April 27, 2020
Daily COVID-19 Literature Surveillance Summary

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This free and open source document represents a good faith effort to provide real time, distilled information for guiding best practices during the COVID-19 pandemic. This document is not intended to and cannot replace the original source documents and clinical decision making. These sources are explicitly cited for purposes of reference but do not imply endorsement, approval or validation.

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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 27th, 2020
Executive Summary

Climate

- One study found that COVID-19 research has had overall low methodological quality
    - Specifically, in doing a literature review appraisal for hydroxychloroquine studies, most lacked randomization, blinding, and standard steps to minimize confounding along with results clouded by selection and residual confounding bias
- Persons with disabilities may be at a higher risk of infection in the pandemic and there are suggestions for this to be the opportunity for significant health reforms
- There are more studies regarding the potential closure of syringe service programs leading to increased overdose and infectious disease transmission rates
    - Currently, there is also concern over the limited sexual and reproductive health services available to the public

Epidemiology

- Preliminary data suggest COVID-19 disease burden may be lower in countries that routinely vaccinate with the BCG tuberculosis vaccine.
- Models based on data from COVID-19 outbreaks in two Chinese provinces predict that contact with asymptomatic carriers is the strongest factor predicting new outbreaks.
- Analysis of lower respiratory tract sputum samples from 92 patients found that viral load exhibits a direct correlation with disease severity.
- A cohort study of 548 hospitalized COVID-19 patients in Wuhan found a 14.2% 15-day mortality rate with age, hypoxia, lymphopenia, high LDH, and multiple organ dysfunction being associated with death.

Transmission & Prevention

- More predictions for summer temperatures reducing COVID-19 transmission.
- Epidemiologists propose an "inverse quarantine," where only high risk uninfected individuals are isolated, as an economically viable method of reducing mortality.
- Researchers performed RT-PCR on throat swabs at 24 hour intervals for 5 days in 22 recovered COVID-19 patients and found that 11 patients had a positive result after 2 or more negatives.
- Using COVID-19 immunity serosurveillance has become a trendy way to discuss how to make the decision to initiate return-to-work, yet, several challenges remain.
    - Calculating sensitivity and specificity of tests requires a gold standard which we still do not have
    - That it is consistent with the acute/infectious period
    - Verifying that the test is not detecting cross-reactivity with other viral pathogens that result in false-positive results
    - How long does the immunity last
    - Making sure that the test is reliable for distribution and is cost-efficient.

Management

- COVID-19 acute respiratory distress syndrome (CARDS) appears to have a component of vascular insult that may require a distinct treatment approach from other ARDS.
    - Two types of CARDS: Type L or Type H.
        - Type L: high compliance, lower lung weight on CT and low response to PEEP

        - Type H: traditional ARDS with extensive CT consolidations, low compliance, higher lung weight on CT and high PEEP response.
- Data trends seem to suggest that prophylactic dose of heparin or DOACs are insufficient to prevent thromboembolic events in patients with COVID-19

Adjusting Practice during COVID-19

- There are new guidelines and recommendations for:
    - Safe ultrasound practices and cleaning equipment in times of COVID-19.
    - Keeping people with epilepsy safe during the pandemic.
    - Allergen immunotherapy
    - Managing diabetes in individuals fasting for Ramadan during the pandemic.
    - Tracheostomy protocols.
- A urology practice found that 44% of their COVID-19-related consultations were effectively managed through telemedicine alone and none of their staff developed infection.
- Obstetricians developed a drive through model for prenatal care that reduces in-person visits by 33%.
- A systematic review of 33 studies including 385 COVID-19 positive pregnant women concluded that infection with the virus during pregnancy exhibits minimal association with poor outcomes.

R&D: Diagnosis & Treatments

- Randomized control trial of how or high dose chloroquine diphosphate found a dose dependent relationship with the dose of chloroquine diphosphate and mortality, leading to the recommendation that dose high as 12g should not be given for more than 10 days.
- Continued reports of B-lines on POCUS and Ground glass opacities on Chest CTs in patients with COVID-19
- Continue data supporting great specificity but questionable sensitivity of nasopharyngeal swabs

Mental Health & Resilience

- The mental health consequences of the pandemic are likely to be present for longer and peak later than the actual pandemic leading experts to urge national strategies for suicide prevention.

Resources

- Multiple articles have come out to provide recommended lists of various resources to access the evolving literature for COVID-19 and have summarized current knowledge of COVID-19 epidemiology, clinical features, diagnostic approaches, proposed therapies, etc.

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Pediatrics

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Neutrophil Extracellular Traps in COVID-19

Tobacco Smoking Increases the Lung Gene Expression of ACE2, the Receptor of SARS-CoV-2.

Inhibition of SARS-CoV-2 Infections in Engineered Human Tissues Using Clinical-Grade Soluble Human ACE2

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Time to consider histologic pattern of lung injury to treat critically ill patients with COVID-19 infection.

COVID-19: A New Virus, but a Familiar Receptor and Cytokine Release Syndrome

Transmission & Prevention

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- High-flow Nasal Cannula May Be No Safer Than Non-Invasive Positive Pressure Ventilation For COVID-19 Patients.

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Acute care

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- Successful recovery of COVID-19 pneumonia in a patient from Colombia after receiving chloroquine and clarithromycin
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- Ventilator Triage Policies During the COVID-19 Pandemic at U.S. Hospitals Associated With Members of the Association of Bioethics Program Directors.
- Title Coronavirus Disease 2019 and Prevalence of Chronic Liver Disease: A Meta-Analysis
- Self-reported olfactory loss associates with outpatient clinical course in Covid-19.

- Clinical value of immune-inflammatory parameters to assess the severity of coronavirus disease 2019
- No adequate evidence indicating hypertension as an independent risk factor for COVID-19 severity.
- Increased amylase and lipase in patients with COVID-19 pneumonia: don´t blame the pancreas just yet!

Emergency Medicine

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Critical Care

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Hematology and Oncology

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- Fibrinolytic abnormalities in acute respiratory distress syndrome (ARDS) and versatility of thrombolytic drugs to treat COVID-19.
- Type and dose of heparin in COVID-19.

Surgical Subspecialties

General Surgery

- Isolation protocol for a COVID-2019 patient requiring emergent surgical intervention: case presentation.
- CORONA-steps for tracheotomy in COVID-19 patients: A staff-safe method for airway management

Otolaryngology

- Tracheostomy guidelines developed at a large academic medical center during the COVID-19 pandemic.

Transplant Surgery

COVID-19 in Solid Organ Transplant Recipients: Initial Report from the US Epicenter.

Earliest cases of coronavirus disease 2019 (COVID-19) identified in solid organ transplant recipients in the United States.

Pediatrics

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Geriatrics

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Alternative Medicine

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Adjusting Practice During COVID-19

For Healthcare Professionals

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World Federation for Ultrasound in Medicine and Biology Position Statement: How to Perform a Safe Ultrasound Examination and Clean Equipment in the Context of COVID-19.

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Diagnosing Pulmonary Thromboembolism in COVID-19: A Stepwise Clinical and Imaging Approach.

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Neurology

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Keeping people with epilepsy safe during the Covid-19 pandemic.

Medical subspecialties

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Asthma and COVID-19.

Dermatology

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Cardiology

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Hematology and Oncology

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Management of hepatocellular carcinoma in the time of COVID-19.

Lymphopenia that may develop in patients treated with temozolomide and immune control check-point inhibitor may be a high risk for mortality during the COVID-19 outbreak.

Managing People with Diabetes Fasting for Ramadan During the COVID-19 Pandemic: A South Asian Health Foundation Update.

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Surgical Subspecialties

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In considerations of robotic colorectal surgery within a COVID-19 pandemic.

General Surgery

Tracheostomy Protocols during COVID-19 Pandemic

COVID-19 and emergency surgery.

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Rapid Deployment of a Drive-Through Prenatal Care Model in Response to the Coronavirus Disease 2019 (COVID-19) Pandemic.

Be aware of misdiagnosis---A 21-Year-Old Primipara with Suspected COVID-19.

Considerations for scaling down fetal echocardiograms during the COVID-19 pandemic.

Successful Treatment of Preterm Labor in Association with Acute COVID-19 Infection.

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Addendum to: Risk Stratification and PPE Use in Pediatric Endoscopy During the COVID-19 Outbreak: A Single-Center Protocol.

Managing Asthma during COVID-19: An Example for Other Chronic Conditions in Children and Adolescents.

Covid-19 and child disabilities: whom to protect and how.

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R&D: Diagnosis & Treatments

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Individuals with mild symptoms in communities experiencing high numbers of COVID-19 hospitalizations

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Connecting clusters of COVID-19: an epidemiological and serological investigation.

Diagnostic accuracy of an automated chemiluminescent immunoassay for anti-SARS-CoV-2 IgM and IgG antibodies: an Italian experience.

COVID-19: a meta-analysis of diagnostic test accuracy of commercial assays registered in Brazil.

Point of care and intensive care lung ultrasound: A reference guide for practitioners during COVID-19.

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Point-of-Care Lung Ultrasound Findings in Patients with Novel Coronavirus Disease (COVID-19) Pneumonia.

Who should perform the rhinopharyngeal swab in COVID-19 positive patients?

Coronavirus (COVID-19) Assessments and the Importance of Calculating the Probability of Illness.

Clinical Pathway for Early Diagnosis of COVID-19: Updates from Experience to Evidence-Based Practice.

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Highly sensitive detection of SARS-CoV-2 RNA by multiplex rRT-PCR for molecular diagnosis of COVID-19 by clinical laboratories.

Reliability and usefulness of a rapid IgM-IgG antibody test for the diagnosis of SARS-CoV-2 infection: a preliminary report.

Early chest computed tomography to diagnose COVID-19 from suspected patients: A multicenter retrospective study.

Rapid and sensitive detection of anti-SARS-CoV-2 IgG using lanthanide-doped nanoparticles-based lateral flow immunoassay

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Salivary diagnostics in COVID-19: Future research implications.

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Screening FMT donors during the COVID-19 pandemic: a protocol for stool SARS-CoV-2 viral quantification.

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Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection: A Randomized Clinical Trial.

An invited commentary on: "Evidence Based Management Guideline for the COVID-19 Pandemic - Review article".

COVID-19 research has overall low methodological quality thus far: case in point for chloroquine/hydroxychloroquine.

Pharmacological Therapeutics Targeting RNA-Dependent RNA Polymerase, Proteinase and Spike Protein: From Mechanistic Studies to Clinical Trials for COVID-19.

Lopinavir/ritonavir did not shorten the duration of SARS CoV-2 shedding in patients with mild pneumonia in Taiwan.

Eculizumab treatment in patients with COVID-19: preliminary results from real life ASL Napoli 2 Nord experience

Current pharmacological treatments for COVID-19: what's next?

Pharmacological Therapeutics Targeting RNA-Dependent RNA Polymerase, Proteinase and Spike Protein: From Mechanistic Studies to Clinical Trials for COVID-19.

Safety signals for QT prolongation or Torsades de Pointes associated with azithromycin with or without chloroquine or hydroxychloroquine.

Vaccines for SARS-CoV-2: Lessons from Other Coronavirus Strains

Photobiomodulation and Antiviral Photodynamic Therapy as a Possible Novel Approach in COVID-19 Management.

Discovery of Potential Multi-Target-Directed Ligands by Targeting Host-specific SARS-CoV-2 Structurally Conserved Main Protease$.

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Does the Direct Renin Inhibitor Have a Role to Play in Attenuating Severity of the Outbreak Coronavirus Disease 2019 (COVID-19)?

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COVID-19: lambda interferon against viral load and hyperinflammation.

The friendly use of chloroquine in the COVID-19 disease: a warning for the G6PD-deficient males and for the unaware carriers of pathogenic alterations of the G6PD gene.

Mental Health & Resilience Needs

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A Multinational, Multicentre Study on the Psychological Outcomes and Associated Physical Symptoms Amongst Healthcare Workers During COVID-19 Outbreak.

Impact on Public Mental Health

The Impact of Online Information on Self-isolation Intention during the COVID-19 Pandemic: A cross-sectional study.

Physical Distancing in COVID-19 May Exacerbate Experiences of Social Isolation among People Living with HIV.

From Helpless to Hero: Promoting Values-Based Behavior and Positive Family Interaction in the Midst of COVID-19.

Effect of COVID-19 on the Mental Health Care of Older People in Canada.

Drawing on Kinship Care Support for Older People during a Pandemic (COVID-19): Practice Considerations for Social Workers in Ghana.

Suicide Risk and Prevention during the COVID-19 Pandemic.

Resources

COVID-19 Research in Brief: 18 April to 24 April, 2020

Keeping up with studies on covid-19: systematic search strategies and resources.

SARS-CoV-2 causing pneumonia-associated respiratory disorder (COVID-19): diagnostic and proposed therapeutic options.

Leveraging open hardware to alleviate the burden of COVID-19 on global health systems.

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Levels of Evidence

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

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

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

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

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

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

Climate

Global

Coronavirus Disease 2019 (COVID-19) in Kenya: Preparedness, response and transmissibility.

Aluga, Martin A
Journal of Microbiology, Immunology, and Infection
2020 Apr 20; PMID: 32331980
Level of Evidence: 5 - Expert Opinion
Type of Article: Perspective

BLUF: This perspective piece discusses the measures taken for prevention by the Kenyan Ministry of Health prior to the diagnosis of their first case of COVID-19 on March 12th, 2020, the restrictions that were placed in response to the emergence of COVID-19, and recommendations for steps going forward with a predicted exponential growth in cases in the coming days.

Abstract:
The world and Kenya face a potential pandemic as the respiratory virus Coronavirus Disease 2019 (COVID-19) affects world populations. Nations have been forced to intervene and issue directions under executive orders to ensure the pandemic is contained. Kenya has reported **110 confirmed COVID-19 cases** (as at 2nd April, 2020), **three persons have succumbed and 2 people have fully recovered**. Most of the affected people had entered/returned to Kenya from different parts of the world. Most of the people who have contracted COVID 19 are between the 16–74 years of age. As a result, since February 2020, Kenya put in place **several precautionary measures to mitigate the pandemic in its early stages**. However, the economic status of the population of country won't be simple to control COVID 19, if government won't integrate the realistic feasible timely plans. This article highlights the **preparedness, response, transmissibility of Covid-19 and proposes intuitions to manage COVID-19 in Kenya**. Currently it is clear that since first confirmation to current, the transmission of the COVID-19 is exponentially increasing in Kenya.

What can countries learn from Hong Kong's response to the COVID-19 pandemic?

