the discontinuation of RAAS inhibitors for hypertension in patients with COVID-19 infection. The authors, two cardiologists from Switzerland, argue that the research is still inconclusive and that recent meta-analysis of a number of research projects suggest a protective factor of RAAS inhibitors against COVID-19 infection.

## Future-proofing cardiac rehabilitation: Transitioning services to telehealth during COVID-19.

Thomas E, Gallagher R, Grace ASL.
Eur J Prev Cardiol.
2020 Apr 23; PMID: 32324047
Level of Evidence: 5 - Expert Opinion
Type of Article: Editorial

**Summary:** This editorial pushes for the transition of care via telehealth, stating that the COVID-19 pandemic is as good a time as ever for this major change to happen. Citing a number of tele-health trials conducted internationally, the author reports the ease of online patient visits actually reduces the number of hospital visits, and that the quality of care is often not compromised due to the advances in technology including text messaging and video calling.

## Restructuring Electrophysiology During the COVID-19 Pandemic: A Practical Guide from a New York City Hospital Network.

Rubin GA, Wan EY, Saluja D, Thomas G, Slotwiner DJ, Goldbarg S, Chaudhary S, Turitto G, Dizon J, Yarmohammadi H, Ehlert F, Rubin DA, Morrow JP, Waase M, Berman J, Kushnir A, Abrams MP, Halik C, Kumaraiah D, Schwartz A, Kirtane A, Kodali S, Goldenthal I, Garan H, Biviano A
Crit Pathw Cardiol
2020 Apr 21; PMID: 32324622
Level of Evidence: 5 - Expert Opinion
Type of Article: Editorial

**BLUF**: Recommendations from the cardiac electrophysiology (EP) teams in the New York-Presbyterian (NYP) enterprise in New York, NY include:

- Measures to allow staff to work from home, including implementation of robust telehealth systems.
- Ensuring multiple procedural attending physicians are available in house and on call.
- Temporary attending privileges for fellows.
- Open two-way communication between EP staff and hospital administration.

**Abstract**: The COVID-19 crisis is a global pandemic of a novel infectious disease with far-ranging public health implications. With regard to cardiac electrophysiology (EP) services, we discuss the "real-world" challenges and solutions that have been essential for efficient and successful **(i) ramping down** of standard clinical practice patterns and **(ii) pivoting of workflow processes** to meet the demands of this pandemic. The aims of these recommendations are to outline: **(1)**

**essential practical steps to approaching procedures**, as well as outpatient and inpatient care of EP patients, with relevant examples, **(2) successful strategies to minimize exposure risk to patients and clinical staff** while also balancing resource utilization, **(3) challenges related to redeployment and restructuring** of clinical and support staff, and **(4) considerations regarding continued collaboration** with clinical and administrative colleagues in order to implement these changes. While process changes will vary across practices and hospital systems, we believe that these experiences from four different EP sections in a large New York city hospital network currently based in the global epicenter of the COVID-19 pandemic will prove useful for other EP practices adapting their own practices in preparation for local surges.
These recommendations are summarized in tables 1 and 2.

Table 1: Challenges, responsibilities and considerations for clinic staff, clinicians and patients during the transition to telehealth visits during the COVID-19 pandemic
EMR = electronic medical record; HIPAA = Health Insurance Portability and Accountability Act; IT = information technology; VPN = virtual private network

| Outpatient Care | | |
|---|---|---|
| **Clinic staff** | **Clinicians** | **Patients** |
| • Consider purchase or loan of iPads or laptops to facilitate staff work from home<br>• Appreciate the enormous effort to call and reschedule patients and prepare them for televisits<br>• Calls must be forwarded from office numbers and fax to physicians' homes<br>• Work with IT staff to arrange password, VPN, remote EMR access from home for division | • If possible, perform telehealth visit through the EMR<br>• As HIPAA regulations have relaxed during the crisis, third party platforms may be used<br>• Document patient consent and time spent during consultation<br>• When using a smartphone, consider if personal phone number is viewable | • Some patients may not have access to technology. A phone-based evaluation suffices<br>• Enlist a young or tech-savvy family member to assist patient<br>• Communicate exact time to patient and advise them that MD may be late if there are several scheduled televisits<br>• Look directly at the camera and advise the patient that if you look away, it is to take notes |

Table 2: Key points when considering administrative restructuring and both external and internal redeployment.

| Restructuring and Redeployment |
|---|
| • One procedure attending in-house per day<br>• One attending at home for procedural back-up; (others on a redeployment wait-list)<br>• Remaining attendings/fellows on a list to be deployed to non-EP areas<br>• Elderly, at-risk physicians reassigned to televisits, overnight calls, teaching duties, curbsides from EP in-house colleagues<br>• Emergency temporary attending privileges granted to fellows<br>• Contingency planning for coverage of fellow duties considered on a daily basis<br>• Designate colleagues to coordinate research efforts with Institutional Review Board |

## Neurology

### MDS-UPDRS use in the COVID era.

Goetz CG, Stebbins GT, Luo S.Goetz CG, et al.
Mov Disord. 2020 Apr 22. PMID: 32320498
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter

**Summary:** Experts of the Movement Disorder Society - Unified Parkinson's Disease Rating Scale (MDS-UPDRS) development program have decided that they **cannot recommend the usage of the MDS-UPDRS during the COVID-19 pandemic** due to not being able to assess rigidity or postural reflexes with telemedicine (without direct patient contact).

### What can Parkinson's disease teach us about COVID-19?

Tipton PW, Wszolek ZK
Neurol Neurochir Pol
2020 Apr 23; PMID: 32323862
Level of Evidence: 5- Expert Opinion
Type of Article: Letter

**Summary**: Authors at Mayo Clinic in Jacksonville, Florida consider SARS-CoV-2 neuronal tropism in the setting of patients with Parkinson's Disease (PD), and **recommend consideration of adamantane derivatives amantadine and/or memantine, PD drugs with antiviral effects,** as potential repurposed antiviral therapy, suggesting that patients currently on amantadine and/or memantine may provide useful in retrospective analysis.

## Oncology

### Management of Locally Advanced Rectal Cancer During The COVID-19 Pandemic: A Necessary Paradigm Change at Memorial Sloan Kettering Cancer Center.

Romesser PB, Wu AJ, Cercek A, Smith JJ, Weiser M, Saltz L, Garcia-Aguilar J, Crane CH.
Adv Radiat Oncol.
2020 Apr 22. Doi; PMID: 32322758
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter

**BLUF:** Before the COVID-19 outbreak, the standard of care for patients with locally advanced rectal cancer was total neoadjuvant therapy (TNT) with long course chemoradiation (LCCRT); however, this method has concerns for increased infectivity due to the need for prolonged and frequent visits. In the setting of the pandemic, the use of short-course radiation therapy (SCRT) must be re-evaluated since it is already a well-validated alternative to LCCRT, but is seldom used due to physician bias.

**Abstract:** The COVID-19 pandemic will consume significant health care resources. Given concerns for rapidly rising infection rates in the US, impending staffing shortages, and potential for resource re-allocation, we rapidly re-evaluated our rectal cancer practice policies during this public health emergency. Previous to the pandemic we commonly utilized total neoadjuvant therapy (TNT) with a strong preference for long course chemoradiation (LCCRT). In the setting of the ongoing pandemic we now mandate short course radiation therapy (SCRT). Despite multiple randomized trials demonstrating no difference in locoregional recurrence, distant recurrence, or overall survival between SCRT and LRCCT, adaptation of SCRT in the United States has been low given concerns for less tumor downstaging and increased toxicity. In the setting of the ongoing and likely prolonged

COVID-19 pandemic, we feel that these concerns must be re-evaluated, as **SCRT presents a well-validated alternative that will allow us to meet the needs of a greater number of potentially curable patients, at a time when our resources are severely and acutely constrained.**

## COVID-19: impact on cancer workforce and delivery of care.

Mayor S.
Lancet Oncol
2020 Apr 20; PMID: 32325021
Level of Evidence: 6 - No Data Cited
Type of Article: News
**Summary:** COVID-19 has added extra challenges to caring for oncology patients by adding the additional task of balancing the risk of infection with the need to continue treatments and by causing a reduction in the number of available health care workers. Oncology teams are adapting to minimize patient risk by **using regimens with less intensive treatment visits, relocating cancer teams away from general hospitals caring for COVID-19 patients, and utilizing telemedicine for outpatient consultations**.

## Cancer Treatment Adaptations in the COVID-19 Era.

Waisberg F, Enrico D, Angel M, Chacón M.
JCO Oncol Pract.
2020 Apr 23; PMID: 32324487
Level of Evidence: 5 - Expert Opinion
Type of Article: Editorial
**Summary:** This editorial written by 4 oncologists at the Alexander Fleming Cancer Institute in Argentina offers a set of recommendations on how to modify treatment approaches for patients diagnosed with cancer. These are namely: **Adapt treatment regimens to reduce patient visits, reduce treatment duration, and consider not prescribing treatment or delaying treatment initiation.**

## Management of advanced melanoma in the COVID-19 era.

Conforti C, Giuffrida R, Di Meo N, Zalaudek I.
Dermatol Ther.
2020 Apr 22; PMID: 32323399
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter
**Summarizing excerpt:** "Based on current considerations of the major oncologic societies ... we suggest (i) patients not discontinue ongoing target therapy or immunotherapy independently, (ii) in case of flu symptoms patients should not discontinue therapy but contact immediately their oncologist, (iii) perform a swab before starting or continuing medical chemotherapy/immunotherapy or in the case of major surgeries, (iv) in case of COVID-19 positive... patients, to evaluate patients on a case-by-case basis and... consider suspending a cycle of treatment for both treatments."

## Meeting the challenge of the 2019 novel coronavirus disease in patients with cancer.

Spiess PE, Greene J, Keenan RJ, Paculdo D, Letson GD, Peabody JW.
Cancer.
2020 Apr 23; PMID: 32324273

Level of Evidence: 5- Expert Opinion
Type of Article: Comment
**Summary:** This commentary proposes a 5-part strategy to cope with COVID-19 and future epidemics in patients with cancer. In brief, that is to screen and test quickly for advanced stages, withhold chemo or radiation treatment in COVID-19 symptomatic patients, update and standardize preventative measures for healthcare providers and family of the patient, develop a COVID-19-specific team in each cancer floor, and for both providers and the community to coordinate identification, triaging, and treatment for patients with cancer and COVID-19.

### Radiation therapy considerations during the COVID-19 Pandemic: Literature review and expert opinions.

Mohindra P, Buckey CR, Chen S, Sio TN, Rong Y.Mohindra P, et al.
J Appl Clin Med Phys.
2020 Apr 23; PMID: 32324950
Level of Evidence: 5 - Expert opinion
Type of Article: Review
**BLUF:** Cases for and against radiation therapy (RT) during COVID-19 (specifics highlighted below), **conclusions for RT during this pandemic remain unclear.**

**Summary:** This article is crafted as a debate between the two sides of the issue. The first half argues for **unchanged radiation therapy including concern for worse outcomes or less safe treatments if needed RT is delayed.** Additionally it is felt that RT **precautions already in place reduce infection risk and denying care would be unfair** considering the high prevalence of asymptomatic COVID-19 carriage. The second half **argues against RT therapy without significant changes to schedule and procedure**. Concerns include **exposure to both patients and staff** considering **evidence for increased risk and worse outcomes with COVID-19 in cancer patients**.

## Gastroenterology

### Low risk of covid-19 transmission in GI endoscopy.

Repici A, Aragona G, Cengia G, Cantù P, Spadaccini M, Maselli R, Carrara S, Anderloni A, Fugazza A, Pace F, Rösch T; ITALIAN GI-COVID19 Working Group
Gut
2020 Apr 22; PMID: 32321857
Level of Evidence: 4-Case series
Type of Article: Research
**BLUF:** Two case series conducted in Northern Italy suggest that **GI endoscopy may not be a major source of COVID-19 spread especially when precautions are taken**.