Wong SYS, Kin On K, Chan FKL.
CMAJ
2020 Apr 24; PMID: 32332040
Level of Evidence: Level 5 - Expert Opinion
Type of Article: Analysis

Summary: Hong Kong has done relatively well in controlling the spread of COVID-19 due to public health measures such as border control, social distancing, high-volume testing for SARS-CoV-2, aggressive contact tracing, quarantine centers, and the use of face masks by most people. The enhanced public health willingness and preparedness by the government and residents of Hong Kong could be due to their experience during the 2003 SARS epidemic.

Canada's role in strengthening global health security during the COVID-19 pandemic.

Chattu VK, Adisesh A, Yaya S.
Glob Health Res Policy.
2020 Apr 20; PMID: 32328533

Level of Evidence: 6 – No data
Type of Article: Commentary
BLUF: Canada has supported global health during the COVID-19 pandemic through their **material support** (eg, supplying PPE), **collaboration with the United States Federal Drugs Administration (FDA)** and **European Medicines Agency (EMA)** to coordinate regulatory responses for vaccines and medicines, and with **research for vaccine and antiviral development clinical trials.**

Abstract:
The world is confronted by the current pandemic of Corona Virus Disease (COVID-19), which is a wake-up call for all nations irrespective of their development status or geographical location. Since the start of the century we have seen five big infectious outbreaks which proved that epidemics are no more regarded as historic and geographically confined threats. The Canadian government underlined that these infectious disease outbreaks are threats to global health security and disrupt societal wellbeing and development. In this context, the Public Health Agency of Canada is proactive and has shown its preparedness for outbreaks of emerging and epidemic-prone diseases, and in dealing with these pathogens. Even before the declaration of pandemic, Canada has proved its global health leadership by ensuring collective action and multisectoral coordination which still remains a serious challenge especially for low and middle- income countries with existing poor health systems. In this article we **discuss how Canada is addressing the global challenges posed by the COVID-19 pandemic through its leadership and practice of global health diplomacy.**

Accessibility of 'essential' alcohol in the time of COVID-19: Casting light on the blind spots of licensing?

Reynolds J, Wilkinson C.
2020 Apr 23; Drug Alcohol Rev.
PMID: 32329548
Level of Evidence: 5 - Expert Opinion
Type of Article: Commentary
BLUF: The authors argue that 'home drinking' is a blind spot of licensing. COVID-19 highlights this point as the closure of pubs and bars may intensify home drinking. Licensing systems should balance the interests of sales as well as safety of off-site consumption, for instance by quantity restrictions or minimum unit pricing.

Abstract: Among the Australian and UK governments' responses to the COVID-19 pandemic has been the designation of outlets selling alcohol for off-premise consumption as 'essential' services, allowing them to remain open while pubs, hotels and restaurants have been forced to close. In a context of restrictions on movement outside the home in both countries, and where alcohol providers are trying to find new ways to reach their customers, this may lead to an intensification of the social and health harms associated with home drinking. By examining the current situation in both Australia and the UK, **we argue that heightened risks from home drinking amid COVID-19 bring into sharp focus long-standing weaknesses within licensing systems in both countries: the regulation of off-premise outlets to minimise harms from drinking at home.** We call for critical conversations on how licensing systems should be revised to take more responsibility for protecting people from the health and social harms associated with home drinking, both under COVID-19 and in the future.

When Past Isn't a Prologue: Adapting Informatics Practice During a Pandemic.

Kannampallil TG, Foraker RE, Lai AM, Woeltje KF, Payne PRO.
J Am Med Inform Assoc.
2020 Apr 25; PMID: 32333757
Level of Evidence: 5 - Expert Opinion
Type of Article: Perspective

BLUF: Four possible strategies on data informatics are presented to help combat the COVID-19 pandemic. Implementing a cross-institutional data analytics leadership team can help coordinate multiple research programs. Data sharing agreements will be vital in propagating local information nationally. Data needs to be presented in the most convenient and usable format for end-users. More promotion of data research is needed.

Abstract:
Data and information technology are key to every aspect of our response to the current COVID-19 pandemic-from **how we diagnose patients and deliver care, to the development of predictive models of disease spread, to the management of personnel and equipment.** The increasing engagement of informaticians at the forefront of these efforts has been a fundamental shift: from an **academic to an operational role**. However, the past history of informatics as a scientific domain and an area of applied practice provides little guidance or prologue for the incredible challenges that we are now tasked with performing. Building upon our recent experiences, we present **four critical lessons-learned** that have helped shape our scalable, data-driven response to COVID-19. We describe each of these lessons within the context of specific solutions and strategies we applied in addressing the challenges that we faced.

Universal Do-Not-Resuscitate Orders, Social Worth, and Life-Years: Opposing Discriminatory Approaches to the Allocation of Resources During the COVID-19 Pandemic and Other Health System Catastrophes

Bledsoe, TA; Jokela, JA; Deep, NN; Snyder Sulmasy, L
Ann Intern Med
2020 Apr 24; PMID: 32330235
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter

Summary: The authors of this opinion letter go over some of the proposed solutions to ethical dilemmas that have arisen in the COVID-19 pandemic. The authors encourage keeping ethical considerations in situations of triage and warn against disproportionate harm to groups of individuals. One way to do so is to approach every patient on an individualized basis.

- Universal Do Not Resuscitate: This violates evidence-based medicine since the presentation of COVID-19 varies from patient to patient and this does not reflect standard of care.
- Social worth: social worth should not play a role in rationing
- Life-years: unfairly disfavors the elderly, disabled, and other groups.

Affecting the Healthcare Workforce

Going to the COVID-19 Gemba: using observation and high reliability strategies to achieve safety in a time of crisis.

Thull-Freedman, Jennifer; Mondoux, Shawn; Stang, Antonia; Chartier, Lucas B
Canadian Journal of Emergency Medicine

2020 Apr 24; PMID: 32327007
Level of Evidence: 6 - No data cited
Type of Article: Comment

BLUF: The authors make a case that Emergency Departments (ED) should focus on utilizing high reliability organizing in order to reduce error rates in high-risk situations associated with this pandemic; they give an example of their work in the Alberta Children's Hospital ED.

Summary: The authors make a case that EDs should implement the five principles of high reliability organizations (HROs) described by Weick and Sutcliff in order to prepare and produce low rates of error in the high-risk circumstances associated with this pandemic. These principles include preoccupation of failure, reluctance to simplify interpretation, sensitivity to operations, commitment to resilience, and deference to expertise. Focusing on these principles in addition to reaching out to those on the frontlines, will ensure that plans are able to be implemented as intended. The authors put forth an example of high reliability organizing for the COVID-19 pandemic with their work in the Alberta Children's Hospital ED where they effectively implemented strategies to reduce the likelihood of error in high-risk processes (e.g. standardized workflows) during situations where high reliability is critical (e.g. resuscitations/intubations).

Disparities

Disability, Urban Health Equity, and the Coronavirus Pandemic: Promoting Cities for All.

Pineda VS, Corburn J.
J Urban Health.
2020 Apr 23; PMID: 32328866
Level of Evidence: Level 5 - Expert opinion
Type of Article: Editorial

BLUF: Many persons with disabilities (PWDs) are at even higher risk of infection or death than non-disabled persons, and they face even more challenges due to social distancing and other measures taken. For inclusive cities in their responses to COVID-19, the authors recommend the following measures:

1. Cities must disseminate public information in accessible manners including audio, Braille, E-pub, and easy-to-understand formats, and avoid discriminatory language.
2. PWDs and disabled persons' organizations should be consulted and assist in designing and implementing public policy.
3. Cities should ensure that persons with disabilities have continued access to essential services, including healthcare and personal assistants.
4. Governments should do more to assist PWDs financially, since most have higher expenses than non-PWDs and 27% of PWDs live below the poverty line.
5. Cities should adopt more anti-discrimination and labor protection laws for PWDs.

Abstract:
Persons with disabilities (PWDs) living in cities during the COVID-19 pandemic response may be four times more likely to be injured or die than non-disabled persons, not because of their "vulnerable" position but because urban health policy, planning and practice has not considered their needs. In this article, the adverse health impacts on PWDs during the COVID-19 pandemic reveals the "everyday emergencies" in cities for PWDs and that these can be avoided through more inclusive community planning, a whole-of-government commitment to equal access, and implementation of universal design strategies. Importantly, COVID-19 can place PWDs at a higher risk of infection since some may already have compromised immune and respiratory systems and policy responses, such as

social distancing, can lead to life-threatening disruptions in care for those that rely on home heath *(sic)* or personal assistants. Living in cities may already present health-damaging challenges for PWDs, such as through lack of access to services and employment, physical barriers on streets and transportation, and smart-city technologies that are not made universally accessible. We suggest that the current pandemic be viewed as an opportunity for significant urban health reforms on the scale of the sanitary and governance reforms that followed ninetieth *(sic)* century urban epidemics. This perspective offers insights for ensuring the twenty-first century response to COVID-19 focuses on promoting more inclusive and healthy cities for all.

Targeting COVID-19 interventions towards migrants in humanitarian settings.

Hargreaves S, Zenner D, Wickramage K, Deal A, Hayward SE.
Lancet Infect Dis
2020 Apr 21; PMID: 32330438
Level of Evidence: 5 - Expert Opinion
Type of Article: Comment

Summarizing Excerpt: "An urgent coordinated effort is now needed to align [refuge and migrant] populations with national and global COVID-19 responses … [T]he Inter-Agency Standing Committee (IASC) has released interim technical guidance on strategies to support outbreak readiness and response among migrants in high-risk camp and slum settings … [T]he recommendations highlight key interventions that will have a positive effect, including maximising site planning for improved distancing among residents and crowd management, and practical interventions to promote infection prevention and control standards. An important component will be strong risk communication and community engagement … The declaration of temporary amnesties (eg, overturning restrictions on access to mainstream health systems) will also be crucial and is occurring in some countries."

Sexual and reproductive health (SRH): a key issue in the emergency response to the coronavirus disease (COVID- 19) outbreak.

Tang K, Gaoshan J, Ahonsi B.
Reprod Health
2020 Apr 23; PMID: 32326943
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter

Summary: Evidence on the impact of COVID-19 on sexual and reproductive health is limited, prompting the authors to call for more research in this area. Many questions remain unanswered about the COVID-19's impact on pregnant patients or fertility. Concerns are also present regarding 1) access to sexual and reproductive health services, including pre- and post-natal checks, HIV/AIDS healthcare, contraception, and safe abortion and 2) increased gender-based violence and domestic violence while self-quarentine policies are in place.

Abstract:
The novel coronavirus disease (COVID-19) outbreak was first declared in China in December 2019, and WHO declared the pandemic on 11 March 2020. A fast-rising number of confirmed cases has been observed in all continents, with Europe at the epicentre of the outbreak at this moment.Sexual and reproductive health (SRH) and rights is a significant public health issue during the epidemics. The novel coronavirus (SARS-CoV-2) is new to humans, and only limited scientific evidence is available to identify the impact of the disease COVID-19 on SRH, including clinical presentation and outcomes of the infection during pregnancy, or for persons with STI/HIV-related

immunosuppression. Beyond the clinical scope of SRH, we should not neglect the impacts at the health system level and disruptions or interruptions in regular provision of SRH services, such as pre- and postnatal checks, safe abortion, contraception, HIV/AIDS and sexually transmitted infections. Furthermore, other aspects merit attention such as the potential increase of gender-based violence and domestic abuse, and effects of stigma and discrimination associated with COVID-19 and their effects on SRH clients and health care providers. Therefore, there is an urgent need for the scientific community to generate sound clinical, epidemiological, and psycho-social behavioral links between COVID-19 and SRH and rights outcomes.

The implications of COVID-19 for the care of children living in residential institutions.

Goldman PS, van Ijzendoorn MH, Sonuga-Barke EJS; Lancet Institutional Care Reform Commission Group.Goldman PS, et al.
Lancet Child Adolesc Health.
2020 Apr 21; PMID: 32330432
Level of Evidence: 6 - No Evidence
Article Type: Correspondence

Summary: This letter of correspondence outlines several ways that residential institutions can support children as they relocate back to their communities during the COVID-19 pandemic. The authors suggest

- Institutions that remain operational should follow public health guidelines and ensure the safety of the children and caregivers.
- Records of children who left institutions and where they relocated to should be maintained.
- Plans regarding the care and protection of children after public health restrictions are lifted should be made.

Ethnicity and COVID-19: an urgent public health research priority.

Pareek M, Bangash MN, Pareek N, Pan D, Sze S, Minhas JS, Hanif W, Khunti K.
Lancet.
2020 Apr 21; PMID: 32330427
Level of Evidence: Level 5 - Expert opinion
Type of Article: Editorial

BLUF: The authors analyzed published papers and national surveillance reports on notifications and outcomes of COVID-19, and **only 2 out of 29 papers reported ethnicity disaggregated data.** Given the cultural and behavioral differences between different ethnicities (as well as the prevalence of certain comorbidities), more research must be urgently done to ascertain how COVID-19 affects ethnicities to inform public health interventions.

The Impact of COVID-19 on Syringe Services Programs in the United States

Glick SN, Prohaska SM, LaKosky PA, Juarez AM, Corcorran MA, Des Jarlais DC.
AIDS and Behavior
2020 Apr 24; PMID: 32333209
Level of Evidence: 4- Cross-sectional
Type of Article: Research

BLUF: Using quantitative and qualitative survey methods in major US cities, it was found that increased closure of Syringe Service Programs (SSPs) due to pandemic policies may lead to increased rates overdose and transmission of infectious diseases among the already vulnerable population of people who inject drugs (PWID).

Summary: Infectious disease experts and the University of Washington and New York University, utilizing quantitative surveys and qualitative interview methods on non-incentivised volunteers from major US cities, found that social distancing policies led to rapid closure of Syringe Service Programs (SSP), with up to one quarter reporting closure of at least 1 site. Authors warn this could have profoundly negative consequences in the already vulnerable population of people who inject drugs (PWID), including increased rates of overdose and transmission of infectious diseases.

Equity360: Gender, Race, and Ethnicity-COVID-19 and Preparing for the Next Pandemic.

O'Connor MI
Clin Orthop Relat Res
2020 Apr 20; PMID: 32332241
Level of Evidence: 5-Expert opinion
Type of Article: Opinion

Summary: In the context of a global pandemic that threatens to increase existing disparities based on race, age, citizenship, and location, the author offers practical options for orthopedic surgeons to help reduce these disparities before our next pandemic. Recommendations include:

- Encourage physical activity
- Address obesity
- Provide care to the underinsured
- Proactively engage patients in electronic medical systems
- Promote policies that increase health equity

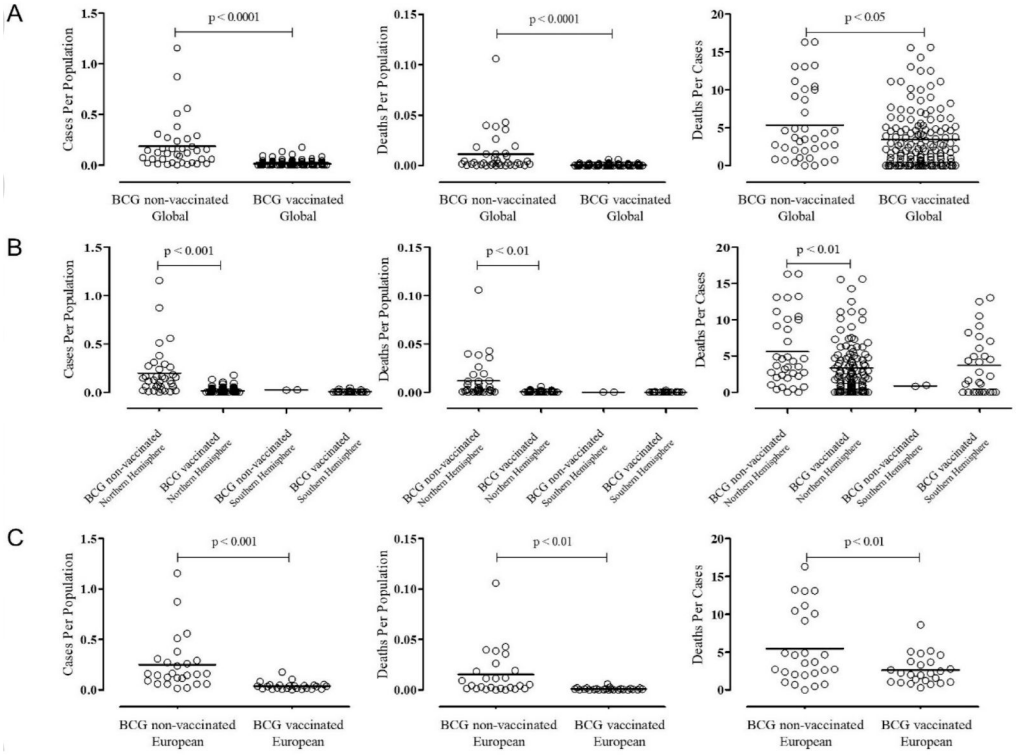
Epidemiology

Is BCG vaccination effecting the spread and severity of COVID-19?

Ozdemir C, Kucuksezer UC, Tamay ZU
2020 Apr 24;
Allergy
PMID: 32330314
Level of Evidence: 4 - Case-control
Type of Article: Research

BLUF: This case-control study compared the number of confirmed Covid-19 cases and deaths between countries that routinely vaccinate with BCG (n=138) and countries that do not routinely vaccinate with BCG (n=37). Mean cases per population, mean deaths per population, and the deaths per cases ratio were significantly lower in BCG vaccinated countries as compared to unvaccinated countries, both globally and within European countries. The authors acknowledge limitations of this observational study, and urge future research to clarify the impact of BCG vaccination on COVID-19.

Summarizing statement: "In our analysis, mean of cases per population ratio is statistically significantly lower in BCGvaccinated countries (n=138) in comparison with BCG-non-vaccinated countries (n=37), [(0.0147 ± 0.027) vs (0.189 ± 0.244), respectively, p<0.0001)] globally. Also, mean deaths per population is found to be significantly lower in BCG-vaccinated countries compared to BCG-non-vaccinated countries [(0.0004 ± 0.001) vs (0.0113 ± 0.020), respectively, p<0.0001)]. Deaths per cases ratio is also significantly lower in BCG-vaccinated countries [(3.4235 ± 3.688) vs (5.3429 ± 4.830), respectively, p<0.05)], (Figure 1A)."



"Legend for Figure 1: Relation between COVID-19 pandemics and BCG vaccination status
A. Global distribution of countries with COVID-19 cases (n=175) with respect to BCG-vaccination status. Mann Whitney-U test was used for comparison of relevant groups. (For Figures 1A-C, lines indicate mean of relevant groups.) B. Distribution of COVID-19 cases in the Northern (n=144) and Southern (n=31) hemispheres, with respect to BCG-vaccination status. ANOVA was used for comparison of groups, and Tukey's test was used as post hoc. C. Effects of BCG-vaccination on COVID-19 pandemics in European Countries [(BCGvaccinated countries (n=25), BCG-non-vaccinated countries (n=26)]. Independent samples T test was used for comparison of relevant groups."

[Understanding Epidemic Data and Statistics: A case study of COVID-19.]

Hoseinpour Dehkordi A, Alizadeh M, Derakhshan P, Babazadeh P, Jahandideh A.Hoseinpour Dehkordi A
J Med Virol
2020 March 18; PMID: 32329522
Level of Evidence: 4 - Case Study
Type of Article: Research

BLUF: Social distancing was one of the most effective policies to limit human to human transmission and reducing mortality and morbidity. To further boost effectiveness and management of COVID-19, a combination of multiple policies such as city lockdowns, shutdown of non essential companies, limiting social interactions and strict isolation protocols of confirmed COVID-19 cases in hospitals were implemented globally.

Abstract:
The 2019-Novel-Coronavirus (COVID-19) has affected 115 countries and out of more than 118,000 confirmed cases. Understanding the transmission dynamics of the infection in each country which affected on a daily basis and evaluating the effectiveness of control policies is critical for our further actions. To date, the statistics of COVID-19 reported cases show more than 80 percent of infected had a mild case of disease, while around 14 percent of infected experienced a severe one and about 5 percent are categorized as critical disease victims. Today's report (2020-03-12; daily updates in the prepared website) shows the **confirmed cases of COVID-19 in China, South Korea, Italy, and Iran are 80932, 7869, 12462 and 10075; respectively. Calculating the total Case Fatality Rate (CFR) of Italy (2020-03-04), about 7.9% of confirmed cases passed away. Compared to South Korea's rate of 0.76% (10% lower than Italy) and China's 3.8% (50% lower than Italy), the CFR of Italy is too high.** There are some effective policies that yield significant changes in the trend of cases. The lockdown policy in China and Italy (the effect observed after 11 days), Shutdown of all non-essential companies in Hubei (the effect observed after 5 days), combined policy in South Korea and reducing working hours in Iran.

Table 1. Top 10 total Confirmed, Deaths & Recovered cases for March-6th

Country/Region	Confirmed	Deaths	Recovered
China	80573	3042	53888
South Korea	6593	42	135
Iran	4747	124	913
Italy	4636	197	523
Germany	670	0	17
France	653	9	12
Japan	420	6	46
Spain	400	5	2
US 278	14	8	
Switzerland	214	1	3

Table 2. Countries with no active cases March-6th

Country/Region	Confirmed	Deaths	Recovered
Vietnam	16	0	16
Macau	10	0	10
Cambodia	1	0	1
Nepal	1	0	1
Sri Lanka	1	0	1

Figure 1. Transmission of Coronavirus Disease 2019-2020 (COVID-19); Blue nodes represents regions with confirmed COVID-19 cases, and Red nodes represents the regions with COVID 19 causes deaths

Doubling Time of the COVID-19 Epidemic by Province, China

Muniz-Rodriguez K, Chowell G, Cheung CH, Jia D, Lai PY, Lee Y, Liu M, Ofori SK, Roosa KM, Simonsen L, Viboud C, Fung IC
Emerg Infect Dis
2020 Apr 24; PMID: 32330410
Level of Evidence: 5 - Basic Research
Type of Article: Research Letter

BLUF: "We analyzed, by province, the number of times coronavirus disease (COVID-19) cumulative incidence doubled and the evolution of the doubling times in mainland China, from January 20 (when nationwide reporting began) through February 9, 2020. We retrieved province-level daily cumulative incidence data from provincial health commissions' websites and conducted 2 sensitivity analyses based on a longer and a shorter time period."

Abstract:
In China, the doubling time of the coronavirus disease epidemic by province increased during January 20-February 9, 2020. Doubling time estimates ranged from 1.4 (95% CI 1.2-2.0) days for Hunan Province to 3.1 (95% CI 2.1-4.8) days for Xinjiang Province. The estimate for Hubei Province was 2.5 (95% CI 2.4-2.6) days.

Modeling

Correlation between climate indicators and COVID-19 pandemic in New York, USA

Bashir MF, Ma B, Bilal, Komal B, Bashir MA, Tan D, Bashir M
Sci Total Environ
2020 Apr 20; PMID: 32334162
Level of Evidence: Ecologic Study
Type of Article: Research

BLUF: Using data pulled from the United States National Weather Service, the authors analyze the impact of specific climate change indicators (temperature, humidity, wind speed, air quality, and rainfall) to determine if there is any correlation between these indicators and the spread of COVID-19 in New York City between March 1 and April 12, 2020. They argue that there was a significant correlation between the spread of COVID-19 and the average and minimum temperature as well as air quality.

Abstract:
This study analyzed the association between COVID-19 and climate indicators in New York City, USA. We used secondary published data from New York city health services and National weather service, USA. The climate in-dicators included in the study are average temperature, minimum temperature, maximum temperature, rainfall,average humidity, wind speed, and air quality. Kendall and Spearman rank correlation tests were chosen for data analysis. We find that average temperature, minimum temperature, and air quality were significantly associated with the COVID-19 pandemic. The findings of this study will help *(sic)* World Health Organization and health regulators such as Center for Disease Control (CDC) to combat COVID-19 in New York and the rest of the world.

Development of an Assessment Method for Investigating the Impact of Climate and Urban Parameters in Confirmed Cases of COVID-19: A New Challenge in Sustainable Development.

Pirouz B, Shaffiee Haghshenas S, Pirouz B, Shaffiee Haghshenas S, Piro P.
Int J Environ Res Public Health
2020 Apr 18; PMID: 32325763
Level of Evidence: Statistical modeling based on case studies
Type of Article: Research

BLUF: The authors developed a multivariate linear regression and trend analysis of 3 large case studies conducted in Italy to investigate the impact of climate and urban parameters in confirmed COVID-19 cases. The developed assessment method predicted a delay from four to eight days between the effect of weather parameters and new confirmed cases.

Abstract:
Sustainable development has been a controversial global topic, and as a complex concept in recent years, it plays a key role in creating a favorable future for societies. Meanwhile, there are several problems in the process of implementing this approach, like epidemic diseases. Hence, in this study, the impact of climate and urban factors on confirmed cases of COVID-19 (a new type of coronavirus) with the trend and multivariate linear regression (MLR) has been investigated to propose a more accurate prediction model. For this purpose, some important climate parameters, including daily average temperature, relative humidity, and wind speed, in addition to urban parameters such as population density, were considered, and their impacts on confirmed cases of COVID-19 were analyzed. The analysis was performed for three case studies in Italy, and the application of the proposed method has been investigated. The impacts of parameters have been considered with a delay time from one to nine days to find out the most suitable combination. The result of the analysis demonstrates the effectiveness of the proposed model and the impact of climate parameters on the trend of confirmed cases. The research hypothesis approved by the MLR model and the present assessment method could be applied by considering several variables that exhibit the exact delay of them to new confirmed cases of COVID-19.

SBDiEM: A New Mathematical Model of Infectious Disease Dynamics.

Bekiros S, Kouloumpou D.
Chaos Solitons Fractals.
2020 Apr 23; PMID: 32327901
Level of Evidence: Statistical modeling
Type of Article: Expert Opinion

BLUF: Authors affiliated with the Hellenic Naval Academy Mathematical Modeling and Applications Laboratory in Greece introduce a **new spatiotemporal approach (SBDiEM**) for "modeling, forecasting and nowcasting infectious dynamics". They postulate that this new model, which utilizes sophisticated mathematics and artificial intelligence, is designed to provide an **accurate representation of contagious disease dynamics** and can be used to **predict, track, and combat global outbreaks** such as the current COVID-19 pandemic.

Abstract:
A worldwide multi-scale interplay among a plethora of factors, ranging from micro-pathogens and individual or population interactions to macro-scale environmental, socio-economic and demographic conditions, entails the development of highly sophisticated mathematical models for robust representation of the contagious disease dynamics that would lead to the improvement of current

outbreak control strategies and vaccination and prevention policies. Due to the complexity of the underlying interactions, both deterministic and stochastic epidemiological models are built upon incomplete information regarding the infectious network. Hence, rigorous mathematical epidemiology models can be utilized to combat epidemic outbreaks. We introduce a new spatiotemporal approach (SBDiEM) for modeling, forecasting and nowcasting infectious dynamics, particularly in light of recent efforts to establish a global surveillance network for combating pandemics with the use of artificial intelligence. This model can be adjusted to describe past outbreaks as well as COVID-19. Our novel methodology may have important implications for national health systems, international stakeholders and policy makers.

Epidemiology of Coronavirus COVID-19: Forecasting the Future Incidence in Different Countries.

Stubinger, Johannes; Schneider, Lucas
Healthcare (Basel)
2020 Apr 15; PMID: 32326512
Level of Evidence: Statistical modeling
Type of Article: Research

BLUF: This group designed an algorithm that utilizes lead-lag effects between different countries and dynamic time warping in order to predict future spread of COVID-19; this was applied to COVID-19 cases of the 10 most affected countries from Jan 1 2020 to Mar 28 2020, using China as the lead, in order to forecast the growth of cases. During the worst case scenario, their model predicts "a future collapse of the healthcare systems of the United Kingdom and Switzerland".

Abstract:
This paper forecasts the future spread of COVID-19 by exploiting the identified lead-lag effects between different countries. Specifically, we first determine the past relation among nations with the aid of **dynamic time warping**. This procedure allows an elastic adjustment of the time axis to find similar but phase-shifted sequences. Afterwards, the established framework utilizes information about the leading country to predict the Coronavirus spread of the following nation. The presented methodology is applied to confirmed Coronavirus cases from **1 January 2020 to 28 March 2020**. Our results show that China leads all other countries in the range of **29 days for South Korea and 44 days for the United States**. Finally, we predict a **future collapse of the healthcare systems of the United Kingdom and Switzerland in case of our explosion scenario**.

Table 2. Population, intensive care unit (ICU) beds, forecast of newly incoming COVID-19 cases between 12 April 2020 and 26 April 2020, and if there is a collapse in the healthcare system of Italy, France, Germany, Spain, Switzerland, United Kingdom (UK), United States (US), South Korea, and Iran.