**Summary:** One case series examined patients at the endoscopy department of the Humanitas Research Hospital Rozzano (Milan), Italy between Jan 27-Mar 13. All patients were contacted by phone to ask about fever, respiratory symptoms or positive COVID-19 diagnosis in the 2 weeks following their appointment. **Of 802 patients completing the survey 1% had suggestive symptoms and 0.12% had laboratory confirmed COVID-19**. A second case series included 968 endoscopy healthcare workers (HCW) across 41 centers in Northern Italy. A web survey filled out in late March by center directors demonstrated a **4.3% infection rate among their HCW with 70% of centers reporting zero cases**. The average Italian HCW infection rate was 10% at the time. During the time period of the study **Italy began implementing policies to decrease clinic**

**volume and increase the use of PPE during endoscopic procedures.** Most of the worker infections were documented prior to this change.

### Expression risk of COVID-19 in Endoscopy ward: a Potential Risk for Gastroenterologists.

Hormati, Ahmad; Niya, Mohammad HK; Ghadir, Mohammadreza; Lankarani, Kamran B; Ajdarkosh, Hossein; Tameshkel, Fahimeh S; Zamani, Farhad
Infection Control & Hospital Epidemiology
2020 Apr 23; PMID: 32321601
Level of Evidence: 34 - Cohort, local non-random sampleSurvey
Type of Article: Letter to Editor

**BLUF:** Due to their high risk of COVID-19 transmission, 480 gastroenterologists from Iranian endoscopic wards were surveyed to understand the prevalence of COVID-19 in this subgroup. 10.6% were shown to have been diagnosed with COVID-19, confirmed with lab findings and this group was further sub-categorized by severity of disease.

**Summary:** This research group aimed to report the **prevalence of COVID-19 among gastroenterologists in Iranian endoscopic wards**, as they are at higher risk for COVID-19 transmission via fecal-oral and respiratory routes. A survey of **480 gastroenterologists** was done (data collection ended on 2020 Mar 26) which showed that **10.6% of them were diagnosed with COVID-19**, confirmed with lab findings. Those with COVID-19 were further categorized into mild (30%), moderate (60%), and severe (10%) disease. For gastroenterologists, it is recommended that they use at least a surgical mask and glasses in the endoscopy ward and use a N95 mask, glasses, shield, and latex gloves during an endoscopy procedure for prevention of COVID-19.

## Nephrology

### How we mitigate and contain COVID-19 outbreak in hemodialysis center (HD): lessons and experiences.

Su K, Ma Y, Wang Y, Song Y, Lv X, Wei Z, Shi M, Ding G, Shen B, Wang H
Infect Control Hosp Epidemiol
2020 Apr 23; PMID: 32321619
Level of Evidence: 5 - Expert opinion
Type of Article: Letter

**Summary:** People's Hospital in Wuhan offers its strategies for reducing the risk of COVID-19 in hemodialysis patients and staff. Implementing the below strategies correlated with a reduction in confirmed COVID-19 infections in patients and staff.

1) Screening every 2 weeks for fever, symptoms, and PCR evidence of SARS-CoV-2
2) Physical separation of confirmed, suspected, possible and unlikely COVID-19 patients within the dialysis patient group
3) Avoid changing dialysis shifts, units and staff to decrease cross-contamination

### Covid-19 pneumonia in a kidney transplant recipient successfully treated with Tocilizumab and Hydroxychloroquine.

Fontana F, Alfano G, Mori G, Amurri A, Lorenzo T, Ballestri M, Leonelli M, Facchini F, Damiano F, Magistroni R, Cappelli G.
Am J Transplant.
2020 Apr 23; PMID: 32324331

Level of Evidence: 5 – Case report
Type of Article: Case Reports
**BLUF:** COVID-19 pneumonia in a kidney transplant recipient with several comorbidities underwent successful treatment with hydroxychloroquine, IVIG, and a single dose of tocilizumab, with a reduction of immunosuppression.

**Abstract:**
Coronavirus disease 2019 (Covid-19) pneumonia has been poorly reported in solid-organ transplanted patients; prognosis is uncertain and best management unclear. We describe the case of a 61-year-old kidney transplant recipient with several co-morbidities who was hospitalized and later received a diagnosis of Covid-19 pneumonia; the infection was successfully managed with the use of hydroxychloroquine and a single administration of Tocilizumab, after immunosuppression reduction; the patient did not require mechanical ventilation. During the rapid spread of SARS-CoV-2 pandemic, transplant clinicians should be readily informed about new cases of Covid-19 pneumonia in solid-organ transplant recipients, with focus on therapeutic strategies employed and their outcome.

## Endocrinology

### COVID-19 and diabetes mellitus: what we know, how our patients should be treated now, and what should happen next.

Angelidi AM, Belanger MJ, Mantzoros CS
Metabolism
2020 Apr 19; PMID: 32320742
Level of Evidence: 5-Expert opinion
Type of Article: Editorial
**Summary:** A thorough review of current knowledge and gaps in knowledge on the associations between diabetes and SARS-CoV-2 infection including theoretical mechanisms for increased severity. The authors highlight the potential benefit of using telemedicine to proactively care for diabetes patients during this time and promote the recommendations of several American medical associations to maintain patients on prescribed RAAS inhibitors. They argue throughout that there is a need for "fast, efficient, but also unbiased, reliable, and valid studies" to fill our current knowledge gaps.

## Rheumatology

### What Is the True Incidence of COVID-19 in Patients With Rheumatic Diseases?

Ennio Giulio Favalli, Francesca Ingegnoli, Rolando Cimaz, Roberto Caporali
Ann Rheum Dis.
2020 Apr 22; PMID: 32321723
Level of Evidence: 3 - Cross sectional study
Type of Article: Correspondence
**Summary:** A survey was administered to 530 patients affected with a rheumatic disease in Milan, Italy to assess the impact of COVID-19. Only 3 patients were found to have mild COVID-19. 10 reported contact with cases of COVID-19 but did not develop symptoms. The low incidence of COVID-19 in this population is said to be attributed to the fact that 90% of these patients reported that they had adopted a preventive strategy against COVID-19 (social distancing and use of PPE).

## Hematology

### Haemophagocytic lymphohistiocytosis in COVID-19 cases?

Tveiten H, Aukrust P, Lehne G, Rodriguez JR, Skjønsberg OH
Tidsskr Nor Laegeforen
2020 Mar 23; PMID: 32321221
Level of Evidence: 5- Expert opinion
Type of Article: Opinion

**Summary excerpt:** Responding to a paper in the Lancet that "discuss[es] whether secondary haemophagocytic lymphohistiocytosis (HLH) can be triggered by coronavirus" the authors comment that "It is not inconceivable that a 'cytokine storm' ... could lead to the development of secondary haemophagocytic lymphohistiocytosis" and assert that HLH may be best treated by immunomodulating drugs, but that clear evidence is lacking. They **recommend that any treatment of suspected HLH in the context of COVID-19 "be undertaken in the form of randomised clinical trials**, which the World Health Organization recommends for all new, experimental therapy to combat this global disease."

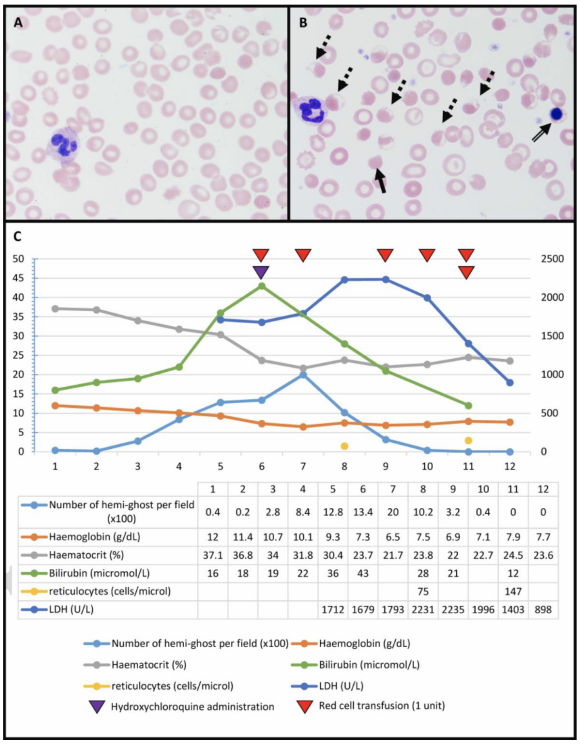
### COVID-19 infection and treatment with hydroxychloroquine cause severe haemolysis crisis in a patient with glucose-6-phosphate dehydrogenase deficiency.

Beauverd Y, Adam Y, Assouline B, Samii K.
Eur J Haematol.
2020 Apr 23; PMID: 32324284
Level of Evidence: 5- Case report
Type of Article: Case Reports

**BLUF:** Clinicians should remain wary of hydroxychloroquine-related haemolytic crisis in patients with G6PD deficiency, particularly in regions with high prevalence of the genetic disorder.

**Abstract:**
Glucose-6-phosphate dehydrogenase (G6PD) deficiency is an inherited genetic disorder caused by red cell enzymatic defects and is associated with haemolytic crisis when patients are exposed to oxidative agents (fava beans, drugs, infections). **Hydroxychloroquine is suspected to trigger haemolytic crisis in G6PD deficient patients**, and off-label administration of this drug to patients infected with the novel coronavirus (SARS-CoV-2) could cause concern. **We report here the first case of severe haemolytic crisis in a patient with G6PD deficiency, initiated by severe COVID-19 infection and hydroxychloroquine use.** With worldwide spread of COVID-19, especially in regions with a high prevalence of G6PD deficiency, our case should alert physicians to this possible correlation.

Figure 1: A) Normal peripheral blood smear before haemolytic crisis (100x magnification). B) Peripheral blood smear during haemolytic crisis with numerous hemi-ghost cells (dotted arrow), microspherocytes (plain arrow) and erythroblast (double arrow) (100x magnification). C) Timeline of blood parameters, blood smear, treatment administration, and blood transfusion.




| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Number of hemi-ghost per field (x100) | 0.4 | 0.2 | 2.8 | 8.4 | 12.8 | 13.4 | 20 | 10.2 | 3.2 | 0.4 | 0 | 0 |
| Haemoglobin (g/dL) | 12 | 11.4 | 10.7 | 10.1 | 9.3 | 7.3 | 6.5 | 7.5 | 6.9 | 7.1 | 7.9 | 7.7 |
| Haematocrit (%) | 37.1 | 36.8 | 34 | 31.8 | 30.4 | 23.7 | 21.7 | 23.8 | 22 | 22.7 | 24.5 | 23.6 |
| Bilirubin (micromol/L) | 16 | 18 | 19 | 22 | 36 | 43 | | 28 | 21 | | 12 | |
| reticulocytes (cells/microl) | | | | | | | | 75 | | | 147 | |
| LDH (U/L) | | | | | 1712 | 1679 | 1793 | 2231 | 2235 | 1996 | 1403 | 898 |

# Radiology

## Radiological Society of North America Expert Consensus Statement on Reporting Chest CT Findings Related to COVID-19. Endorsed by the Society of Thoracic Radiology, the American College of Radiology, and RSNA

Simpson S, Kay FU, Abbara S, Bhalla S, Chung JH, Chung M, Henry TS, Kanne JP, Kligerman S, Ko JP, Litt H

J Thorac Imaging
2020 Apr 21; PMID: 32324653
Level of Evidence: 5 – Expert Opinion
Type of Article: Research

**BLUF:** The authors, a group of radiologists, present a case for using standardized, inclusive, and specific language to describe CT findings related to COVID-19. **The authors cite the current lack of standardization, overlap of CT findings with other clinical syndromes,** and **mixed results of CT specificity for COVID-19** as reasons for adopting a standard COVID-19-related lexicon. Highlighted language choices include use of **"viral pneumonia" instead of explicit COVID-19 diagnosis** in cases of incidental findings without secondary confirmation, noting that **CT** is widely **not recommended for COVID-19 diagnosis**.

**Abstract:**
Routine screening CT for the identification of COVID-19 pneumonia is currently not recommended by most radiology societies. However, the number of CTs performed in persons under investigation (PUI) for COVID-19 has increased. We also anticipate that some patients will have incidentally detected findings that could be attributable to COVID-19 pneumonia, requiring radiologists to decide **whether or not to mention COVID-19 specifically** as a differential diagnostic possibility. We aim to **provide guidance to radiologists** in reporting CT findings potentially attributable to

COVID-19 pneumonia, including **standardized language to reduce reporting variability** when addressing the possibility of COVID-19. When typical or indeterminate features of COVID-19 pneumonia are present in endemic areas as an incidental finding, we **recommend contacting the referring providers to discuss the likelihood of viral infection**. These incidental findings do not necessarily need to be reported as COVID-19 pneumonia. In this setting, using the term **"viral pneumonia" can be a reasonable and inclusive alternative**. However, if one opts to use the term "COVID-19" in the incidental setting, consider the provided standardized reporting language. In addition, practice patterns may vary, and this document is meant to serve as a guide. Consultation with clinical colleagues at each institution is suggested to establish a consensus reporting approach. The goal of this expert consensus is to **help radiologists recognize findings of COVID-19 pneumonia** and aid their communication with other healthcare providers, assisting management of patients during this pandemic.

# Surgery

## SAGES and EAES recommendations for minimally invasive surgery during COVID-19 pandemic.

Francis N, Dort J, Cho E, Feldman L, Keller D, Lim R, Mikami D, Phillips E, Spaniolas K, Tsuda S, Wasco K, Arulampalam T, Sheraz M, Morales S, Pietrabissa A, Asbun H, Pryor A.
Surg Endosc.
2020 Apr 22; PMID: 32323016
Level of Evidence: 5 – Expert Opinion
Type of Article: Recommendations
**Summary:** There is very little evidence regarding the relative risks of minimally invasive surgery (MIS) versus the open approach, specific to COVID-19. It is strongly recommended, however, that consideration be given to the possibility of viral contamination to staff during open, laparoscopic, or robotic surgery and that protective measures are strictly employed for OR staff. Proven benefits of MIS of reduced length of stay and complications should be strongly considered.

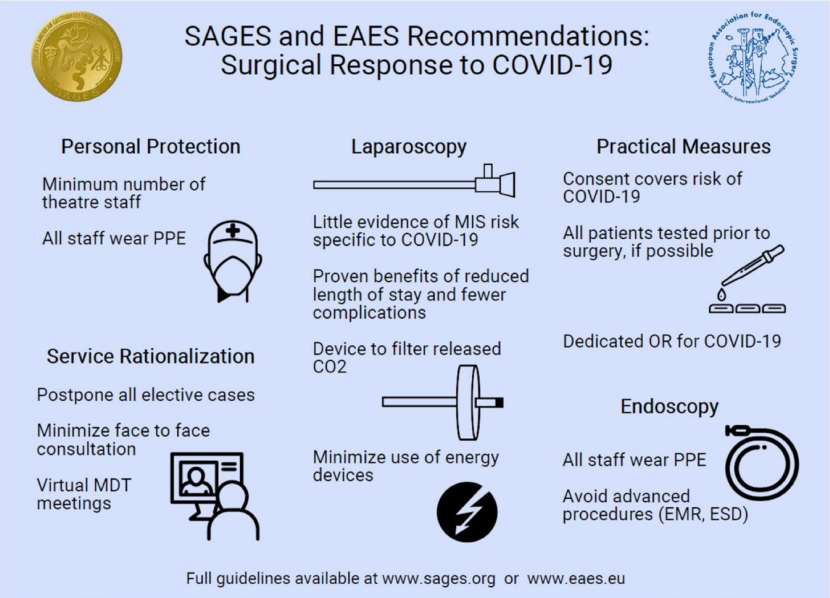



**Fig. 1** Infographic illustration of SAGES/EAES recommendations for COVID-19 and surgery

## ENT/Otolaryngology

### Esophageal oncologic surgery in SARS-CoV-2 (COVID-19) emergency.

Barbieri L, Talavera Urquijo E, Parise P, Nilsson M, Reynolds JV, Rosati R.
Dis Esophagus
2020 Apr 23, PMID: 32322892
Level of Evidence: 5 - Expert Opinion
Article Type: Research

**Summary:** The authors provide recommendations for the management of patients with esophageal cancer. Priority should be given to patients in which the tumor is causing symptoms or the patient has an advanced stage.

# Pediatrics

### Systemic Immunosuppressive Therapy for Inflammatory Skin Diseases in Children: Expert-Consensus-Based Guidance for Clinical Decision Making During the COVID-19 Pandemic

Reynolds SD, Mathur AN, Chiu YE, Brandling-Bennett HA, Pope E, Siegel MP, Holland KE, Paller AS, Siegfried EC, Tom WL, Lara-Corrales I, Tollefson MM, Maguiness S, Eichenfield LF, Sugarman J, Frieden IJ, Oza VS, Cipriano SD, Huang JT, Shah SD, Lauren CT, Castelo-Soccio L, McMahon P, Cordoro KM.Reynolds SD, et al.
Pediatric Dermatology
2020, April 22; PMID: 32320494
Level of Evidence: 5 - Expert opinion
Type of Article: Review

**BLUF**: Researchers with the Pediatric Dermatology COVID-19 Response Task Force address the concern over the susceptibility of children to COVID-19 while taking immunosuppressive therapies to treat inflammatory skin diseases. They acknowledge the lack of research in this area, and suggest the following:

- Avoid giving specific advice via mass communication, this can cause misinterpretation of information; however, the dissemination of general information to these patients is important.
- The continuation and initiation of immunosuppressive therapy is dependent on an individual's specific risk factors (such as stability of underlying disease).
- In patients with exposure to or confirmed COVID-19, systemic and biological medications should be discontinued (with the exception of systemic steroids).
- Patients with URI symptoms but unknown COVID-19 status should be handled on a case to case basis.
- Reduced laboratory monitoring is suggested for patients who have been taking long-term systemic agents without prior complications.

**Abstract:**
Background/objectives: The COVID-19 pandemic has raised questions about the approach to management of systemic immunosuppressive therapies for dermatologic indications in children. Given the absence of data to address concerns related to SARS-CoV-2 infection while on these agents in an evidence-based manner, a Pediatric Dermatology COVID-19 Response Task Force (PDCRTF) was assembled to offer time-sensitive guidance for clinicians.

Methods: A survey was distributed to an expert panel of 37 pediatric dermatologists on the PDCRTF to assess expert opinion and current practice related to three primary domains of systemic therapy: initiation, continuation, and laboratory monitoring.
Results: Nearly all respondents (97%) reported that the COVID-19 pandemic had impacted their decision to initiate immunosuppressive medications. The majority of pediatric dermatologists (87%) reported that they were pausing or reducing the frequency of laboratory monitoring for certain immunosuppressive medications. In asymptomatic patients, continuing therapy was the most popular choice across all medications queried. The majority agreed that patients on immunosuppressive medications who have a household exposure to COVID-19 or test positive for acute infection should temporarily discontinue systemic and biologic medications, with the exception of systemic steroids, which may require tapering.
Conclusions: The ultimate decision regarding initiation, continuation and laboratory monitoring of immunosuppressive therapy during the pandemic requires careful deliberation, consideration of the little evidence available, and discussion with families. Consideration of an individual's adherence to COVID-19 preventive measures, risk of exposure, and the potential severity if infected must be weighed against the dermatological disease, medication, and risks to the patient of tapering or discontinuing therapies.

# Palliative

## Virtual Reality as a Bridge in Palliative Care during COVID-19

Wang, Samuel S Y; Teo, Wendy Z W; Teo, Winnie Z Y; Chai, Yong Woon
J Palliat Med
2020 Apr 22; PMID: 32324080
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter
**Summarizing Excerpt:** “Virtual reality (VR) has a burgeoning role to play in palliative care, particularly during COVID-19 where physical interactions are strictly prohibited till death.1 Currently, video conferencing (VC) is the choice of communication, but recent advances in VR technologies has opened up experiential modalities that can push the boundaries of communication in ways that VC cannot offer.”

# R&D: Diagnosis & Treatments

## Current Diagnostics

### Characteristic CT findings distinguishing 2019 novel coronavirus disease (COVID-19) from influenza pneumonia.

Wang H, Wei R, Rao G, Zhu J, Song B.
Eur Radiol.
2020 Apr 22. Doi; PMID: 32323011
Level of Evidence: 4 - Case Series
Type of Article: Research

**BLUF:** CT can play a role in the diagnosis of COVID-19 in the case of no epidemic exposure, as well as be used for the differential diagnosis of influenza and COVID-19 with satisfactory accuracy. CT findings characteristic of COVID-19 included a patchy or combination of ground glass opacities and consolidation opacities with peripheral distribution and balanced lobe predominance.

**Abstract:**
Objectives: To investigate the different CT characteristics which may distinguish influenza from 2019 coronavirus disease (COVID-19).
Methods: A total of 13 confirmed patients with COVID-19 were enrolled from January 16, 2020, to February 25, 2020. Furthermore, 92 CT scans of confirmed patients with influenza pneumonia, including 76 with influenza A and 16 with influenza B, scanned between January 1, 2019, to February 25, 2020, were retrospectively reviewed. Pulmonary lesion distributions, number, attenuation, lobe predomination, margin, contour, ground-glass opacity involvement pattern, bronchial wall thickening, air bronchogram, tree-in-bud sign, interlobular septal thickening, intralobular septal thickening, and pleural effusion were evaluated in COVID-19 and influenza pneumonia cohorts.
Results: Peripheral and non-specific distributions in COVID-19 showed a markedly higher frequency compared with the influenza group ($p < 0.05$). Most lesions in COVID-19 showed balanced lobe localization, while in influenza pneumonia they were predominantly located in the inferior lobe ($p < 0.05$). COVID-19 presented a clear lesion margin and a shrinking contour compared with influenza pneumonia ($p < 0.05$). **COVID-19 had a patchy or combination of GGO and consolidation opacities**, while a cluster-like pattern and bronchial wall thickening were more frequently seen in influenza pneumonia ($p < 0.05$). The lesion number and attenuation, air bronchogram, tree-in-bud sign, interlobular septal thickening, and intralobular septal thickening were not significantly different between the two groups (all $p > 0.05$).
Conclusions: Though viral pneumonias generally show similar imaging features, there are **some characteristic CT findings which may help differentiating COVID-19 from influenza pneumonia**.

### In Defense of Evidence-Based Medicine for the Treatment of COVID-19 ARDS.

Rice TW, Janz DR.Rice TW, et al.
Ann Am Thorac Soc.
2020 Apr 22; PMID: 32320268
Level of Evidence: 5 - Expert Opinion
Type of Article: Article in Press

**Summary:** During the COVID-19 epidemic numerous studies are being published, but too many of those articles are limited based on a small sample size or uncontrolled experiments without consent or regulatory oversight. With severe acute respiratory failure already being a challenge to intensivists

worldwide, **the authors urges clinicians to fall back on good evidenced based medicine when managing and treating patients from ARDS**. As the authors remind clinicians, "Not giving a medication lacking high quality evidence of benefit does not equal just standing there and doing nothing. [On] the contrary, providing evidence based critical care is more than just doing something for our patients. It is providing them with the best possible chance of surviving without complications and not putting them at risk for poor outcomes from non-evidence based care."