Country	Population	ICU Beds	COVID-19 Cases Explosion	Collapse
Italy	60,431,280	7500	14,258	No
France	66,987,240	7500	14,804	No
Germany	82,927,920	24,000	9540	No
Spain	46,723,750	5000	20,039	Unclear
Switzerland	8,516,540	1000	40,346	Yes
UK	66,488,990	4500	49,621	Yes
US	327,167,430	205,000	138,211	No
South Korea	51,635,260	5500	1620	No
Iran	81,800,270	4000	4442	No

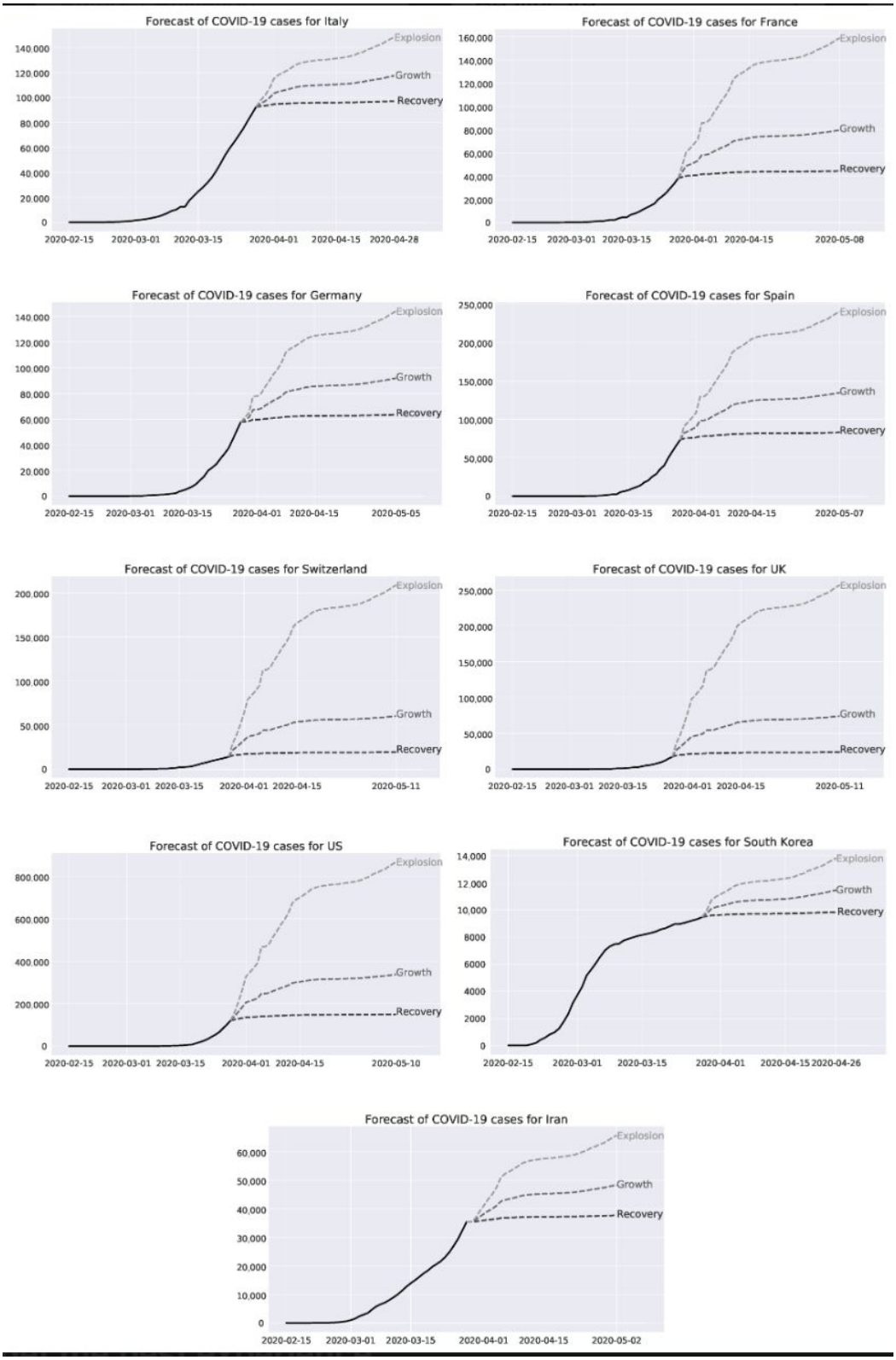


Figure 4: Forecast of COVID-19 ases for Italy, France, Germany, Spain, Switzerland, UK, US, South Korea, and Iran.

Dynamic models for Coronavirus Disease 2019 and data analysis.

Shao N, Zhong M, Yan Y, Pan H, Cheng J, Chen W
Math Methods Appl Sci
2020 May 15; PMID: 32327866
Level of Evidence: Computational model
Type of Article: Letter

BLUF: An introduction to two computational models of COVID-19 spread, the Time Delay Dynamical–Novel Coronavirus Pneumonia (TDD-NCP) model and the Fudan-Chinese Centers for Disease Control and Prevention (Fudan-CCDC) model, with an analysis of how the severity of isolation strategies in Japan could impact containment. The paper also looks briefly at China, Singapore and the Diamond Princess cruise ship. Their model suggests the severity of the epidemic highly depends on early isolating measures.

Abstract:
In this letter, two time delay dynamic models, a Time Delay Dynamical–Novel Coronavirus Pneumonia (TDD-NCP) model and Fudan-Chinese Center for Disease Control and Prevention (CCDC) model, are introduced to track the data of Coronavirus Disease 2019 (COVID-19). The TDD-NCP model was developed recently by Chengąŕs group in Fudan and Shanghai University of Finance and Economics (SUFE). The TDD-NCP model introduced the time delay process into the differential equations to describe the latent period of the epidemic. The Fudan-CDCC model was established when Wenbin Chen suggested to determine the kernel functions in the TDD-NCP model by the public data from CDCC. By the public data of the cumulative confirmed cases in different regions in China and different countries, these models can clearly illustrate that the containment of the epidemic highly depends on early and effective isolations.

Estimating the Effects of Asymptomatic and Imported Patients on COVID-19 Epidemic Using Mathematical Modeling.

Sun T, Weng D.Sun T, et al.
J Med Virol.
2020 Apr 24; PMID: 32330299
Level of Evidence: Predictive modeling
Type of Article: Mathematical model

BLUF: The authors discuss the process of creating and the predictions from a mathematical model based on data from COVID-19 outbreaks in two Chinese provinces. Their model predicts that contact with asymptomatic carriers is the strongest factor predicting new outbreaks. Based on this they recommend continued strict restrictions in China.

Summary: Confirmed and recovered cases were used to create a mathematical model predicting COVID-19 outbreaks. The authors analyzed data from the time period 1/23/2020-3/31/2020 in Jiangsu and Anhui provinces in China and created three sequential models, to find the best fit for the data. The final model incorporated five population variables: susceptible, closely observed, “including people under public health intervention [quarantine]”, infected, recovered, and asymptomatic. Their model also incorporates time in quarantine, recovery rate, and transitions from asymptomatic to diagnosed cases. Based on this model their model predicts higher asymptomatic carriers freely moving within the population predict “faster outbreaks and larger outbreak sizes compared with imported patients” and based on this they recommend continued restrictions in China.

Spread and dynamics of the COVID-19 epidemic in Italy: Effects of emergency containment measures

Gatto, Marino; Bertuzzo, Enrico; Mari, Lorenzo; Miccoli, Stefano; Carraro, Luca; Casagrandi, Renato; Rinaldo, Andrea
Proc Natl Acad Sci U S A
2020 Apr 23; PMID: 32327608
Level of Evidence: Statistical Modeling
Type of Article: Research

BLUF: In their modeling of the COVID-19 endemic in Italy, mobile and human-to-human interaction restrictions were found to reduce transmission by 45%. With this data, the authors support the use of emergency restrictions such as these.

Abstract:
The spread of coronavirus disease 2019 (COVID-19) in Italy prompted drastic measures for transmission containment. We examine the effects of these interventions, based on modeling of the unfolding epidemic. We test modeling options of the spatially explicit type, suggested by the wave of infections spreading from the initial foci to the rest of Italy. We estimate parameters of a metacommunity Susceptible-Exposed-Infected-Recovered (SEIR)-like transmission model that includes a network of 107 provinces connected by mobility at high resolution, and the critical contribution of presymptomatic and asymptomatic transmission. We estimate a generalized reproduction number ([Formula: see text] = 3.60 [3.49 to 3.84]), the spectral radius of a suitable next-generation matrix that measures the potential spread in the absence of containment interventions. The model includes the implementation of progressive restrictions after the first case confirmed in Italy (February 21, 2020) and runs until March 25, 2020. We account for uncertainty in epidemiological reporting, and time dependence of human mobility matrices and awareness-dependent exposure probabilities. We draw scenarios of different containment measures and their impact. **Results suggest that the sequence of restrictions posed to mobility and human-to-human interactions have reduced transmission by 45% (42 to 49%).** Averted hospitalizations are measured by running scenarios obtained by selectively relaxing the imposed restrictions and total about 200,000 individuals (as of March 25, 2020). Although a number of assumptions need to be reexamined, like age structure in social mixing patterns and in the distribution of mobility, hospitalization, and fatality, we conclude that verifiable evidence exists to support the planning of emergency measures.

Symptoms and Clinical Presentation

Adults

Characteristics of Hospitalized Adults With COVID-19 in an Integrated Health Care System in California.

Myers LC, Parodi SM, Escobar GJ, Liu VX
JAMA
2020 Apr 24; PMID: 32329797
Level of Evidence: 3 - Retrospective cohort study
Type of Article: Research

Summary: The authors of this retrospective cohort study out of Kaiser Permanente of Northern California (KPNC) demonstrate the characteristics (age, gender, comorbidities and diagnostic studies) of adult COVID-19 positive patients admitted to KPNC hospitals during the month of March (see

Figure below). Of the 1,299 COVID-19 positive patients, 377 (29%) were hospitalized, 113 (8.7%) of which in the ICU, which is similar to CDC's report of the US as a whole (21%-31% and 5-12% respectively).

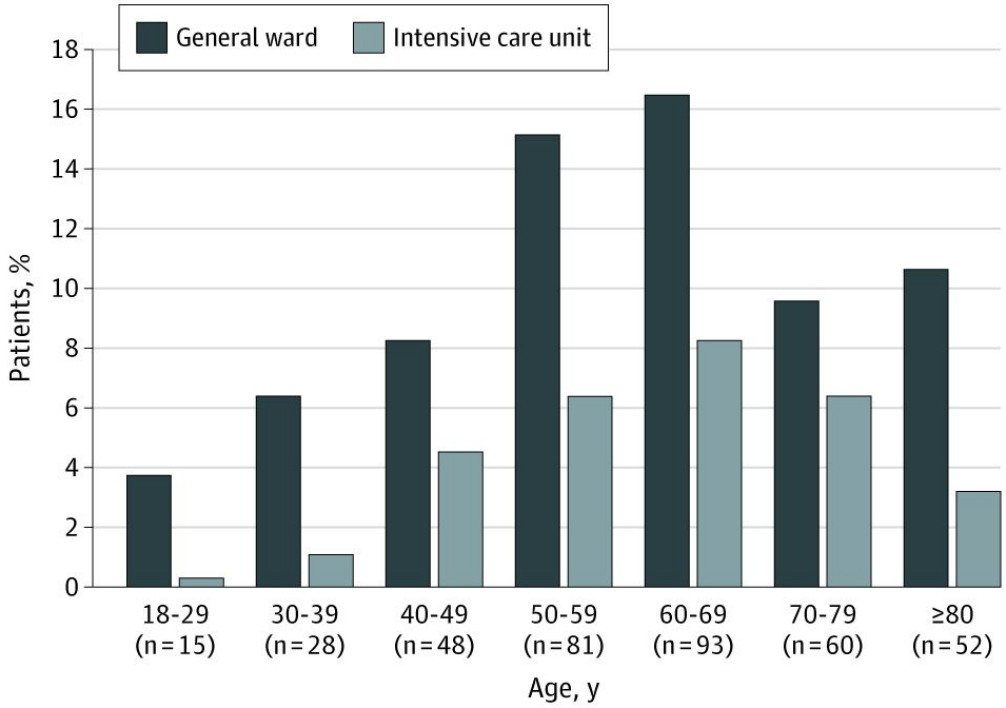
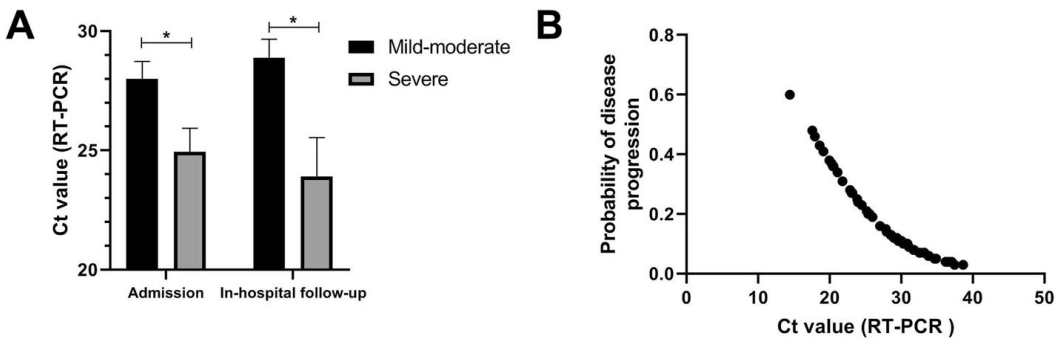


Figure. Distribution by Age Group of Adult Patients Admitted to General Ward and Intensive Care Unit With Coronavirus Disease 2019

SARS-CoV-2 viral load in sputum correlates with risk of COVID-19 progression.

Yu X, Sun S, Shi Y, Wang H, Zhao R, Sheng J.
Crit Care.
2020 Apr 23; PMID: 32326952
Level of Evidence: Level 3 - Cohort/follow-up study
Type of Article: Research

Summary: Researchers collected sputum samples from the lower respiratory tracts from 92 patients with confirmed COVID-19 who were admitted to the First Affiliated Hospital of Zhejiang University. The levels of viral nucleic acid were determined by a real-time PCR (RT-PCR) approach and indicated by the cycle threshold (Ct) values of RT-PCR assays. **Severe patients and patients who became severe during their hospitalization had a significantly higher viral load (and thus lower Ct value) than patients with mild-moderate illness.**



15-day mortality and associated risk factors for hospitalized patients with COVID-19 in Wuhan, China: an ambispective observational cohort study.

Wang K, Zhang Z, Yu M, Tao Y, Xie M.
Intensive Care Med.
2020 Apr 23; PMID: 32328724
Level of Evidence: 3 - Observational cohort
Type of Article: Letter

Summary: A single-center, ambispective cohort study prospectively followed up on 548 patients to assess death within 15 days of hospitalization. The study found that 14.2% of patients in the cohort reached the primary endpoint of death within 15-day hospitalization. Aging, hypoxia, lymphopenia, high LDH level and multiple organ dysfunction were associated with increased 15-day in-hospital mortality from COVID-19.

Clinical and virologic characteristics of the first 12 patients with coronavirus disease 2019 (COVID-19) in the United States.

COVID-19 Investigation Team
Nature Medicine
2020 Apr 23; PMID: 32327757
Level of Evidence: 4 - Case Series
Type of Article: Letter

BLUF: This is a case series of the first 12 US patients confirmed to have COVID-19 from 20 Jan 2020 to 5 Feb 2020, where they report a mean age of 53 years and more tha half were men. The initial symptoms were cough and fever and most patients developed mild to moderate illness. Despite 7 being hospitalized none required ventilation.

Abstract:
Data on the detailed clinical progression of COVID-19 in conjunction with epidemiological and virological characteristics are limited. In this case series, we describe the first 12 US patients confirmed to have COVID-19 from 20 January to 5 February 2020, including 4 patients described previously(1-3). Respiratory, stool, serum and urine specimens were submitted for SARS-CoV-2 real-time reverse-transcription polymerase chain reaction (rRT-PCR) testing, viral culture and whole genome sequencing. Median age was 53 years (range: 21-68); 8 patients were male. Common symptoms at illness onset were cough (n = 8) and fever (n = 7). Patients had mild to moderately severe illness; seven were hospitalized and demonstrated clinical or laboratory signs of worsening during the second week of illness. No patients required mechanical ventilation and all recovered. All had SARS-CoV-2 RNA detected in respiratory specimens, typically for 2-3 weeks after illness onset. Lowest real-time PCR with reverse transcription cycle threshold values in the upper respiratory tract were often detected in the first week and SARS-CoV-2 was cultured from early respiratory specimens. These data provide insight into the natural history of SARS-CoV-2. Although infectiousness is unclear, highest viral RNA levels were identified in the first week of illness. Clinicians should anticipate that some patients may worsen in the second week of illness.

The role of self-reported olfactory and gustatory dysfunction as a screening criterion for suspected COVID-19.

Wee LE, Chan YFZ, Teo NWY, Cherng BPZ, Thien SY, Wong HM, Wijaya L, Toh ST, Tan TT
Eur Arch Otorhinolaryngol

2020 Apr 24; PMID: 32328771
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter
Summary Excerpt: "[S]elf-reported olfactory or taste disorders (OTD) had high specificity as a screening criterion for COVID-19 in an Asian cohort. Patients with COVID-19 appeared to have higher odds of OTD compared to those positive for other respiratory viruses. Routine screening in patients with new-onset OTD can improve case detection during a COVID-19 outbreak."

Neurological complications of coronavirus and COVID-19.

Carod-Artal FJ
Rev Neurol
2020 May 1; PMID: 32329044
Level of Evidence: 5 - Expert Opinion
Type of Article: Editorial (Full text Spanish only as of 25 Apr 2020)
BLUF: Authors examine various factors of SARS-CoV-2, including:

- Typical clinical manifestations of cough, fatigue, sputum production, and dyspnea
- Neurological complications of coronaviruses and COVID-19 specific neurological complications including smell and taste disorders, encephalopathy, encephalitis, necrotising hemorrhagic encephalopathy, Guillain-Barre syndrome, and cerebrovascular complications
- Potential pathogenic mechanisms including hematological dissemination, transsynaptic transference, ACE2 receptor regulation, hypoxia, and neurological-mediated damage
- RT-PCR as the fastest and most efficient method for detection

Abstract:
Introduction: Clinical and experimental studies have shown that the coronavirus family has a certain **tropism for the central nervous system**. Seven types of coronavirus can infect humans. Development: Coronaviruses are not always confined to the respiratory tract, and under certain conditions they can invade the central nervous system and cause neurological pathologies. The potential for neuroinvasion is well documented in most human coronaviruses (OC-43, 229E, MERS and SARS) and in some animal coronaviruses (porcine haemagglutinating encephalomyelitis coronavirus). **Neurological symptoms have been reported in patients affected by COVID-19, such as headache, dizziness, myalgia and anosmia, as well as cases of encephalopathy, encephalitis, necrotising haemorrhagic encephalopathy, stroke, epileptic seizures, rhabdomyolysis and Guillain-Barre syndrome, associated with SARS-CoV-2 infection.**
Conclusions:Future epidemiological studies and case records should elucidate the real incidence of these neurological complications, their pathogenic mechanisms and their therapeutic options.

Neurological Complications of Coronavirus Disease (COVID-19): Encephalopathy.

Filatov A, Sharma P, Hindi F, Espinosa PS
Cureus
2020 Mar 21; PMID: 32328364
Level of Evidence: 4 - Case Study
Type of Article: Research
Summary: Neurologists at the Charles E. Schmidt College of Medicine and Boca Raton Regional Hospital in Florida present a case study of a 74-year-old Dutch man with a past medical history significant for atrial fibrillation, cardioembolic stroke, parkinson disease, COPD, and recent cellulitis

who re-presented to the emergency department eight days after arriving to the United States with encephalopathy. He was subsequently found to have COVID-19, suggesting that **encephalopathy may be a presenting sign of COVID-19, especially in older patients with comorbid conditions.**

Pediatrics

Neurologic manifestations in an infant with COVID-19

Dugue, Rachelle; Cay-Martínez, Karla C; Thakur, Kiran; Garcia, Joel A; Chauhan, Lokendra V; Williams, Simon H; Briese, Thomas; Jain, Komal; Foca, Marc; McBrian, Danielle K; Bain, Jennifer M; Lipkin, W Ian; Mishra, Nischay
Neurology
2020 Apr 23; PMID: 32327489
Level of Evidence: 4 - Case Report
Type of Article: Research

Summary: A 6-week-old term infant presented with a brief episode of sustained upward gaze and bilateral leg stiffening in the setting of one day fever and cough. Patient was found to be COVID-19 and rhinovirus positive. Authors encourage practitioners to be wary of co-infections and possible neurological manifestations of COVID-19 in children.

Acral cutaneous lesions in the Time of COVID-19.

Recalcati S, Barbagallo T, Frasin LA, Prestinari F, Cogliardi A, Provero MC, Dainese E, Vanzati A, Fantini F.
J Eur Acad Dermatol Venereol.
2020 Apr 24; PMID: 32330324
Level of Evidence: 4 – Case Report
Type of Article: Letter to the Editor

BLUF: This letter reports peculiar (perniosis-like) lesions observed in young outpatients who visited the Dermatologic Unit in the last 4 weeks of COVID-19 pandemic (March-April 2020). They suspected that these cutaneous manifestations could be COVID-19 related.

Abstract:
Coronavirus disease 2019 (COVID-19) has become a pandemic condition, yet little is known about its dermatologic manifestations. We report here on peculiar (perniosis-like) skin lesions, unreported in the previous years, observed in young outpatients visited in our Dermatologic Unit in the last 4 weeks of COVID-19 pandemic (March-April 2020). Similar cases were referred to us in the same period by Pediatricians and Dermatologists from Italy and European countries.

Figure 1. Clinical images. (a) Violaceous papules and digital swelling on the feet of a 14 year-old female. A small overlying blister is visible on the big toe. (b) Purple macules on the right foot of a 18 year-old female. (c) Erythematous macules on the right hand of a 14 year-old female. Targetoid lesions are present. (d) Targetoid lesions on the elbows of a 11 year-old male.

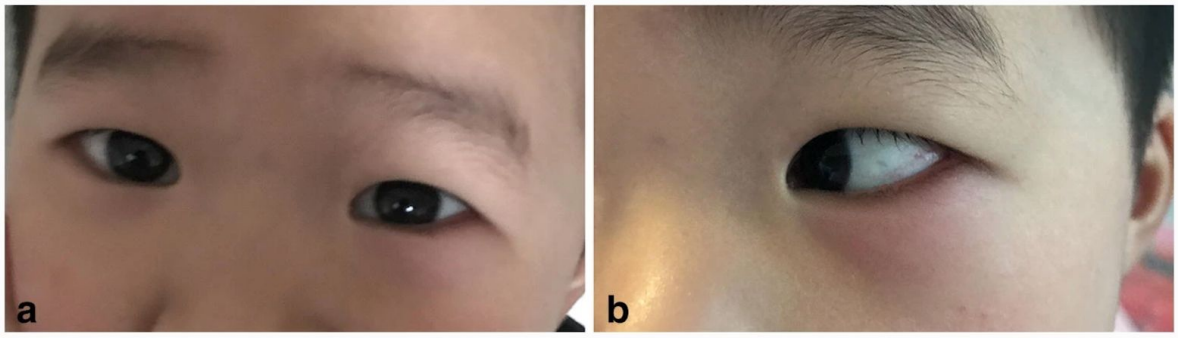
A child confirmed COVID-19 with only symptoms of conjunctivitis and eyelid dermatitis.

Wu P, Liang L, Chen C, Nie S.Wu P, et al.
Graefes Arch Clin Exp Ophthalmol.
2020 Apr 24; PMID: 32333104
Level of Evidence: 4- Case Report
Article Type: Letter to the Editor

BLUF: This case reports on a SARS-CoV-2 confirmed boy with conjunctivitis and eyelid dermatitis, possibly the first pediatric case presenting solely with ocular symptoms.

Summary: The authors report on a SARS-CoV-2 positive, boy (2 years and 10 months old) with conjunctivitis and eyelid dermatitis without any other presenting symptoms. He was initially asymptomatic when he tested positive for SARS-CoV-2 nucleic acid from nasopharyngeal swabs. **After 7 days, he developed conjunctivitis and eyelid dermatitis**, and was admitted to the hospital. Inpatient testing reconfirmed SARS-CoV-2 with RT-PCR. Myocardial damage and atypical change in lymphocyte count was also observed (Table 1), while chest CT was normal. His conjunctivitis and eyelid dermatitis gradually resolved 5 days after admission. The authors reason that the abnormally high lymphocyte count is in part due to the higher count of lymphocytes in children less than 5 compared to adults. **The authors discuss that ACE2 is expressed in the conjunctiva and cornea, which could explain this child's presentation.**

There has been previous reports of conjunctivitis in SARS-CoV-2 adult cases, but this may be the first case reported with an infected child having ocular symptoms.



a and **b** Day 1 of admission. The pictures showed conjunctival congestion and eyelid redness and swelling in the left eye

	1st day	11th day	Reference range
White blood cell count, *10^9/L	9.57	5.02	3.5–9.5
Lymphocyte count,*10^9/L	4.48	3.20	1.1–3.2
Neutrophil count,*10^9/L	4.29	1.22	1.8–6.3
Platelet count,*10^9/L	289	298	125–350
Procalcitonin (PCT), ng/mL	< 0.05	–	0–0.05
C- reactive protein (CRP), mg/L	6.5	0.5	0–10
Troponin I (CTnI), μg/L	< 0.01	< 0.01	0–0.01
Myoglobin (MYO), μg/L	17	60	10–46
Creatine kinase (CK), IU/L	295	–	50–310
Creatine kinase isoenzyme–MB (CKMB), μg/L	6.38	6.77	0–5.1
Lactate dehydrogenase (LDH), IU/L	329	–	120–250
Alanine aminotransferase (ALT), U/L	24	20	9–50
Aspartate minotransferase (AST), U/L	35	30	15–40
Urea, mmol/L	5.37	–	3.1–8.0
Creatinine, umol/L	27.1	–	57–97

"–" represents no retests in this admission

Table 1: Partial results of blood tests after admission

Advanced age

Age, Frailty and Diabetes - Triple Jeopardy for Vulnerability to COVID-19 Infection

Sinclair, A J; Abdelhafiz, A H
EClinicalMedicine
2020 Apr 23; PMID: 32328575
Level of Evidence: 5 – Expert Opinion
Type of Article: Commentary

Summary: In an epidemiological analysis of 72,314 cases of COVID-19 in China the proportion of cases in the elderly was 44.1% and the mortality rate also increased proportionally with age, 8% in those aged 70-79 years and 14.8% in those over 80. In addition, patients with diabetes mellitus were more likely to require intensive care treatment (22.2% vs 5.9%) and have a higher mortality rate (7.3% vs .9%) compared to those who did not.

Understanding the Pathology

In silico

The Architecture of SARS-CoV-2 Transcriptome.

Kim D, Lee JY, Yang JS, Kim JW, Kim VN, Chang H.
Cell
2020 Apr 18; PMID: 32325421
Level of Evidence: 5-Basic research
Type of Article: Short Communication

BLUF: Here the authors use two two complementary sequencing approaches, Illumina-based sequencing (DRS) and nanopore-based sequencing (SBS) in order to get a better understanding of the transcriptomic signature of SARS-CoV-2 in infected cells. They map genomic RNA, subgenomic RNA (sgRNAs), open reading frames (ORFs), and transcription-regulatory sequences (TRSs). "An in-depth analysis of the joint reads [reveal] a highly complex landscape of viral RNA synthesis."

Abstract:
SARS-CoV-2 is a betacoronavirus responsible for the COVID-19 pandemic. Although the SARS-CoV-2 genome was reported recently, its transcriptomic architecture is unknown. Utilizing two complementary sequencing techniques, **we present a highresolution *(sic)* map of the SARS-CoV-2 transcriptome and epitranscriptome.** DNA nanoball sequencing shows that the transcriptome is highly complex owing to numerous discontinuous transcription events. In addition to the canonical genomic and 9 subgenomic RNAs, SARS-CoV-2 produces transcripts encoding unknown ORFs with fusion, deletion, and/or frameshift. Using nanopore direct RNA sequencing, we further find at least 41 RNA modification sites on viral transcripts, with the most frequent motif, AAGAA. Modified RNAs have shorter poly(A) tails than unmodified RNAs, suggesting a link between the modification and the 30 tail. **Functional investigation of the unknown transcripts and RNA modifications discovered in this study will open new directions to our understanding of the life cycle and pathogenicity of SARS-CoV-2.**

Coronavirus in Hematologic Malignancies: Targeting Molecules Beyond the Angiotensin-Converting Enzyme 2 (ACE2) Wall in COVID-19

Tsiambas E, Papanikolaou V, Chrysovergis A, Mastronikolis N, Ragos V, Kavantzas N, Lazaris AC, Kyrodimos E
Pathol Oncol Res
2020 Apr 24; PMID: 32333199
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter to the editor

Summary: Here the authors speculate about the relationship between the requirement of SARS-CoV-2 for furin mediated entry and hypoxia. They offer their opinion that "..Vascular Endothelial Growth Factor/receptor (VEGF- band 6p21.1 /VEGFR), Mas receptor (MasR-6q25.3) and Hypoxia - Inducible Factor 1-alpha (HIF-1a - band14q23.2) should be analyzed in conjunction with hACE2 and Furin/GBP/PACS 1 complex for understanding the complete mechanism of SARS-CoV-2 - dependent severe pneumonia complicated or not with pulmonary embolism in the general population and especially in immunocompromised patients with hematologic malignancies and HSCTs."