## Diagnostic Options for Coronavirus Disease 2019 (COVID-19).

Xiao Y, Peng Z, Tan C, Meng X, Huang X, Wu A, Li C.Xiao Y, et al.
Infect Control Hosp Epidemiol.
2020 Apr 23; PMID: 32321609
Level of Evidence: 5- Expert Opinion
Type of Article: Letter

**Summary**: This letter discusses some challenges posed by COVID-19, highlighting that diagnoses may be missed due to false negative tests. They made a case for using more than one form of diagnostic testing. They continue to describe each of the following test options: Nucleic acid amplification test, viral sequences, serological testing, rapid antigen tests, and imaging examinations. They discuss various factors of each such as cost and speed. They aim to inform clinicians to more effectively decide how to approach COVID-19 patients.

## The continuing evolution of COVID-19 imaging pathways in the UK: a British Society of Thoracic Imaging expert reference group update

Hare, S. S., Rodrigues, J., Nair, A., Jacob, J., Upile, S., Johnstone, A., Mcstay, R., Edey, A., & Robinson, G.
Clin Radiol.
2020 Apr 15; PMID: 32321645
Level of Evidence: 5 – Expert Opinion
Type of Article: Editorial

**BLUF:** The chest radiograph along with computed tomography and CT angiogram will be important in the diagnosis of COVID-19 as well as emerging thrombotic incidents.

**Summary:** The chest radiograph (CXR) has emerged as the frontline diagnostic imaging test, in conjunction with clinical history and key blood biomarkers: C-reactive protein (CRP) and lymphopenia. However, any design of local diagnostic imaging algorithms would be contingent on RT-PCR sensitivity. Computed tomography (CT) can also be justifiably used in a cohort of patients with high clinical probability but suspected false-negative RT-PCR results. Although sensitive, CT findings of COVID-19 are not specific. When performed, a low-dose unenhanced CT technique should be utilized and consideration given to an additional CT pulmonary angiogram (CTPA). The need for CTPA is to ensure occult pulmonary embolism (PE) is excluded, particularly in light of increasing reports of pro-thrombotic risk in COVID-19.

# Developments in Treatments

## Anti-SARS-CoV-2 virus antibody levels in convalescent plasma of six donors who have recovered from COVID-19.

Zhang L, Pang R, Xue X, Bao J, Ye S, Dai Y, Zheng Y, Fu Q, Hu Z, Yi Y.Zhang L, et al.
Aging (Albany NY).
2020 Apr 22, PMID: 32320384
Level of Evidence: 4 - Case Series
Type of Article: Research

**BLUF:** A 64 year-old female received convalescent plasma (CP) and was removed from her mechanical ventilation 11 days later. Serologies of six CP donors who recently recovered from COVID-19 were analyzed: five out of six of the donors had high IgG titers (≥1:320); five out of the six donors had positive IgM titers. These results may help inform CP donor screening protocols of cutoff titer values.

**Abstract**:
Background: Anti-SARS-CoV-2 virus **antibody levels in convalescent plasma (CP)**, which may be useful in severe Anti-SARS-CoV-2 virus infections, have been rarely reported.
Methods: Anti-SARS-CoV-2 antibodies including IgM and IgG were measured by two enzyme-linked immunosorbent assays (ELISA) in convalescent plasma from six donors who have recovered from coronavirus disease 2019 (COVID-19) in Nanjing, China. **CP was also utilized for the treatment of one severe COVID-19 patient.**
Results**:** A total of eight donors were considered for enrollment; two of them were excluded because of ineligible routine check. Of the six remaining participants, **five samples were tested weakly positive by the IgM ELISA**. Meanwhile, **high titers of IgG were observed in five samples**. The patient treated with CP did not require mechanical ventilation 11 days after plasma transfusion, and was then transferred to a general ward.
Conclusions: Our serological findings in convalescent plasma from recovered patients may help facilitate understanding of the SARS-CoV-2 infection and **establish CP donor screening protocol in COVID-19 outbreak.**

## Operational protocol for donation of anti-COVID-19 convalescent plasma in Italy.

Franchini M, Marano G, Velati C, Pati I, Pupella S, Liumbruno GM.
Vox Sang.
2020 Apr 23; PMID: 32324899
Level of Evidence: 6 - No data cited
Type of Article: Letter to the Editor

**Summary:** The usage of convalescent plasma from recovered COVID-19 patients containing antibodies against SARS-CoV-2 as a COVID-19 treatment is currently being explored in Italy. To donate plasma, **donors must have documentation of COVID-19 infection and recovery**, negative history of blood component transfusion, negative results for parvovirus B19 and hepatitis A & E. The sample must be processed with a pathogen reduction method, clearly labeled, and kept separately from other blood products.

## Some drugs for COVID-19

No authors listed
Med Lett Drugs Ther
2020 Apr 6; PMID: 32324177

Level of Evidence: 5 - Literature Review
Type of Article: Comment
**Summary:** In this brief review, the authors summarize a number of involved or questioned drugs in relation to the COVID-19 pandemic such as angiotensin-converting enzyme inhibitors (ACE), corticosteroids, or immunomodulators.

## Tocilizumab: A new opportunity in the possible therapeutic arsenal against COVID-19.

Ortiz-Martínez Y.Ortiz-Martínez Y.
Travel Med Infect Dis.
2020 Apr 20; .PMID: 32325121
Level of Evidence: 5 - Mechanism Based Reasoning
Type of Article: Letter to the Editor
**BLUF: Tocilizumab** has demonstrated some therapeutic utility for COVID-19 and **may be an option for severe disease but evidence is currently limited.**

**Summary:** In response to an article proposing treatments for COVID-19 the authors discuss **Tocilizumab as a potential option**, particularly **for severe complications** including lung injury and cytokine storm. They reference **a Chinese study (n=21) which showed decreased inflammatory markers and earlier discharge**, an **Italian case study showing partial resolution on CT**, and another **case study from Switzerland** whose subject was on an IL-2R blocker and **developed a mild case despite other comorbidities**. Additionally, Tocilizumab is currently the **subject of a single arm phase 2 trial in Italy.** For all these reasons they feel Tocilizumab is a promising prospect.

## Prevention and Therapy of COVID-19 via Exogenous Estrogen Treatment for Both Male and Female Patients.

Suba Z.
J Pharm Pharm Sci
2020 Apr 23; PMID: 32324533
Level of Evidence: 5 - Expert Opinion
Type of Article: Commentary
**Summary:** Based on observational studies in China and U.S. that suggest that COVID-19 has a higher infection and mortality rate in men and women and mouse studies of SARS that suggested that estrogen receptor (ER) signalling contributed to improved survival of female mice, the author speculates that insufficient ER signalling may contribute to the excessive inflammatory response and resultant respiratory distress in COVID-19 cases. Premarin, an estrogen preparation, is recommended as a potential preventative agent for COVID-19.

**Abstract:** The presented work summarizes the results of studies underlining the crucial role of estrogen receptor (ER) signaling in both innate and adaptive immune responses as well as in tissue repairing processes during respiratory virus infection. Experimental studies justify that there are no quite different pathways for immune defenses against respiratory virus infection in males and females, but rather the physiologically weaker ER signaling results in an increased morbidity and mortality among men with pulmonary virus infection. In animal experiments, estrogen treatment silences the inflammatory reactions and decreases virus titers leading to improved survival rate; it seems to be an ideal prevention and therapy against COVID-19. We should overcome the widespread reluctance to estrogen therapy as we have a unique estrogen formula; Premarin deriving from natural

sources. Premarin can exert similar ER upregulative and gene repairing power like endogenous estrogen without any risk for adverse reactions. Premarin is capable of stopping the COVID-19 pandemic.

## Potential use of hydroxychloroquine, ivermectin and azithromycin drugs in fighting COVID-19: trends, scope and relevance.

Choudhary R, Sharma AK, Choudhary R.
New Microbes New Infect.
2020 Apr 22; PMID: 32322397
Level of Evidence: 5 - Qualitative Data
Type of Article: Literature Review

**Summary**: The authors review three classes of drugs that may potentially be effective for COVID-19. However, it remains unclear which drug has better efficacy either as monotherapy or in combination with other drugs. Some in vitro and poorly controlled or uncontrolled clinical trials revealed hydroxychloroquine has activity against SARS-CoV-2. Studies show azithromycin may work similarly to hydroxychloroquine. Ivermectin can inhibit viral replication under *in vitro* conditions.

## Vaporization, bioactive formulations and a marine natural product: different perspectives on antivirals.

Manning TJ, Thomas-Richardson J, Cowan M, Beard T.Manning TJ, et al.
Drug Discov Today.
2020 Apr 20; PMID: 32325124
Level of Evidence: 5 - Mechanism-Based Reasoning
Type of Article: Research

**Summary:** This is a **preliminary discussion of antiviral delivery via vaporization**. The authors tested **varying concentrations of Hydroxychloroquine and Bryostatin**, a marine natural product with antiviral activity in a base formulation. They demonstrated that **vaporization was an effective way to deliver fractions of these components to an aqueous medium** (specific concentrations not given). They also discuss mechanisms whereby the base itself may have antiviral and bioactive properties. These in-vitro studies suggest **vaporization may be effective for antiviral delivery**.

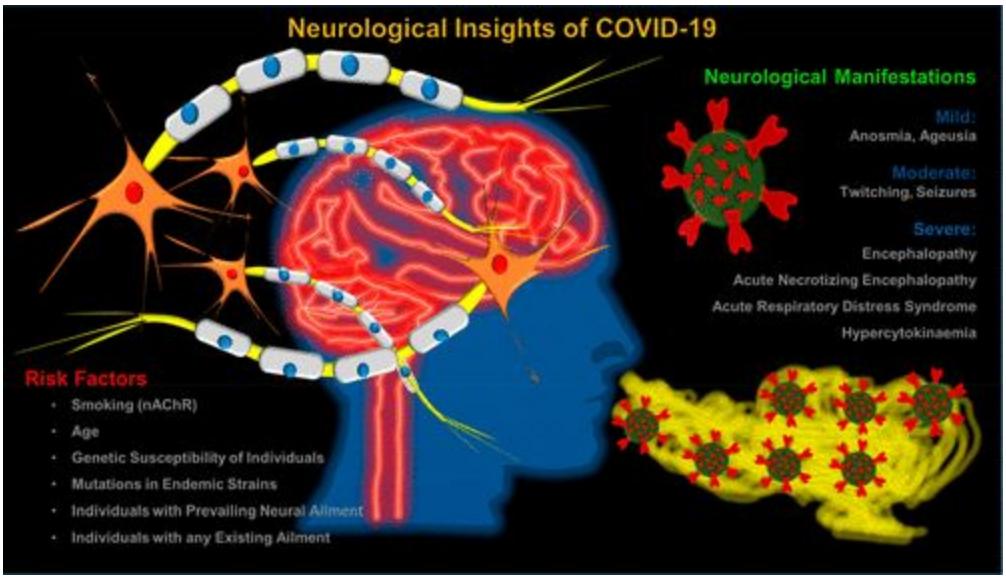
## Neurological Insights of COVID-19 Pandemic.

Das G, Mukherjee N, Ghosh S
ACS Chem Neurosci
2020 Apr 22; PMID: 32320211
Level of Evidence: 5 - Expert Opinion
Type of Article: Viewpoint

**BLUF**: Authors at the CSIR-Indian Institute of Chemical Biology examine SARS-CoV-2's uniquely strong binding affinity for the ACE2 protein, neurological systems ranging from anosmia to severe encephalopathy (figure 1), the observed cytokine storm, the link between infection severity and smoking, and the implications of ethnicity and regional diversity on susceptibility. They suggest consideration of peptide-based therapies, epitope-targeting antibody drugs, and use of the receptor-binding domain (RBD) in a subunit vaccine as potential therapeutic targets.