Genetic Roadmap for Kidney Involvement of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection.

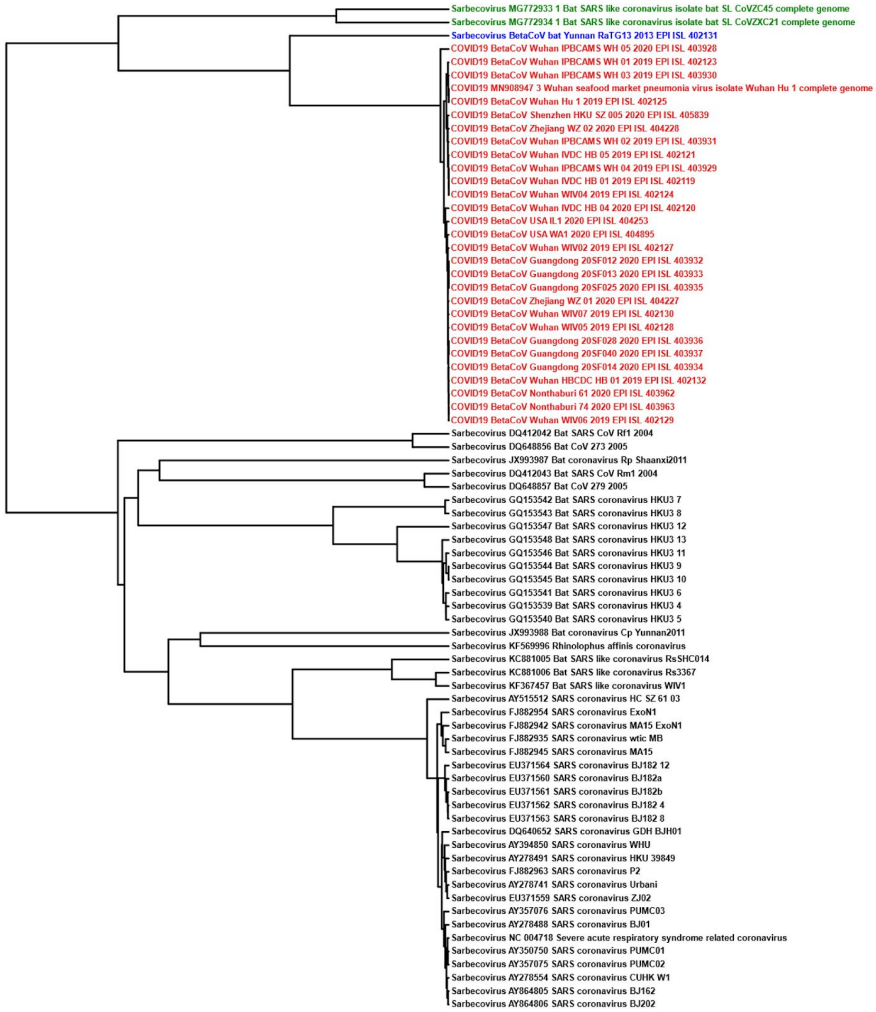
Zhang YM, Zhang H
Clin J Am Soc Nephrol

2020 Apr 23; PMID: 32327413
Level of Evidence: 5 - Mechanistic
Type of Article: Research
Summary: Human angiotensin-converting enzyme 2 (ACE2) has been identified as the functional receptor of SARS-CoV-2. A genetic analysis of the spatial distribution of human ACE2 expression found 49 variants in kidney tubulointerstitial tissue ($p < 0.05$). The spatial characteristics of RNA, protein expression of human ACE2, and kidney-specific eQTL (expression quantitative trait loci) indicate that SARS-COV-2 could affect the kidneys of the general population infected with the virus. This study suggests that **tubular injury might be the main pathologic manifestation of kidney involvement in patients with SARS-CoV-2.**

Machine learning using intrinsic genomic signatures for rapid classification of novel pathogens: COVID-19 case study

Randhawa GS, Soltysiak MPM, El Roz H, de Souza CPE, Hill KA, Kari L.Randhawa GS
PLoS One
2020 April 24; PMID: 32330208
Level of Evidence: 4 Case Study
Type of Article: Research
BLUF: Using a machine learning-based approach for classification of SARS-CoV-2 genomes, researchers classify the virus as sarbecovirus, within betacoronavirus.

Abstract:
The 2019 novel coronavirus (renamed SARS-CoV-2, and generally referred to as the COVID-19 virus) has spread to 184 countries with over 1.5 million confirmed cases. Such major viral outbreaks demand early elucidation of taxonomic classification and origin of the virus genomic sequence, for strategic planning, containment, and treatment. This paper identifies an intrinsic COVID-19 virus genomic signature and uses it together with a **machine learning-based alignment-free approach for an ultra-fast, scalable, and highly accurate classification of whole COVID-19 virus genomes.** The proposed method combines supervised machine learning with digital signal processing (MLDSP) for genome analyses, augmented by a decision tree approach to the machine learning component, and a Spearman's rank correlation coefficient analysis for result validation. These tools are used to analyze a large dataset of over 5000 unique viral genomic sequences, totalling 61.8 million bp, including the 29 COVID-19 virus sequences available on January 27, 2020. Our results support a hypothesis of a bat origin and classify the **COVID-19 virus** as **Sarbecovirus, within Betacoronavirus.** Our method achieves **100% accurate classification** of the COVID-19 virus sequences, and discovers the most relevant relationships among over 5000 viral genomes within a few minutes, ab initio, using raw DNA sequence data alone, and without any specialized biological knowledge, training, gene or genome annotations. This suggests that, for novel viral and pathogen genome sequences, this alignment-free whole-genome machine-learning approach can provide a reliable real-time option for taxonomic classification.



In vitro

Neutrophil Extracellular Traps in COVID-19

Zuo Y, Yalavarthi S, Shi H, Gockman K, Zuo M, Madison JA, Blair CN, Weber A, Barnes BJ, Egeblad M, Woods RJ, Kanthi Y, Knight JS

JCI Insight
2020 Apr 24; PMID: 32329756
Level of Evidence: 4 – Cohort study
Type of Article: Research

BLUF: This correlative study investigates the **role of neutrophil extracellular traps** (NETs) in the **serum of patients with COVID-19 versus control healthy patients (n=89)**. The authors describe the functionality of NETs as mechanisms to combat disease, and they highlight cases of **NETs contributing to progression of influenza** due to **thrombotic events**. Key findings of this study include significantly **higher levels of NET markers in COVID-19 patients**, and the ability of serum from COVID-19 patients to induce more NET formation. They acknowledge the need for further study into whether NETs drive disease or are a consequence of another process.

Abstract:
In severe cases of coronavirus disease 2019 (COVID-19), viral pneumonia progresses to respiratory failure. Neutrophil extracellular traps (NETs) are extracellular webs of chromatin, microbicidal

proteins, and oxidant enzymes that are released by neutrophils to contain infections. However, when not properly regulated, **NETs have potential to propagate inflammation and microvascular thrombosis** - including in the lungs of patients with acute respiratory distress syndrome. While elevated levels of blood neutrophils predict worse outcomes in COVID-19, the role of NETs has not been investigated. We now report that sera from patients with COVID-19 (n = 50 patients, n = 84 samples) have elevated levels of **cell-free DNA, myeloperoxidase (MPO)-DNA, and citrullinated histone H3 (Cit-H3)**; the latter two are highly specific markers of NETs. Highlighting the potential clinical relevance of these findings, **cell-free DNA strongly correlated** with acute phase reactants including **C-reactive protein, D-dimer, and lactate dehydrogenase, as well as absolute neutrophil count**. MPO-DNA associated with both cell-free DNA and absolute neutrophil count, while Cit-H3 correlated with platelet levels. Importantly, **both cell-free DNA and MPO-DNA** were **higher** in hospitalized **patients receiving mechanical ventilation** as compared with hospitalized patients breathing room air. Finally, **sera** from individuals with **COVID-19 triggered NET release from control neutrophils** in vitro. In summary, these data reveal high levels of NETs in many patients with COVID-19, where they may contribute to cytokine release and respiratory failure. Future studies should investigate the predictive power of circulating NETs in longitudinal cohorts, and determine the extent to which NETs may be novel therapeutic targets in severe COVID-19.

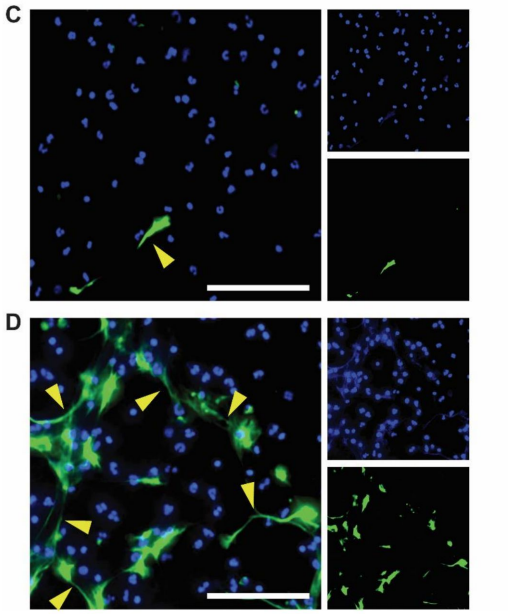


Figure 4. COVID-19 sera trigger control neutrophils to release NETs. COVID-19 samples (for which sufficient sera were available) were tested for their ability to trigger neutrophils isolated from healthy controls to undergo NETosis. **C.** Representative image of control neutrophils cultured with 10% heterologous control serum (upper) or COVID-19 serum (lower). Neutrophil elastase is stained green and DNA is stained blue. Scale bar=100 microns. The yellow arrows highlight some examples of NET strands.

Tobacco Smoking Increases the Lung Gene Expression of ACE2, the Receptor of SARS-CoV-2.

Cai G, Bossé Y, Xiao F, Kheradmand F, Amos CI
Am J Respir Crit Care Med
2020 Apr 24; PMID: 32329629
Level of Evidence: 5- Meta Analysis of Mechanistic research
Type of Article: Research

Summary: Researchers examine transcriptomic datasets to understand the association between smoking status and expression of genes potentially relevant to SARS-CoV-2 infection. They find that ACE2 expression is increased in ever-smokers as is FURIN to a lesser extent. They additionally find

that ACE2 expression in smokers is more likely to be associated with goblet cells while it is associated with club cells in non-smokers.

Inhibition of SARS-CoV-2 Infections in Engineered Human Tissues Using Clinical-Grade Soluble Human ACE2

Monteil V, Kwon H, Prado P, Hagelkrüys A, Wimmer RA, Stahl M, Leopoldi A, Garreta E, Hurtado Del Pozo C, Prosper F, Romero JP, Wirnsberger G, Zhang H, Slutsky AS, Conder R, Montserrat N, Mirazimi A, Penninger JM

Cell

2020 Apr 17; PMID: 32333844

Level of Evidence: 5- Mechanism based reasoning

Type of Article: Research

BLUF: Based on the knowledge that SARS-CoV-2 can use angiotensin converting enzyme 2 (ACE2) as an entry receptor, the authors use *in vitro* studies with wild type SARS-CoV-2 virus and demonstrate that clinical-grade human recombinant soluble ACE2 (hrsACE2) can significantly reduce viral infection in Vero E6 cells (normally used to grow virus in the lab). Furthermore, they create both human blood vessel- and human kidney-based organoids and show that these organoids could be infected by SARS-CoV-2 and that infection was reduced after using hrsACE2 early during infection.

Abstract:

We have previously provided the first genetic evidence that angiotensin converting enzyme 2 (ACE2) is the critical receptor for severe acute respiratory syndrome coronavirus (SARS-CoV), and ACE2 protects the lung from injury, providing a molecular explanation for the severe lung failure and death due to SARS-CoV infections. **ACE2 has now also been identified as a key receptor for SARS-CoV-2** infections, and it has been proposed that inhibiting this interaction might be used in treating patients with COVID-19. However, it is not known whether human recombinant soluble ACE2 (hrsACE2) blocks growth of SARS-CoV-2. **Here, we show that clinical grade hrsACE2 reduced SARS-CoV-2 recovery from Vero cells by a factor of 1,000-5,000. An equivalent mouse rsACE2 had no effect. We also show that SARS-CoV-2 can directly infect engineered human blood vessel organoids and human kidney organoids, which can be inhibited by hrsACE2. These data demonstrate that hrsACE2 can significantly block early stages of SARS-CoV-2 infections.**

SARS-CoV-2 entry factors are highly expressed in nasal epithelial cells together with innate immune genes.

Sungnak W, Huang N, Bécavin C, Berg M, Queen R, Litvinukova M, Talavera-López C, Maatz H, Reichart D, Sampaziotis F, Worlock KB, Yoshida M, Barnes JL; HCA Lung Biological Network.

Nat Med.

2020 Apr 23, PMID: 32327758

Level of Evidence: 5 - Bench Research

Article Type: Research

BLUF: Utilizing multiple human tissue samples, researchers determined that ACE2 was present in high amounts in nasal epithelium and cornea in SARS-CoV-2 patients. These results may indicate the virus spends time in the nasal goblet cells in pre-symptomatic phase and drugs administered intranasally may be effective against SARS-CoV-2.

Abstract:

We investigated SARS-CoV-2 potential tropism by surveying expression of viral entry-associated genes in single-cell RNA-sequencing data from multiple tissues from healthy human donors. We

co-detected these transcripts in specific respiratory, corneal and intestinal epithelial cells, potentially explaining the high efficiency of SARS-CoV-2 transmission. These genes are co-expressed in nasal epithelial cells with genes involved in innate immunity, highlighting the cells' potential role in initial viral infection, spread and clearance. The study offers a useful resource for further lines of inquiry with valuable clinical samples from COVID-19 patients and we provide our data in a comprehensive, open and user-friendly fashion at www.covid19cellatlas.org.

Time to consider histologic pattern of lung injury to treat critically ill patients with COVID-19 infection.

Copin MC, Parmentier E, Duburcq T, Poissy J, Mathieu D, Lille COVID-19 ICU and Anatomopathology Group.
Intensive Care Med.
2020 Apr 23; PMID: 32328726
Level of Evidence: 5 – Mechanism-based reasoning
Type of Article: Letter to the Editor

BLUF: Analysis of postmortem lung biopsies from COVID-19 patients displayed a pattern of injury inconsistent with diffuse alveolar damage. Understanding the pathophysiology of COVID-19 is crucial for applying the most appropriate treatment.