**Abstract**: The novel coronavirus SARS-CoV-2, which was identified after a recent outbreak in Wuhan, China, in December 2019, has kept the whole world in tenterhooks due to its severe life-threatening nature of the infection. The virus is unlike its previous counterparts, SARS-CoV and MERS-CoV, or anything the world has encountered before both in terms of virulence and severity of

the infection. If scientific reports relevant to the SARS-CoV-2 virus are noted, it can be seen that the virus owes much of its killer properties to its **unique structure that has a stronger binding affinity with the human angiotensin-converting enzyme 2 (hACE2) protein, which the viruses utilize as an entry point to gain accesses to its hosts**. Recent reports suggest that it is not just the lung that the virus may be targeting; the **human brain** may soon emerge as the new abode of the virus. Already instances of patients with COVID-19 have been reported with **mild (anosmia and ageusia) to severe (encephalopathy) neurological manifestations**, and if that is so, then it gives us more reasons to be frightened of this killer virus. Keeping in mind that the situation does not worsen from here, **immediate awareness and more thorough research regarding the neuroinvasive nature of the virus** is the immediate need of the hour. Scientists globally also need to up their game to design more specific therapeutic strategies with the available information to counteract the pandemic. In this Viewpoint, we provide a brief outline of the currently known neurological manifestations of COVID-19 and discuss some probable ways to design therapeutic strategies to overcome the present global crisis.




## Neuropsychiatric adverse events of chloroquine: a real-world pharmacovigilance study using the FDA Adverse Event Reporting System (FAERS) database.

Sato K, Mano T, Iwata A, Toda T.Sato K, et al.
Biosci Trends
2020 Apr 22.; PMID: 32321905
Level of Evidence: 4 - Retrospective Review
Type of Article: Research

**Summary :** The authors of this study used a large self-reporting database to study the neuropsychiatric adverse events (AE) associated with chloroquine (or hydroxychloroquine) between the fourth quarter of 2012 and the fourth quarter of 2019. There were 2,389,474 AE cases, among which 520 cases developed neuropsychiatric AE following the use of chloroquine. Exposure to chloroquine was associated with a statistically significant high reporting of amnesia, delirium, hallucinations, depression, and loss of consciousness, (lower 95% confidence interval of the adjusted ROR > 1).

## To consider or not antimalarials as a prophylactic intervention in the SARS-CoV-2 (COVID-19) pandemic

Spinelli, FR, Ceccarelli F, Di Franco M
Ann Rheum Dis
2020 Apr 22; PMID: 32241791
Level of Evidence: 5 – Expert Opinion
Type of Article: Letter

**Summary:** A small pilot study of patients from China with COVID-19 showed no difference between chloroquine and hydroxychloroquine (HCQ) treated patients compared with a control group in terms of negative conversion rate of pharyngeal swabs, duration of fever and radiographic progression on CT chest images. Given the interest, large clinical trials to assess the efficacy and safety of antimalarial treatments in patients with COVID-19 infection are needed.

## Drug Development and Medicinal Chemistry Efforts Toward SARS-Coronavirus and Covid-19 Therapeutics.

Ghosh AK, Brindisi M, Shahabi D, Chapman ME, Mesecar AD.
ChemMedChem.
2020 Apr 23; PMID: 32324951
Level of Evidence: 5 – Mechanism-Based Reasoning
Type of Article: Literature Review

**Summary**: Biochemical events critical to the coronavirus replication cycle provided a number of attractive targets for drug development: including the spike protein that binds to host cell surface receptors, proteolytic enzymes essential for processing polyproteins into mature viruses, and RNA dependent RNA polymerase. This paper reviews potential therapeutic targets and notes important kinetic properties that must be taken into consideration for drug design.

## Recent progress and challenges in drug development against COVID-19 coronavirus (SARS-CoV-2) - an update on the status.

El-Aziz TMA, Stockand JD.El-Aziz TMA, et al.
Infect Genet Evol.
2020 Apr 19;.PMID: 32320825
Level of Evidence: 5 - Mechanism-based reasoning
Type of Article: Review

**BLUF:** Vaccine development is expected to extend to the end of the year. Many drugs are currently being tested for its effectiveness against COVID-19-associated pathologies: Favilavir is used in various countries for symptomatic relief (not approved by U.S. FDA); antimalarial drugs are being used for severe, hospitalized patients (FDA Approved); Remdesivir is undergoing clinical trials. The following drugs have shown efficacy against COVID-19 either *in vitro* or in case reports, but they have not been approved for usage: antiretroviral drugs (lopinavir/ritonavir, darunavir), ivermectin, and Tociluzumab.

**Abstract**:
Coronaviruses are a large group of viruses known to cause illnesses that vary between the common cold and more severe diseases to include severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS). A novel coronavirus was identified in December 2019 in Wuhan city, Hubei province, China. This virus represents a new strain that has not been previously identified in humans. The virus is now known as the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the resulting disease is called coronavirus disease 2019 (COVID-19). The World Health Organization (WHO) declared the novel coronavirus outbreak a global pandemic in March 2020. Despite rigorous global containment and quarantine efforts, the incidence of COVID-19 continues to rise, with more than 1,948,617 laboratory-confirmed cases and over 121,846 deaths worldwide. Currently, no specific medication is recommended to treat COVID-19 patients. However, governments and pharmaceutical companies are **struggling to quickly find an effective drug to defeat the coronavirus**. In the current review, we summarize the existing state of knowledge about COVID-19, available medications, and treatment options. **Favilavir is an antiviral drug that is approved in Japan for common influenza treatment and is now approved to treat symptoms of COVID-19 in China.** Moreover, Chloroquine and hydroxychloroquine, drugs used to treat malaria and arthritis, respectively, were recommended by the National Health Commission of the People's Republic of China for treatment of COVID-19. Presently, **chloroquine and hydroxychloroquine are under investigation by the US Food and Drug Administration (FDA) as a treatment for COVID-19**. The first COVID-19 **vaccine is not expected to be ready for clinical trials before the end of the year.**

## Urgent avenues in the treatment of COVID-19: Targeting downstream inflammation to prevent catastrophic syndrome

Quartuccio, Luca; Semerano, Luca; Benucci, Maurizio; Boissier, Marie-Christophe; De Vita, Salvatore
J Joint Bone Spine
2020 May Issue; PMID: 32321634
Level of Evidence: 5 - Mechanism-Based Reasoning
Type of Article: Editorial
**Summarizing Excerpt:** "First, **giving priority to targeting the inflammatory response to the COVID19 infection appears more feasible in some patient subsets,** seemingly the more severe ones, when disease has already evolved, and likely also for those in earlier stages, but at higher risk. **Secondly, when available, concomitant etiological, antiviral therapy remains in any case a cornerstone** in all patients. Immunosuppressant can make the viral clearance more difficult, and an antiviral therapy should be combined when an immunosuppressant is given, in the absence of additional data at present. Thirdly, besides IL-6 pathways blockers, other biologic drugs currently used by rheumatologists may be employed in selected patients. **In our opinion, targeting IL1 and complement activation have a strong rationale."**

## Chloroquine and Hydroxychloroquine for the Prevention or Treatment of Novel Coronavirus Disease (COVID-19) in Africa: Caution for Inappropriate Off-Label Use in Healthcare Settings.

Abena PM, Decloedt EH, Bottieau E, Suleman F, Adejumo P, Sam-Agudu NA, Muyembe TamFum JJ, Seydi M, Eholie SP, Mills EJ, Kallay O, Zumla A, Nachega JB.
Am J Trop Med Hyg.
2020 Apr 22; PMID: 32323646
Level of Evidence: 5 - Expert Opinion
Type of Article: Perspective piece

**BLUF:** These authors suggest that some African nations may be at risk of poor health outcomes due to poorly regulated off-label distribution of chloroquine and hydroxychloroquine as a result of shortages amidst a growing popularity of these drugs during the COVID-19 pandemic.

**Summary:**In this perspective piece, the authors warn of downstream consequences of the growing popularity and widespread use of Chloroquine and Hydroxychloroquine in the treatment of COVID-19, particularly in African countries. Some of these consequences include potential drug resistance in the treatment of Plasmodium falciparum malaria and more importantly shortages of these medications and thus widespread use of poorly regulated off-label CQ/HCQ due to the relatively weak drug monitoring systems in sub-saharan African countries. The authors call for a collaborative network for coordinated production, distribution and surveillance of any approved COVID-19 medications and recommend African countries to implement more rigorous prescription monitoring protocols.

## Is GSK3β a molecular target of chloroquine treatment against COVID-19?

Embi, Mohammed N; Ganesan, Nagesswary, Sidek, Hasidah M
Drug Discoveries & Therapeutics
2020 Apr 21; PMID: 32321878
Level of Evidence: 5 - Mechanism Based Reasoning
Type of Article: Letter
**BLUF:** This research group uses experimental animal melioidosis to make a case that chloroquine modulates cytokine levels via the phosphorylation and subsequent inhibition of glycogen synthase kinase-3β (GSK3β) signalling in the liver. The reported efficacy of chloroquine in recent clinical trials as a treatment for COVID-19 may also be due to a similar mechanism of action.

**Abstract:**
The recent clinical trial reports pertaining to the efficacy of chloroquine and hydroxychloroquine against COVID-19 albeit yet to be validated with larger clinical trials, have sparked much interest globally to evaluate whether this anti-malarial drug can be repurposed for the treatment of COVID-19. In addition to its anti-viral activity, the anti-inflammatory activity of chloroquine may also contribute to its efficacy. Based on our data obtained from an **animal infection model of melioidosis** (a disease caused by the bacteria Burkholderia pseudomallei), **treatment with chloroquine can result in the phosphorylation and consequent inhibition of glycogen synthase kinase-3β (GSK3β).** This serine/threonine protein kinase is now recognised as a point of convergence for host inflammatory response. In view of this, it is **plausible** that the mechanism for the **anti-inflammatory effect of chloroquine against COVID-19 involves inhibition of host GSK3β**.

## Mesenchymal stem cells as a potential treatment for critically ill patients with coronavirus disease 2019.

Ji F, Li L, Li Z, Jin Y, Liu W.Ji F, et al.
Stem Cells Transl Med.
2020 Apr 22; PMID: 32320535
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter
**Summary:** Mesenchymal stem cells (MSCs), currently in study for its potential to resolve acute respiratory distress (ARDS) in a clinical trial, should be considered as a potential treatment for COVID-19 patients. Its potential is being evaluated for COVID-19 patients.

## Plea for multitargeted interventions for severe COVID-19.

Gaborit BJ, Bergmann JF, Mussini C, Arribas JR, Behrens G, Walmsley S, Pozniak A, Raffi F.
Lancet Infect Dis.
2020 Apr 20; PMID: 32325035
Level of Evidence: 5 – Expert Opinion
Type of Article: Correspondence

**Summary**: Most clinical trials to date have assessed single drugs with a clinical endpoint using the WHO seven point ordinal scale. The author urges investigators to join their efforts in proposing, rather than adaptive or sequential studies of a single strategy, combined approaches through multifactorial designs. It is likely both antivirals and blockage of inflammatory pathways are needed to optimize responses.