Summary:
Previous studies have described different phenotypes of COVID-19 pneumonia, whereby worsening patients progress from a 'type L' to a 'type H.' Type L is characterized by low elastance, low ventilation to perfusion ratio, low lung weight, and low lung recruitability. In contrast, type H, which has high elastance, high right-to-left shunt, high lung weight, and high lung recruitability. Herein, the authors sought to **analyze postmortem lung tissue biopsies from COVID-19 positive patients** to further explore the pathophysiology of COVID-19 pneumonia. In one patient who died at 5 days after the beginning of fever, a **lymphocytic viral pneumonia** (Fig. 1A) was identified, consistent with type L. In five patients who died later in their disease course (around 20 days after beginning of symptoms), the histologic pattern was an **acute fibrinous and organizing pneumonia (AFOP)**, characterized by an extensive intra-alveolar fibrin deposition called fibrin 'balls,' **rather than hyaline membranes**. Additionally, organizing pneumonia consisting of intraluminal loose connective tissue was observed within the alveolar ducts and bronchioles associated with the fibrinous acute injury (Fig. 1B). Fibroblastic bodies and fibroblasts surrounding intra-alveolar fibrin were seen in all cases (Fig. 1C), as well as a moderate interstitial T-cell lymphocytic, a plasma cells infiltrate, and type 2 pneumocyte hyperplasia with cytologic atypia. Vascular injury was also a prominent feature readily, demonstrated by endothelial injury with cytoplasmic vacuolization and cell detachment in small to medium-sized pulmonary arteries (1D).

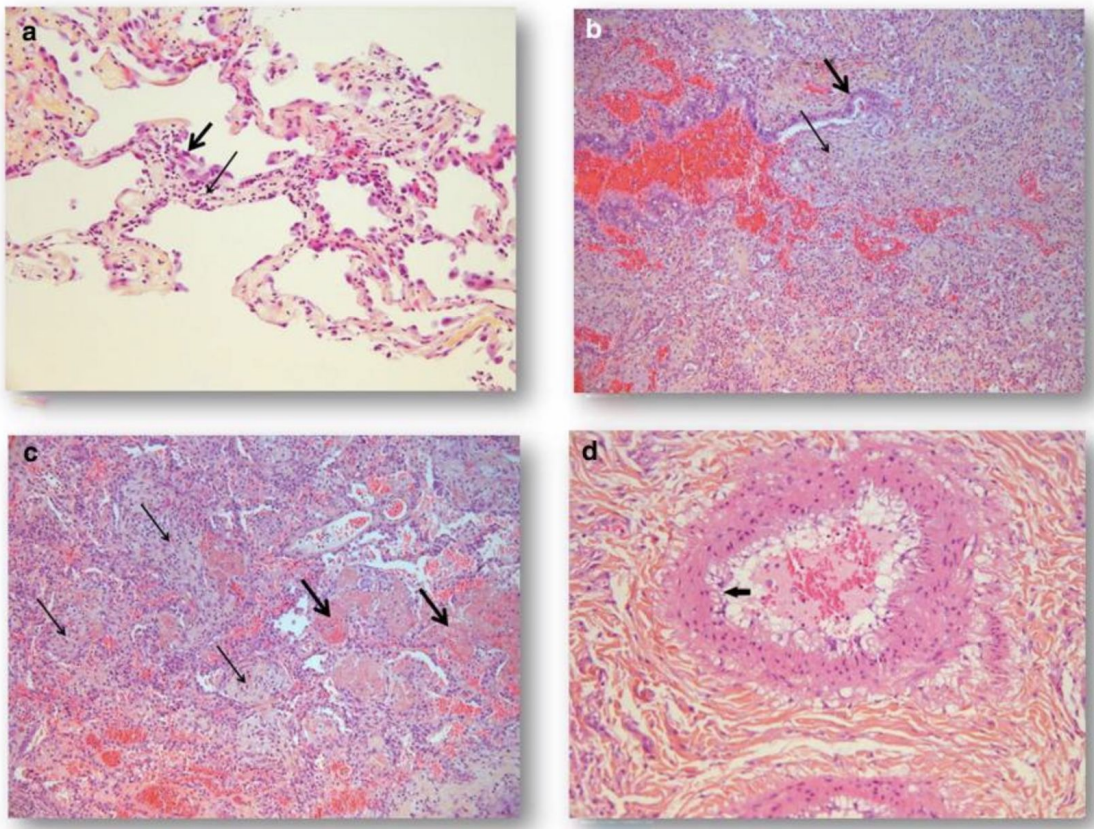


Fig. 1. COVID-19 pulmonary histological findings. a Infiltration of alveolar walls by numerous lymphocytes and edema (thin arrow). Type 2 pneumocyte hyperplasia with cytologic atypia (thick arrow). HES × 200. b Intraluminal loose connective tissue (thin arrow) within bronchiole (bronchiolitis obliterans). Bronchiolar epithelium, thick arrow HES × 200. c Organizing pneumonia (thin arrow) within the alveolar ducts coexisting with fibrin balls (thick arrow). HES × 200. d Endothelial damage: cytoplasmic vacuolization of endothelial cells (arrow). HES × 200

COVID-19: A New Virus, but a Familiar Receptor and Cytokine Release Syndrome

Hirano T, Murakami M.Hirano T
Immunity
2020, April 19; PMID: 32325025
Level of Evidence: 4- Review
Type of Article: Literature Review

BLUF: Review of key literature shows that ACE2 is the cellular entry point of COVID-19 and may serve as an effective target for therapeutic treatment during the initial phase of infection. "In its later phase, the potential dysregulation of the AngIIAT1R pathway downstream of ACE2 could lead to cytokine release syndrome as observed in COVID-19 patients that may require targeting of cytokine pathways, particularly IL-6-STAT3 axis."

Abstract:

Zhou et al. (Nature) and Hoffmann et al. (Cell) identify ACE2 as a SARS-CoV-2 receptor, and the latter show its entry mechanism depends on cellular serine protease TMPRSS2. These results may explain proinflammatory cytokine release via the associated angiotensin II pathway and a possible therapeutic target via the IL-6-STAT3 axis.

Transmission & Prevention

Developments in Transmission & Prevention

Is temperature reducing the transmission of COVID-19?

Tobías, Aurelio; Molina, Tomás
Environ Res
2020 Apr 18; PMID: 32330766
Level of Evidence: 4 - Cross-sectional Study
Type of Article: Letter to the Editor

Summary: The authors analyzed daily incidence rates of COVID-19 cases confirmed by PCR in the Barcelona Health Region in Spain and compared them to daily temperatures to create a quasi-Poisson regression model. **Using this model, they conclude that the arrival of summer may reduce COVID-19 transmission.** Limitations include only using a small number of days and temperature variance over the region that COVID-19 was confirmed in.

Anal swab findings in an infant with COVID-19.

Fan Q, Pan Y, Wu Q, Liu S, Song X, Xie Z, Liu Y, Zhao L, Wang Z, Zhang Y, Wu Z, Guan L, Lv X.
Pediatr Investig.
2020 Mar; PMID: 32328338
Level of Evidence: 4- Case Study
Type of Article: Case Report

Summary: This case report tested oropharyngeal and rectal swabs of a COVID-19 positive 3-month old girl from Jingzhou via RT-PCR on days 1, 7, 10, 14 17, 21, and 28 since onset of illness and found that anal swabs remained positive for COVID-19 on day 28 while oropharyngeal swabs remained positive only until day 10. These findings present viral RNA via rectum and suggest the possibility of fecal-oral transmission of COVID-19 for up to 28 days.

TABLE 1 Results of real-time RT-PCR tests for the novel SARS-CoV-2

Specimen	Day 1	Day 7	Day 10	Day 14	Day 17	Day 21	Day 28
Oropharyngeal swab	+	+	+	–	–	–	–
Anal swab	NT	NT	+	+	+	+	+

+, positive; –, negative; NT, not tested.

Positive RT-PCR test results after consecutively negative results in patients with COVID-19.

Liang C, Cao J, Liu Z, Ge F, Cang J, Miao C, Luo J
Infect Dis (Lond)
2020 Apr 24; PMID: 32329388
Level of Evidence: 4- Case series
Type of Article: Letter

Summary: A case series examines the **sequential RT-PCR results of throat swabs** from 22 COVID-19 patients at a Wuhan hospital. The infections were initially confirmed by RT-PCR of throat swabs and chest CT. After symptom recovery and a single negative RT-PCR throat swab, 4 additional swabs were collected at 24 hour intervals. They find that **11/22 had a positive result after 2 or more negatives, which is the standard accepted for hospital discharge. Virus infectivity in these samples was not assessed.**

Table 1. The Characteristics of these cases with COVID-19 and the five consecutively virus nucleic acid tests.

	Age	Sex	Symptoms and signs	Abnormalities on CT Scan	Initial Nucleic acid test	Five consecutively Nucleic acid tests				
Case1	62	Female	+	+	+	−	−	−	+	−
Case2	63	Female	−	+	+	−	−	−	−	−
Case3	75	Male	+	+	+	−	−	+	−	−
Case4	61	Male	+	+	+	−	+	−	−	−
Case5	74	Female	+	+	+	−	−	+	−	−
Case6	80	Female	−	+	+	−	−	−	+	−
Case7	65	Male	−	+	+	−	−	−	−	−
Case8	31	Male	+	+	+	−	+	−	−	−
Case9	65	Female	−	+	+	−	−	+	−	−
Case10	34	Female	+	+	+	−	+	−	−	+
Case11	62	Female	+	+	+	−	+	−	−	−
Case12	66	Female	+	+	+	−	−	+	+	−
Case13	69	Female	−	+	+	−	−	−	−	−
Case14	75	Female	+	+	+	−	−	+	+	−
Case15	72	Female	+	+	+	−	+	−	−	−
Case16	67	Male	−	+	+	−	−	+	−	−
Case17	65	Male	+	+	+	−	+	−	−	−
Case18	69	Male	−	+	+	−	−	−	−	−
Case19	44	Male	+	+	+	−	+	−	−	−
Case20	44	Male	−	+	+	−	−	−	+	−
Case21	63	Male	+	+	+	−	+	−	+	−
Case22	52	Male	−	+	+	−	−	+	−	−

+: positive; −: negative. Symptoms and signs positive: Patients with at least one of following items: Fever, Cough, Fatigue and Diarrhoea.

Applications of 3D Printing Technology to Address COVID-19 Related Supply Shortages.

Ishack S, Lipner SR.
American Journal of Medicine.
2020 Apr 21; PMID: 32330492
Level of Evidence: 5 - Mechanism based evidence
Type of Article: Recommendation

Summary: This article describes how the use of 3D printing technology could combat the shortage of personal protective equipment (PPE) by producing masks with the same synthetic polymer biomaterials used in standard manufacturing grade products (such as N95 masks). The authors discuss the methods by which a mask could be made as well as the benefits of using these masks including cost and availability.

Barrier Shields: Not Just for Intubations in Today's COVID-19 World?

Tsai PB
Anesth Analg
2020 Apr 21; PMID: 32324597
Level of Evidence: 5 – Expert Opinion
Type of Article: Letter

Summary: In the situation of **PPE scarcity amidst the COVID-19 pandemic**, the author, a California anesthesiologist, highlights recent innovations to limit spread of contamination, namely the aerosol box. He further suggests that **intubation barrier shields might be low-cost PPE substitutes for physicians**, though he acknowledges the patient-specific (body habitus) or circumstantial limitations might preclude its use.

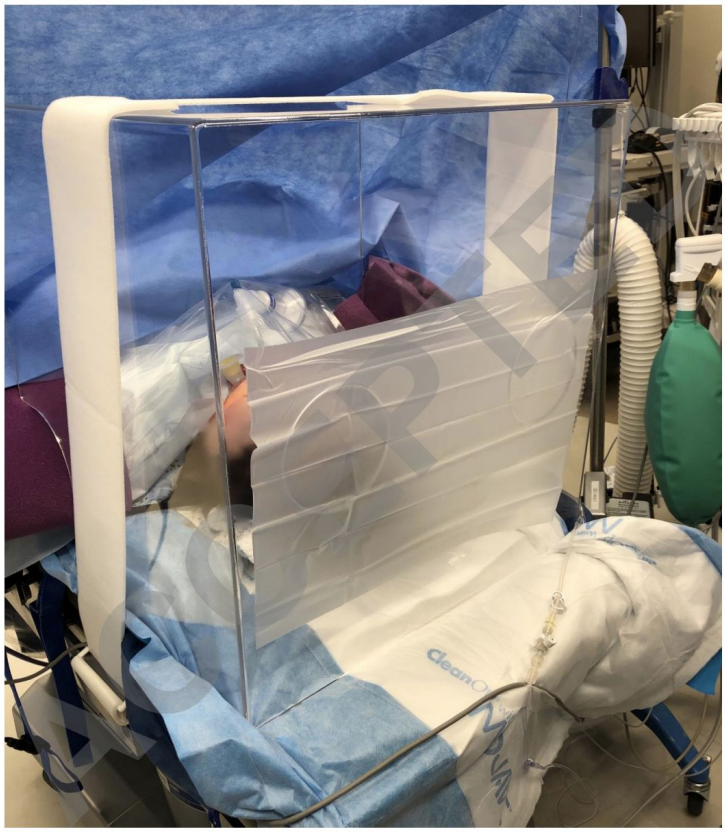


Figure 1. Intubation barrier shield as a PPE-substitute to prevent COVID-19 spread.

Asymptomatic SARS-CoV-2 Infection in Household Contacts of a Healthcare Provider, Wuhan, China

Yi Luo, Edwin Trevathan, Zhengmin Qian, Yirong Li, Jin Li, Wei Xiao, Ning Tu, et al.
Emerg Infect Dis.
2020 Apr 24; PMID: 32330112
Level of Evidence: 4 - Case series
Type of Article: Research letter

BLUF: This single-household observation study found a high attack rate for asymptomatic SARS-CoV-2 infection among the immediate family members of a symptomatic COVID-19 patient.

Summary: This observation study conducted on a family of 6 to assess the attack rate of COVD-19 when one member (patient 1) is symptomatic. **All 5 household contacts of patient 1 had laboratory evidence of SARS-CoV-2 infection but remained asymptomatic** throughout the period of observation (February 11–March 1). All household contacts who had throat swab specimens tested for SARS-CoV-2 were positive by PCR except for one contact who stool specimen was positive for SARS-CoV-2.

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Vertical Transmission in Neonates Born to Mothers With Coronavirus Disease 2019 (COVID-19) Pneumonia.