## Structure-based design of antiviral drug candidates targeting the SARS-CoV-2 main protease.

Dai, Wenhao; Zhang, Bing; Su, Haixia; Li, Jian; Zhao, Yao; Xie, Xiong; Jin, Zhenming; Liu, Fengjiang; Li, Chunpu; Li, You; Bai, Fang; Wang, Haofeng; Cheng, Xi; Cen, Xiaobo; Hu, Shulei; Yang, Xiuna; Wang, Jiang; Liu, Xiang; Xiao, Gengfu; Jiang, Hualiang; Rao, Zihe; Zhang, Lei-Ke; Xu, Yechun; Yang, Haitao; Liu, Hong
Science
22 Apr 2020; PMID: 32321856
Level of Evidence: 5 - Mechanism-Based Reasoning
Type of Article: Research

**BLUF:** This group designed and synthesized two novel inhibitors **(11a and 11b)** targeting the SARS-CoV-2 Mpro protease, which plays an essential role in the life cycle of COVID-19. These were evaluated for SARS-CoV-2 Mpro inhibition activity with a (FRET)-based cleavage assay and in vitro, for their pharmacokinetic properties, and for their in vivo toxicity, yielding a compound (**11a**) that shows promise to be a good candidate for further clinical studies.

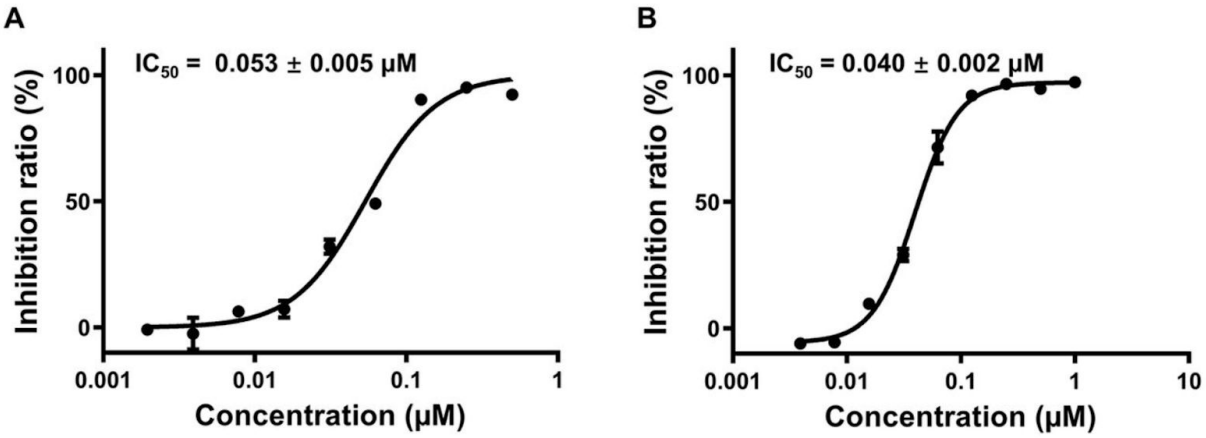



**Fig. 2 Inhibitory activity profiles of compounds 11a (A) and 11b (B) against SARS-CoV-2 Mpro.**

**Abstract:**

SARS-CoV-2 is the etiological agent responsible for the global COVID-19 outbreak. The **main protease (Mpro) of SARS-CoV-2** is a **key enzyme** that plays a pivotal role in mediating viral replication and transcription. We designed and synthesized two lead compounds (**11a** and **11b**)

targeting Mpro. Both exhibited **excellent inhibitory activity and potent anti-SARS-CoV-2 infection activity**. The X-ray crystal structures of SARS-CoV-2 Mpro in complex with **11a** or **11b**, both determined at 1.5 Å resolution, showed that the **aldehyde groups of 11a and 11b are covalently bound to Cys145 of Mpro**. Both compounds showed **good PK properties in vivo**, and **11a** also exhibited **low toxicity**, suggesting that these compounds are promising drug candidates.

## Pharmacologic Therapy for COVID-19 Infection.

Nusbaum, Neil
J Community Health
2020 Apr 20; PMID: 32314081
Level of Evidence: 6 - No data cited
Type of Article: Comment

**BLUF:** There may already be a large cohort of patients available who unintentionally received treatments for other potential diagnoses such as influenza, while actually having COVID-19. Retrospective case-control studies of these patients can be used to identify differences in COVID-19 mortality rates related to these medications (including antipyretics, antibacterial drugs, antiviral drugs, and/or corticosteroids), which may help identify existing medications that can be repurposed to treat COVID-19 patients.

**Abstract:** The COVID-19 pandemic has focused attention on issues of epidemiology, public health, and vaccine design. I submit that attention to COVID-19 pharmacologic therapy needs similar emphasis, including **identifying any existing medications that can be repurposed to treat COVID-19 patients**.

# Mental Health & Resilience Needs

## Affective temperament, attachment style, and the psychological impact of the COVID-19 outbreak: an early report on the Italian general population

Moccia L, Janiri D, Pepe M, Dattoli L, Molinaro M, De Martin V, Chieffo D, Janiri L, Fiorillo A, Sani G, Di Nicola M.Moccia L, et al.
Brain Behav Immun
2020 Apr 20; PMID: 32325098
Level of Evidence: 4 - Cross-sectional
Type of Article: Research

**Summary:** This study investigated possibly the first psychological impact of COVID19 in Italy by identifying the psychological distress (using the Kessler 10 Psychological Distress Scale) from early phases of COVID-19 by assessing the general Italian population of their temperament and adult style attachment (AAS) through an online survey of n= 500 participants ages 18-75. The results showed the risk factor for mild distress was an anxious temperament (OR=1.39; p=0.008), and risk factors for mod-severe distress were “cyclothymic (OR=1.24; p<0.001), depressive (OR=1.52; p<0.001) and anxious (OR: 1.58; p = 0.002) temperaments, and the attachment style questionnaire (ASQ) subscales of “Need for approval” (OR: 1.08; p = 0.01).” While the male gender (OR: 0.5; p = 0.012) was a protective factor for mild distress, and the “ASQ “Confidence” (OR: 0.89; p = 0.002) and “Discomfort with closeness” subscales were protective (OR: 0.92; p = 0.001).”

**Abstract:** The outbreak of COVID-19 is severely affecting mental health worldwide, although individual response may vary. **This study aims to investigate the psychological distress perceived by the Italian general population during the early phase of the COVID-19 pandemic, and to analyze affective temperament and adult attachment styles as potential mediators**. Through an **online survey, we collected sociodemographic and lockdown-related information** and evaluated distress, temperament, and attachment using the Kessler 10 Psychological Distress Scale (K10), the Temperament Evaluation of Memphis, Pisa, Paris and San Diego-Autoquestionnaire short version (TEMPS-A) and the Attachment Style Questionnaire (ASQ). **In our sample (n=500), 62% of the individuals reported no likelihood of psychological distress, whereas 19.4% and 18.6% displayed mild and moderate-to-severe likelihood.** Cyclothymic (OR: 1.24; p<0.001), depressive (OR: 1.52; p<0.001) and anxious (OR: 1.58; p=0.002) temperaments, and the ASQ "Need for approval" (OR: 1.08; p=0.01) were risk factors for moderate-to-severe psychological distress compared to no distress, while the ASQ "Confidence" (OR: 0.89; p=0.002) and "Discomfort with closeness" were protective (OR: 0.92; p=0.001). Cyclothymic (OR: 1.17; p=0.008) and depressive (OR: 1.32; p=0.003) temperaments resulted as risk factors in subjects with moderate-to-severe psychological distress compared to mild distress, while the ASQ "Confidence" (OR: 0.92; p=0.039) and "Discomfort with closeness" (OR: 0.94; p=0.023) were protective. Our data indicated that a relevant rate of individuals may have experienced psychological distress following the COVID-19 outbreak. Specific affective temperament and attachment features predict the extent of mental health burden. To the best of our knowledge, these are the first data available on the psychological impact of the early phase of the COVID-19 pandemic on a sizeable sample of the Italian population. Moreover, our study is the first to investigate temperament and attachment characteristics in the psychological response to the ongoing pandemic. Our results provide further insight into developing targeted intervention strategies.

## Generalized anxiety disorder, depressive symptoms and sleep quality during COVID-19 outbreak in China: a web-based cross-sectional survey.

Huang Y, Zhao N
Psychiatry Res.
2020 Apr 12; PMID: 32325383
Level of Evidence: 4 - Cross-sectional study
Type of Article: Research

**BLUF:** To investigate the impact of the Covid-19 pandemic on mental health in China, an online survey was administered to 7,236 self-selected participants from the Chinese public, collecting information on demographics, generalized anxiety disorder, depressive symptoms, and sleep quality. There was a high level of generalized anxiety disorder among the public (35%), and this was associated with time spent focusing on COVID-19. Poor sleep quality was particularly prevalent in healthcare workers (23.6%), as compared to teachers/student (14.3%) and institution/enterprise workers (12.7%).

**Abstract:** China has been severely affected by Coronavirus Disease 2019(COVID-19) since December, 2019. We aimed to assess the mental health burden of Chinese public during the outbreak, and to explore the potential influence factors. Using a web-based cross-sectional survey, we collected data from 7,236 self-selected volunteers assessed with demographic information, COVID-19 related knowledge, generalized anxiety disorder (GAD), depressive symptoms, and sleep quality. **The overall prevalence of GAD, depressive symptoms, and sleep quality of the public were 35.1%, 20.1%, and 18.2%,** respectively. **Younger people reported a significantly higher prevalence of GAD and depressive symptoms than older people.** Compared with other occupational group, **healthcare workers were more likely to have poor sleep quality.** Multivariate logistic regression showed that age (< 35 years) and **time spent focusing on the COVID-19 (≥ 3 hours per day) were associated with GAD**, and healthcare workers were at high risk for poor sleep quality. Our study identified a major mental health burden of the public during the COVID-19 outbreak. Younger people, people spending too much time thinking about the outbreak, and healthcare workers were at high risk of mental illness. Continuous surveillance of the psychological consequences for outbreaks should become routine as part of preparedness efforts worldwide.

## Self-harm and COVID-19 Pandemic: An emerging concern - A report of 2 cases from India.

Sahoo S, Rani S, Parveen S, Pal Singh A, Mehra A, Chakrabarti S, Grover S, Tandup C
2020 Apr 16; PMID: 32325391
Asian J Psychiatr.
Level of Evidence: 4 - Case report
Type of Article: Research

**BLUF:** Case report of two suidice attempts due to distress caused by the COVID-19 pandemic. In both cases, the patients developed excessive worry about exposure to and contraction of COVID-19. Both patients closely followed the news, which highlighted the mortality rate and potential for a painful death. Over about 2 weeks the patients progressed to sadness, anhedonia, the thought that they would die soon anyways due to COVID-19, and eventually to self-harm.

**Summarizing statement: "**These cases highlight the fact that how **information overload can lead to increase in psychological distress among normal people too.** One of the case developed severe anxiety and depression, after learning that the person with whom he came in contact with, was found to be COVID-19 positive and the second case developed anxiety and

depressive symptoms, due to apprehension of possible infection, after coming in contact with people with travel history. While the first case had a direct contact with a COVID-19 positive case, the second subject had merely met a foreign couple. In both the cases, the depression and anxiety were fueled by the information overload in the media, with respect to COVID-19. Media reports have been highlighting the possible painful deaths and significant higher mortality with COVID-19 infection. **Both the scenarios, depict that both the suicidal attempts could have been prevented, if proper awareness about the infection is done, by providing the necessary information about spread of infection, rather than talking about mortality rates and type of death."**

## Challenges and Priorities in Responding to COVID-19 in Inpatient Psychiatry.

Li L.Li L
Psychiatr Serv.
2020 Apr 23; PMID: 32321388
Level of Evidence: 5 - Expert Opinion
Type of Article: Open Forum

**BLUF:** The open forum offers suggestions on how inpatient psychiatry should respond to COVID-19 based on the 5 contingency planning strategies outlined in this article. These are "**including COVID-19-specific precautions, visitor restrictions, physician workforce considerations, operational adjustments, and group therapy changes**. **Organized leadership and clear communication are identified as early priorities in pandemic response to minimize misinformation and address immediate challenges."**

**Abstract:**This **Open Forum focuses on specific challenges, contingency planning considerations, and downstream impacts of COVID-19 on inpatient psychiatric care.** COVID-19 is a novel coronavirus that has been declared a pandemic. Challenges for inpatient psychiatry include risky close contact among staff and patients, space constraints, and structural barriers in care delivery. **Nuanced considerations of five contingency planning strategies in response to COVID-19 are described, including COVID-19-specific precautions, visitor restrictions, physician workforce considerations, operational adjustments, and group therapy changes**. **Organized leadership and clear communication are identified as early priorities in pandemic response to minimize misinformation and address immediate challenges.**

## Optimizing psychiatric care during the COVID-19 pandemic.

Moesmann Madsen M, Dines D, Hieronymus F
Acta Psychiatr Scand.
2020 Apr 22; PMID: 32323297
Level of Evidence: 5 - Expert Opinion
Type of Article: Opinion

**BLUF:** The authors outline several challenges to optimal psychiatric care due to the Covid-19 pandemic. These include: change in routines, social isolation, massive exposure to the news regarding the pandemic, incorporation of the pandemic's catastrophic narrative into delusions, reduced in-person support, reduced care seeking due to fear of nosocomial infection, risk for PTSD, higher infection risk for several reasons including residential instability, risk of spread in inpatient and outpatient settings.

**Summarizing statement:** "We foresee an increasing tension between optimizing psychiatric care and minimizing the overall health impact of COVID-19. We also expect that increased psychological

stress in the population and among healthcare workers shall lead to increased mental health pathology (likely depression, anxiety, PTSD and higher suicide rates). More studies, as well as more knowledge sharing is imperative as we continue our work in the frontline of mental healthcare in this new pandemic context."

## Three insights on psychoneuroimmunology of mood disorders to be taken from the Covid-19 pandemic.

Brietzke E, Magee T, Freire RCR, Gomes FA, Milev R.
Brain Behav Immun Health
2020 Apr 22; PMID: 32322822
Level of Evidence: 5 - Expert Opinion
Type of Article: Viewpoint

**BLUF:** The COVID-19 pandemic presents an opportunity to further our understanding of the relationship between neurotropic viruses and mental health disorders. The authors pose three avenues for future study: 1) " COVID-19 is an opportunity for investigation of the naturalistic association between psychiatric symptoms and viral respiratory infections," 2) "If the hypothesis of immunosenescence is correct, COVID-19 response in individuals with mood disorders will be similar to elderly people," and 3) "If COVID-19 and mood disorders are associated, it is possible that anti-SARS-CoV-2 medications have a therapeutic utility in mood disorders."

**Abstract:** In the recent months, the world was taken by surprise by the outbreak of a coronavirus (SARS-CoV-2) pandemic (COVID-19). The COVID-19 pandemic is a unique opportunity to advance the understanding of the association of respiratory viruses with mood disorders and suicide. In this editorial, we explore three insights to the neuropsychoneuroimmunology of mood disorders that could be taken from the COVID-19 pandemic.

## Vicarious traumatization: A psychological problem that cannot be ignored during the COVID-19 pandemic.

Li Z, Ge J, Yang M, Feng J, Liu C, Yang C
Brain Behav Immun.
2020 Apr 20; PMID: 32325097
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter

**BLUF:** Authors respond to two critiques of their recent paper on traumatization from COVID-19: 1) enrollment bias and 2) confounding factors. Strict isolation prevented them from conducting large-scale, face to face studies, and data addressing the confounding factors was not included due to space limitations. They note the main goal of their study is to highlight the phenomenon of vicarious traumatization in medical stuff and the public during the COVID-19 pandemic.

**Summarizing statement:** "Our research was a cross-sectional study and found that the vicarious traumatization of non-front-line medical staff was more serious than that of front-line medical staff during the COVID-19 outbreak. It is noteworthy that the evolution of psychological problems is a developmental process. After short-term medical support work for COVID-19 control, the effects of various psychological stressors may be strengthened, and psychological problems will gradually emerge. The onset of psychological crisis is commonly 3 months after the end of medical support work, and its peak is approximately 6 months later (Hsiao et al., 2020). Therefore, even though the COVID-19 epidemic is over, it is of great importance to continue tracking the development of vicarious traumatization in medical staff as well as the general public."

## Coronavirus Disease 2019 (COVID-19) and Firearms in the United States: Will an Epidemic of Suicide Follow?

Mannix R, Lee LK, Fleegler EW
Ann Intern Med
2020 Apr 22; PMID: 32320463
Level of Evidence: 5- Expert opinion
Type of Article: Ideas and Opinions

**Summary:** The authors draw on previous research about the associations between suicide rates and economic upheaval, natural disasters, social isolation, and access to guns to argue that **we are on the brink of a potential suicide epidemic** in the United States due to the coronavirus pandemic. They suggest potential mitigation strategies such as increasing economic support and social connectedness, while arguing that the most **significant impact will come from policy changes** that decrease gun purchases, increase gun buy-backs, and support safe storage. **Clinicians can be central to mitigation efforts through patient screening and counseling and distribution of safety devices.**

# COVID-19's impact on healthcare workforce

## Geographical distance to the epicenter of Covid-19 predicts the burnout of the working population: Ripple effect or typhoon eye effect?

Zhang SX, Huang H, Wei F.
Psychiatry Res.
2020 Apr 14; PMID: 32325386
Level of Evidence: 5 - Local non-random sample
Type of Article: Letter to the editor

**BLUF:** In this letter to the editor, researchers present preliminary survey results investigating the relationship between distance to the epicenter of an outbreak and burnout. Researchers surveyed 308 working adults in China at locations varying in distance from Wuhan and found an inverted U-shaped relationship between the distance to the epicenter and burnout, suggesting that both psychological ripple effect and typhoon eye effect are present in China in the aftermath of COVID-19.

**Abstract:**
Covid-19 originated in Wuhan and rippled across China. We investigate how the geographical distance of working adults to the epicenter of Wuhan predicts their burnout - emotional, physical and mental exhaustion due to excessive and prolonged stress. **Preliminary results of a survey of 308 working adults in 53 cities showed working adults' distance to the epicenter of Wuhan had an inverted U-shaped relationship with their burnout**. Such results help to identify regions where people may need more psychiatric assistance, with direct implications for healthcare practitioners and policymakers.

# Silver Linings

## COVID-19 transforms health care through telemedicine: evidence from the field.

Mann DM, Chen J, Chunara R, Testa PA, Nov O.Mann DM, et al.
J Am Med Inform Assoc.
2020 Apr 23; PMID: 32324855
Level of Evidence: 4 - Case Series
Type of Article: Research

**BLUF: In one large health system in New York, use of telemedicine for both urgent and non-urgent care increased dramatically during the COVID-19 pandemic (135% and 4345% increases, respectively).** "[T]he changes instigated initially by the COVID-19 pandemic have likely irreversibly altered the position of telemedicine in the US healthcare system."

**Abstract:**
This study provides data on the feasibility and impact of video-enabled telemedicine use among patients and providers and its impact on urgent and non-urgent health care delivery from one large health system (NYU Langone Health) at the epicenter of the COVID-19 outbreak in the United States. Between March 2nd and April 14th 2020, telemedicine visits increased from 369.1 daily to 866.8 daily (135% increase) in urgent care after the system-wide expansion of virtual health visits in response to COVID-19, and from 94.7 daily to 4209.3 (4345% increase) in non-urgent care post expansion. Of all virtual visits post expansion, 56.2% and 17.6% urgent and non-urgent visits, respectively, were COVID-19-related. Telemedicine usage was highest by patients aged 20-44, particularly for urgent care. The COVID-19 pandemic has driven rapid expansion of telemedicine use for urgent care and non-urgent care visits beyond baseline periods. This reflects an important change in telemedicine that other institutions facing the COVID-19 pandemic should anticipate.

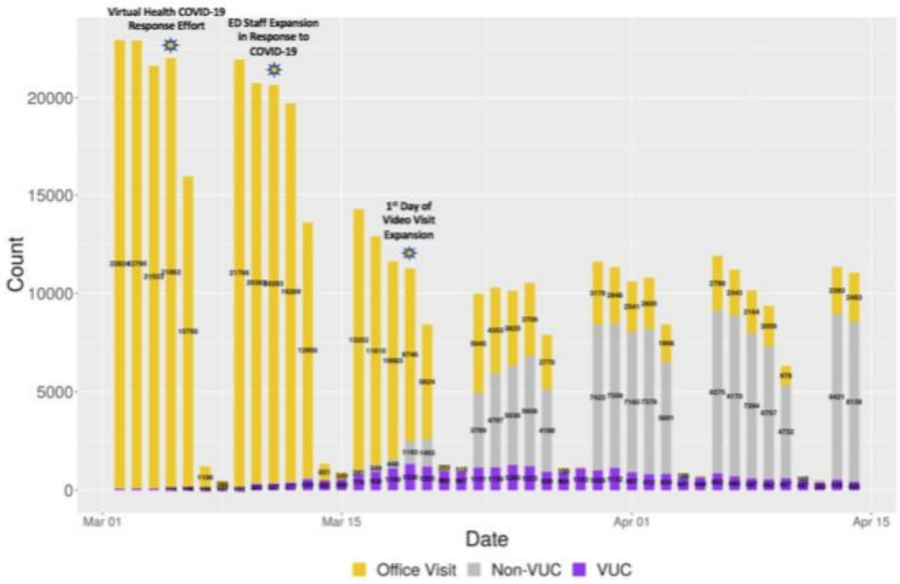



Figure 1. Visit volumes increase in telemedicine urgent care (VUC) and non-urgent care (non-VUC), and decrease in in-person care. Each bar represents one day. Key dates are annotated above corresponding bars.

## Non-pharmaceutical interventions used for COVID-19 had a major impact on reducing influenza in China in 2020.

Sun J, Shi Z, Xu H.
J Travel Med.
2020 Apr 24. Doi; PMID: 32324879
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter

**BLUF:** Non-pharmaceutical interventions implemented by the Chinese government not only effectively contained China's COVID-19 outbreak by March 2020, but also led to a decrease in the incidence of influenza cases in China from 47.7% to 1.2% in the first 6 weeks of 2020.

**Summary:** The Chinese government implemented **strict non-pharmaceutical interventions** (NPIs), including active case detection and isolation of infected persons, maintaining social distance, closure of schools and universities and most businesses, working from home where possible, quarantining and monitoring close contacts, and releasing multi-media epidemic and protection information. These measures **effectively contained China's COVID-19 epidemic by March 2020**. Additionally, data from the CDC Weekly China Influenza Surveillance Report showed that in the first 6 weeks of 2020, the incidence of laboratory-confirmed influenza cases at sentinel hospitals nationwide dropped from the highest (47.7%) to the lowest (1.2%) level in recent years, leading to the conclusion that **NPIs had a significant impact on reducing influenza** in China as well.

## Socially distanced school-based nutrition program feeding under COVID 19 in the rural Niger Delta.

Francis NN, Pegg S.
Extr Ind Soc
2020 Apr 21; PMID: 32322535
Level of Evidence: 6 - No data cited
Type of Article: Comment

**BLUF:** A Niger Delta primary school continues to offer weekly nutritional program feedings in a socially distanced form despite school closures due to the COVID-19 outbreak.

**Abstract:**
The Niger Delta region of Nigeria is widely recognized as a complex and contentious space for oil exploration and production. Over the past few decades, the Niger Delta has witnessed large-scale mass peaceful mobilizations and rebellion-like conditions from violent militia groups. Oil companies have been implicated in violence perpetrated by Nigerian security forces. Local host communities have suffered greatly from corruption, political instability, violence and the environmental devastation of their farmlands and fishing grounds. Oil companies have increasingly turned to corporate social responsibility (CSR) initiatives to attempt to build or repair relations with oil-producing communities. There are also governmental and non-governmental humanitarian actors supporting various initiatives in the oil-producing areas. This article **highlights the challenges that one long running micro-scale development project has faced due to the COVID 19 disease outbreak and the closure of all schools in Rivers State, Nigeria in March 2020**. The school closures have halted some initiatives, but our **weekly nutritional program feedings have continued in new, socially distanced forms**.

# Resources

## The epidemiological and clinical features of COVID-19 and lessons from this global infectious public health event.

Tu H, Tu S, Gao S, Shao A, Sheng J.
J Infect
2020 Apr 18; PMID: 32315723
Level of Evidence: 5 - Review of literature
Type of Article: Research

**BLUF:** The article summarizes the etiology, epidemiology, clinical features, diagnosis, and current interventions related to the COVID-19 pandemic, which is caused by SARS-CoV-2. The pandemic in China is improving, although a lack of financial support, healthcare and public health infrastructure, equipment and protective gear, testing, and national disease control systems continue to limit control of the COVID-19 pandemic.

**Abstract:**
**Coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and represents a potentially fatal disease of great global public health importance**. As of March 26, 2020, the outbreak of COVID-19 has resulted in 462,801 confirmed cases and 20,839 deaths globally, which is more than those caused by SARS and Middle East respiratory syndrome (MERS) in 2003 and 2013, respectively. The epidemic has posed considerable challenges worldwide. **Under a strict mechanism of massive prevention and control, China has seen a rapid decrease in new cases of coronavirus**; however, the global situation remains serious. Additionally, the **origin of COVID-19 has not been determined and no specific antiviral treatment or vaccine is currently available**. Based on the published data, this review systematically discusses the etiology, epidemiology, clinical characteristics, and current intervention measures related to COVID-19 in the hope that it may provide a reference for future studies and aid in the prevention and control of the COVID-19 epidemic.

## The emergence of SARS, MERS and novel SARS-2 coronaviruses in the 21st century.

da Costa VG, Moreli ML, Saivish MV.
Arch Virol
2020 Apr 22; PMID: 32322993
Level of Evidence: 5 - Expert opinion
Type of Article: Review

**BLUF:** The authors of this piece compare the history and epidemiology of the three main coronaviruses that have caused significant human illness in the 21st century: SARS, MERS and COVID-19.

**Abstract:**
At the beginning of the 21st century, a new deadly infectious disease known as severe acute respiratory syndrome (SARS) was recognized as a global public health threat. Subsequently, ten years after the initial SARS cases occurred in 2002, new cases of another atypical respiratory disease caused worldwide concern. This disease became known as Middle East respiratory syndrome (MERS) and was even more lethal than SARS. Currently, history has repeated itself with the emergence of a new Chinese epidemic at the end of 2019. For this respiratory disease, called COVID-19, a novel coronavirus (SARS-CoV-2) was identified as the etiologic agent. In sum, SARS, MERS and COVID-19

are caused by recently discovered coronaviruses that cause flu-like illnesses, but with a clinical outcome that tends to be more severe. As a result of the current importance of coronaviruses in global public health, we conducted a review to summarize and update, above all, the epidemiological historical aspects of the three major diseases in humans caused by coronaviral infection.

## Scientific research progress of COVID-19/ SARS-CoV-2 in the first five months.

Li, Hua; Liu, Zhe; Ge, Junbo
J Cell Mol Med
2020 Apr 23; PMID: 32320516
Level of Evidence: 5 - Expert Opinion
Type of Article: Review
**BLUF:** In this article, the current known knowledge regarding epidemiological, pathogenesis, pathology, clinical features, comorbidities, and treatment of COVID-19/SARS-CoV-2 is summarized.

**Abstract:** A cluster of pneumonia (COVID-19) cases have been found in Wuhan China in late December, 2019 and subsequently a novel coronavirus with a positive stranded RNA was identified to be the etiological virus (severe acute respiratory syndrome coronavirus 2, SARS-CoV-2), which has a phylogenetic similarity to severe acute respiratory syndrome coronavirus (SARS-CoV). SARS-CoV-2 transmits mainly through droplets and close contact and the elder or people with chronic diseases are high-risk population. People affected by SARS-CoV-2 can be asymptomatic, which brings about more difficulties to control the transmission. COVID-19 has become pandemic rapidly after onset and so far the infected people have been above 2,000,000 and more than 130,000 died worldwide according to COVID-19 situation dashboard of World Health Organization (https://covid19.who.int). Here, we **summarized the current known knowledge regarding epidemiological, pathogenesis, pathology, clinical features, comorbidities and treatment of COVID-19/ SARS-CoV-2** as reference for the prevention and control COVID-19.

## 2019 Novel coronavirus (COVID-19) overview.

Mohammadi M, Meskini M, do Nascimento Pinto AL.Mohammadi M, et al.
Z Gesundh Wiss
2020 Apr 19; PMID: 32313806
Level of Evidence: Systematic Review-2
Article Type: Research
**BLUF:** The authors summarize current research for COVID-19 treatment, including observing molecules in-vitro and human-based SARS-CoV and MERS-Cov trials, evaluating type I and II interferon antiviral activity, considering combination therapy with lopinavir/ritonavir, pegylated interferon and ribavirin, and possible future research in remdesivir therapy. Suggestions for prevention include hand washing with disinfectant solutions, minimal contact with patients, immediate provision of PPE, medicine supply chains, and hospital supplies.

**Abstract:** Novel coronaviruses (CoVs) are zoonotic pathogens, but the first human-to-human transmission has been reported. CoVs have the best known genome of all RNA viruses, and mutations in the genome have now been found. A pneumonia of unknown cause detected in Wuhan, China, was first reported to the WHO Country Office in China on 31 December 2019. **This study aims to report early findings related to COVID-19 and provide methods to prevent and treat it.**

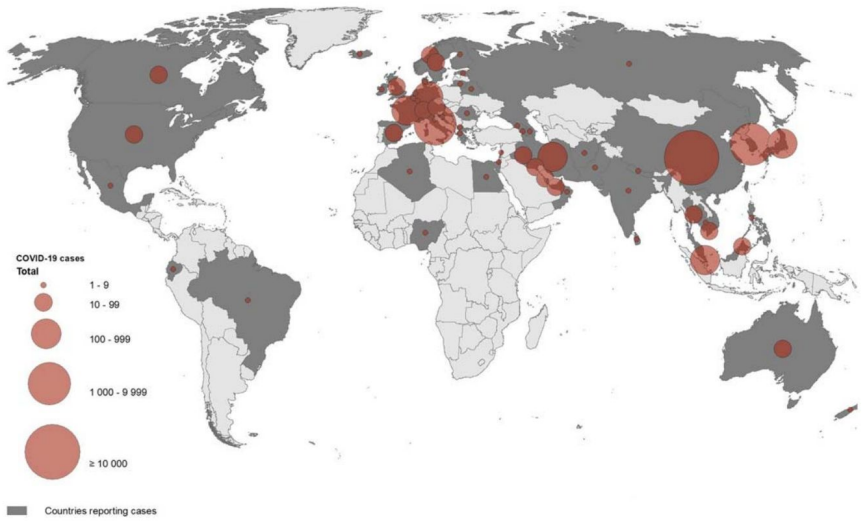



**Fig. 1** Geographic distribution of COVID-19 cases worldwide, as of March 1, 2020

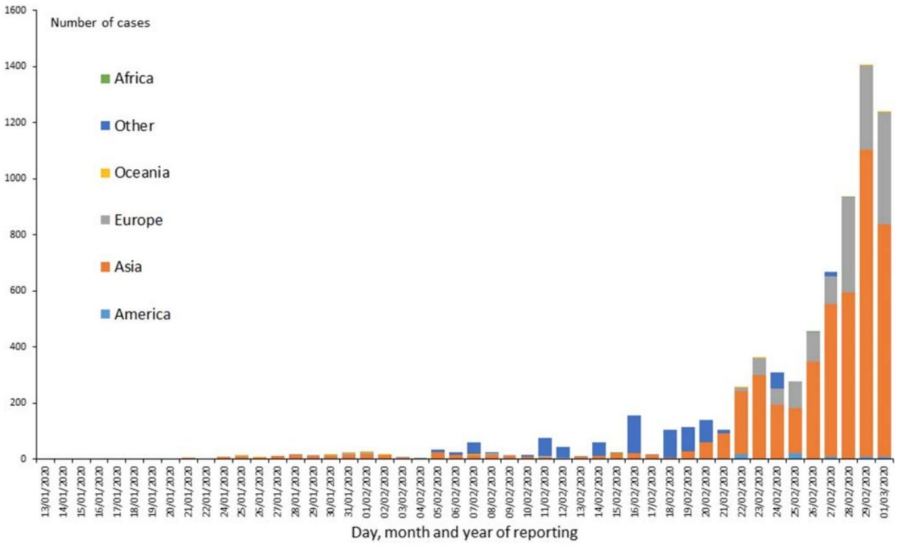



**Fig. 2** Distribution of COVID-19 cases by continent (except China), as of March 1, 2020

## Covid-19: Simulation models for epidemics.

Kristiansen, Ivar Sonbo; Burger, Emily Annika; Blasio, Birgitte Freiesleben de
Tidsskr Nor Laegeforen
2020 Mar 18; PMID: 32321234
Level of Evidence: 5 - Expert opinion
Type of Article: Commentary

**BLUF:** The authors describe how infectious disease models can predict the course of an epidemic and the effects of interventions such as quarantine, school closures, drug treatments and vaccines.

**Abstract:** Statistical modelling is being used on an increasing level nationally and internationally to understand and manage epidemics. Infectious disease models are **based on infectious disease theories and previous epidemics**. During an epidemic, knowledge of the consequences of the

epidemic is important. Public health authorities need to know how the **number of infected people is likely to develop over time, how many will require hospitalization or respiratory support, and how many may die**. In the course of an epidemic, first there is a **period of exponential growth** in the number of infected individuals, after which the proportion of **susceptible individuals in the population falls and the epidemic dies out**. Modelling allows for the simulation of the effects of **interventions such as quarantine, school closures, drug treatment and vaccines where appropriate.**

# Acknowledgements


## Contributors and Associate Contributors:

**University of Arizona, College of Medicine-Phoenix**

Diep Nguyen, MS3[1]
Abel De Castro, MS1[2]
Akshara Malla, MS4[2]
Allison Hansen, MS3[2]
Allen Doan, MS3[2]
Ann Staudinger Knoll, MS1[2]
Bhupinder (Rose) Kaur, MS4[2]
Celina Virgen, MS3[2]
Charlotte Archuleta, MS3[2]
John Michael Sherman, MS1[2]
Julie Tran, MS3[2]
Kathleen Hanlon, MS4[2]
Kylie Jenkins, MS4[2]
Maggie Donovan, MS1[2]
Marzia Shah, MS4[2]
Michael Olson, MS1[2]
Michelle Arnold, MS3[2]
Nour Bundogji, MS3[2]
Sameer Kandula, MS3[2]
Shandiin Sam, MS4[2]

**University of Washington, School of Medicine**

Avery Forrow, MS2[1]
Daniel Lee, MS3[1]
Luke Johnson, MS4[1]
Sangeetha Thevuthasan, MS2[1]
Amanda Nguyen, MS3[2]
Colin Bartz-Overman, MS3[2]
Dax Cvancara, MS1[2]
Jeremiah Sims, MS3[2]
Kyle Ellingsen, MS3[2]
Sara Rutz, MS1[2]

**Western University of Health Sciences**

Kersti Bellardi, MS3[2]

Kealapono Richardson, Technology & Design
Kaitlin Howard, Strategic Outreach
Jenny Jensen, MS1

Contributor[1], Associate Contributor[2]