Hu X, Gao J, Luo X, Feng L, Liu W, Chen J, Benachi A, De Luca D, Chen L.
Obstet Gynecol
2020 Apr 24; PMID: 32332320
Level of Evidence: 4 - Case Series

Type of Article: Research Letter

Summary: This article presents seven cases of COVID-19 during late pregnancy from late January to late February in Wuhan. All of the patients had C-sections planned to minimize the risk of vertical transmission (one delivered vaginally before a C-section could be performed). Amniotic fluid samples collected from each patient tested negative by RT-PCR. Nasopharyngeal swabs were performed on all of the neonates between 24-36 hours of life; one neonate, delivered by cesarean, had a positive RT-PCR. All patients ultimately recovered. The authors speculate that vertical transmission of COVID-19 may be a possible but relatively rare occurrence and indicate a need for more research in this area.

Asymptomatic COVID-19 infection in late pregnancy indicated no vertical transmission.

Lu D, Sang L, Du S, Li T, Chang Y, Yang XA.

J Med Virol
2020 Apr 24; PMID: 32330313
Level of Evidence: 4 - Case Study
Type of Article: Short Communication

BLUF: This article presents a case study of a 22 year old 38-weeks pregnant patient who presented to a hospital in the Anhui Province of China in February with asymptomatic COVID-19. The neonate was delivered by emergency cesarean and had negative PCR results on nasopharyngeal, oropharyngeal, and blood samples collected immediately after delivery. Amniotic fluid samples could not be collected. The neonate was isolated from her mother for 14 days. No COVID-19 symptoms were observed during this time. The neonate had a negative stool nucleic acid test on day six of life and a normal CT on day 13 of life. The authors conclude that there was not evidence of vertical transmission in this case, but more research in this area is needed.

Abstract:
Objective: This study is to investigate the clinical characteristics of late pregnancy with asymptomatic 2019 novel coronavirus disease (COVID-19) infection, evaluate the outcome of maternal and fetal prognosis, and identify the evidence of intrauterine vertical transmission.
Methods: A 22 years old pregnant woman with asymptomatic COVID-19 infection who was admitted to our hospital on Feb 11, 2020 was enrolled in this study. Clinical data including laboratory test results and chest computed tomography (CT) scanning were collected and reviewed.
Results: Diagnosis of late pregnancy with asymptomatic COVID-19 infection was made. Lumbar anesthesia for cesarean section was performed and a female baby was delivered uneventfully, with the Apgar score of 9-10 points. Three times of COVID-19 nucleic acid test for the baby was negative after delivery. The puerpera returned to normal after the operation and two times of throat swab COVID-19 nucleic acid test were all negative after antiviral therapy.
Conclusion: We reported an asymptomatic COVID-19 pregnant woman with detailed clinical information and our result indicated that for late pregnant women with asymptomatic COVID-19 infection, there might be no intrauterine infection caused by vertical transmission. This article is protected by copyright. All rights reserved.

Prevention in the Community

Reusable and Recyclable Graphene Masks With Outstanding Superhydrophobic and Photothermal Performances

Zhong H, Zhu Z, Lin J, et al.

J ACS Nano.
2020 Apr 23; PMID: 32327566
Level of Evidence: 5- Mechanism-Based Research
Type of Article: Research

BLUF: Researchers from The Hong Kong Polytechnic Institute report a novel method for converting single-use disposable surgical masks into a reusable and self-cleaning product. The technique involves depositing a graphene coat on the masks, which has superhydrophobic and photothermal properties that allow for solar-driven cleaning under sunlight. These have not been tested for clinical efficacy.

Abstract:
The 2019 coronavirus outbreak (COVID-19) is affecting over 210 countries and territories, and it is spreading mainly by respiratory droplets. The use of disposable surgical masks is common for patients, doctors, and even the general public in highly risky areas. However, the **current surgical masks cannot self-sterilize** in order to reuse or be recycled for other applications. The resulting **high economic and environmental costs** are further damaging societies worldwide. Herein, we reported a **unique method for functionalizing commercially available surgical masks with outstanding self-cleaning and photothermal properties**. A dual-mode laser-induced forward transfer method was developed for depositing few-layer graphene onto low-melting temperature nonwoven masks. Superhydrophobic states were observed on the treated masks' surfaces, which can cause the incoming aqueous droplets to bounce off. Under sunlight illumination, the surface temperature of the functional mask can quickly increase to over 80 °C, making the masks reusable after sunlight sterilization. In addition, this graphene-coated mask can be recycled directly for use in solar-driven desalination with outstanding salt-rejection performance for long-term use. These roll-to-roll production-line-compatible masks can provide us with better protection against this severe virus. The environment can also benefit from the direct recycling of these masks, which can be used for desalinating seawater.

Managing Close Contacts of COVID-19 Confirmed Cases in Metropolitan Areas in China.

Ding J, Tuan WJ, Temte JL.Ding J
J Public Health Manag Pract
2020 April 19; PMID: 32332481
Level of Evidence: 5 Expert Opinion
Type of Article: Rapid Report

BLUF: The authors propose a community-driven preparedness strategy involving the collaboration of local health departments, public safety authorities, neighborhood councils, and community health centers with an emphasis on a centralized infection database, case investigations, home visits to infected individuals, and enforced quarantine measures in order to strengthen the control and management of COVID-19 in China.

Abstract:
The novel coronavirus (COVID-19) outbreak has rapidly spread across the world. As medical systems continue to develop vaccines and treatments, **it is crucial for the public health community to establish nonpharmaceutical interventions (NPIs) that can effectively mitigate the rate of SARS-Coronavirus-2 (SARS-CoV-2) spread across highly populated residential areas**, especially among individuals who have close contact with confirmed cases. A community-driven preparedness strategy has been implemented in metropolitan areas in China. The Chinese Center for

Disease Control and Prevention (CCDC) has required that all COVID-19 confirmed cases be recorded and documented in a national notifiable disease surveillance system (NDSS). After receiving reports of newly confirmed cases, an epidemiological services team at the CCDC or trained medical professionals at local clinical facilities start a case-contact investigation. A task force performs home visits to infected individuals. Persons under investigation (PUIs) can stay in designated quarantine facilities for 14 days or in special circumstances can be quarantined at home. This community-based approach involved all stakeholders including local public health departments, public safety authorities, neighborhood councils, and community health centers.

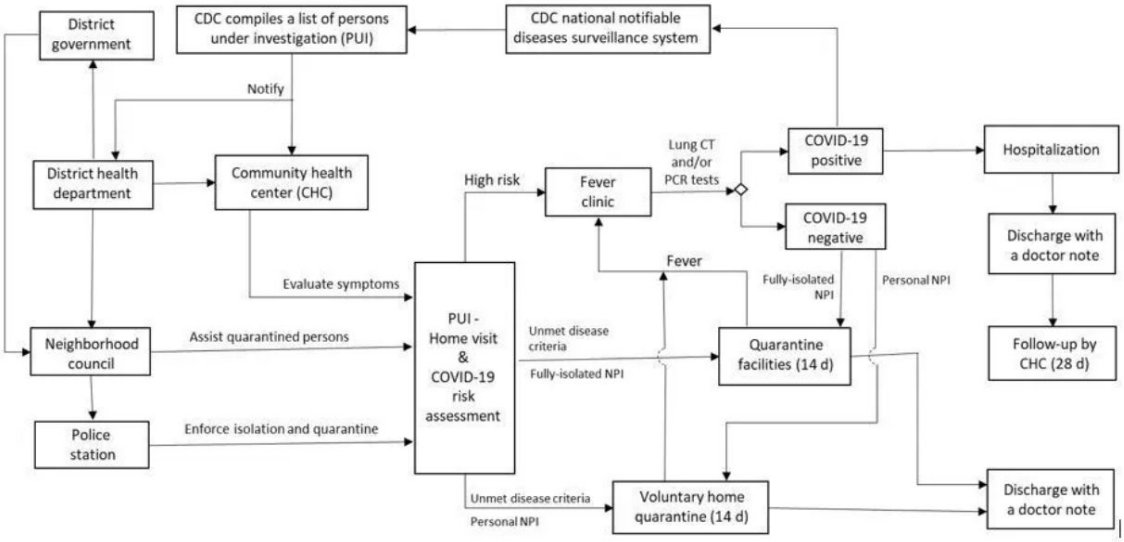


Figure: Processing Summary for Monitoring Individuals Who Had Close Contact to Confirmed Cases

Slum Health: Arresting COVID-19 and Improving Well-Being in Urban Informal Settlements.

Corburn J, Vlahov D, Mberu B, Riley L, Caiaffa WT, Rashid SF, Ko A, Patel S, Jukur S, Martínez-Herrera E, Jayasinghe S, Agarwal S, Nguendo-Yongsi B, Weru J, Ouma S, Edmundo K, Oni T, Ayad H.
J Urban Health.
2020 Apr 24; PMID: 32333243
Level of Evidence: 5 - Expert Opinion
Type of Article: Comment
BLUF: The following article devises an 8-step plan to slow down the spread of COVID-19 in slum neighborhoods in the Global South. The plan consists of implementing emergency stations, putting holds on rent, and maintaining food, water, and waste.

Abstract:
"The informal settlements of the Global South are the least prepared for the pandemic of COVID-19 since basic needs such as water, toilets, sewers, drainage, waste collection, and secure and adequate housing are already in short supply or non-existent. Further, space constraints, violence, and overcrowding in slums make physical distancing and self-quarantine impractical, and the rapid spread of an infection highly likely. Residents of informal settlements are also economically

vulnerable during any COVID-19 responses. Any responses to COVID-19 that do not recognize these realities will further jeopardize the survival of large segments of the urban population globally. Most top-down strategies to arrest an infectious disease will likely ignore the often-robust social groups and knowledge that already exist in many slums. Here, we offer a set of practice and policy suggestions that aim to (1) dampen the spread of COVID-19 based on the latest available science, (2) improve the likelihood of medical care for the urban poor whether or not they get infected, and (3) provide economic, social, and physical improvements and protections to the urban poor, including migrants, slum communities, and their residents, that can improve their long-term well-being. Immediate measures to protect residents of urban informal settlements, the homeless, those living in precarious settlements, and the entire population from COVID-19 include the following: (1) institute informal settlements/slum emergency planning committees in every urban informal settlement; (2) apply an immediate moratorium on evictions; (3) provide an immediate guarantee of payments to the poor; (4) immediately train and deploy community health workers; (5) immediately meet Sphere Humanitarian standards for water, sanitation, and hygiene; (6) provide immediate food assistance; (7) develop and implement a solid waste collection strategy; and (8) implement immediately a plan for mobility and health care. Lessons have been learned from earlier pandemics such as HIV and epidemics such as Ebola. They can be applied here. At the same time, the opportunity exists for public health, public administration, international aid, NGOs, and community groups to innovate beyond disaster response and move toward long-term plans."

Aerosol Filtration Efficiency of Common Fabrics Used in Respiratory Cloth Masks.

Konda A, Prakash A, Moss GA, Schmoldt M, Grant GD, Guha S
ACS Nano
2020 Apr 24; PMID: 32329337
Level of Evidence: 5-Basic science
Type of Article: Research

BLUF: An experimental setup demonstrates the effectiveness of various common materials at filtering particles between 10nm and 6μm, spanning the likely range of sizes for transmission of viral particles. The results suggest **increased efficacy when multiple different materials are combined** and highlight the **need for careful fitting to avoid air leakage**. These results can guide future efforts at producing effective cloth masks for the public.

Abstract:
The emergence of a pandemic affecting the respiratory system can result in a significant demand for face masks. This includes the use of cloth masks by large sections of the public, as can be seen during the current global spread of COVID-19. However, there is limited knowledge available on the performance of various commonly available fabrics used in cloth masks. Importantly, there is a need to evaluate filtration efficiencies as a function of aerosol particulate sizes in the 10 nm to 10 μm range, which is particularly relevant for respiratory virus transmission. We have carried out these studies for several common fabrics including cotton, silk, chiffon, flannel, various synthetics, and their combinations. Although the filtration efficiencies for various fabrics when a single layer was used ranged from 5 to 80% and 5 to 95% for particle sizes of <300 nm and >300 nm, respectively, the efficiencies improved when multiple layers were used and when using a specific combination of different fabrics. Filtration efficiencies of the hybrids (such as cotton–silk, cotton–chiffon, cotton–flannel) was >80% (for particles <300 nm) and >90% (for particles >300 nm). We speculate that the enhanced performance of the hybrids is likely due to the combined effect of mechanical and electrostatic-based filtration. Cotton, the most widely used material for cloth masks performs better at higher weave densities (*i.e.*, thread count) and can make a significant difference in filtration

efficiencies. Our studies also imply that gaps (as caused by an improper fit of the mask) can result in over a 60% decrease in the filtration efficiency, implying the need for future cloth mask design studies to take into account issues of "fit" and leakage, while allowing the exhaled air to vent efficiently. Overall, we find that combinations of various commonly available fabrics used in cloth masks can potentially provide significant protection against the transmission of aerosol particles.

Figure 3

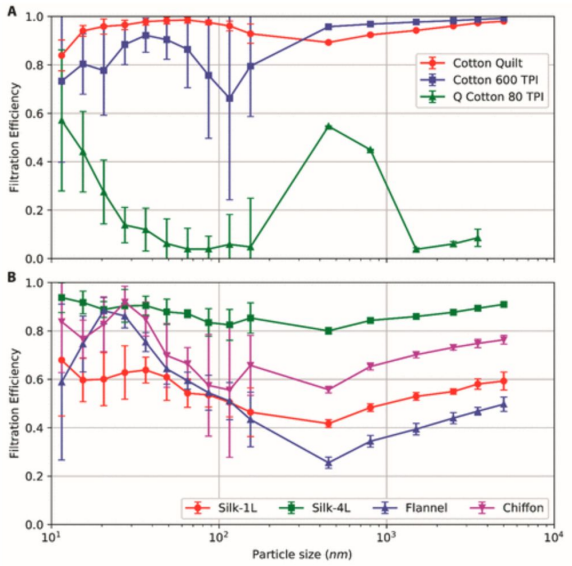


Figure 3. Filtration efficiency of individual fabrics at a flow rate of 1.2 CFM (without gap). (a) Plot showing the filtration efficiencies of a cotton quilt consisting of two 120 threads per inch (TPI) cotton sheets enclosing a ~0.5 cm thick cotton batting, 80 TPI quilters cotton (Q Cotton 80 TPI), and a 600 TPI cotton (cotton 600 TPI). (b) Plot showing the filtration efficiencies of one layer of natural silk (Silk-1L), four layers of natural silk (Silk-4L), one layer of flannel, and one layer of chiffon. The error bars on the <300 nm measurements are higher, particularly for samples with high filtration efficiencies because of the small number of particles generated in this size range, the relatively poorer counting efficiency of the detector at <300 nm particle size, and the very small counts downstream of the sample. The sizes of the error bars for some of the data points (>300 nm) are smaller than the symbol size and hence not clearly visible.

Figure 4

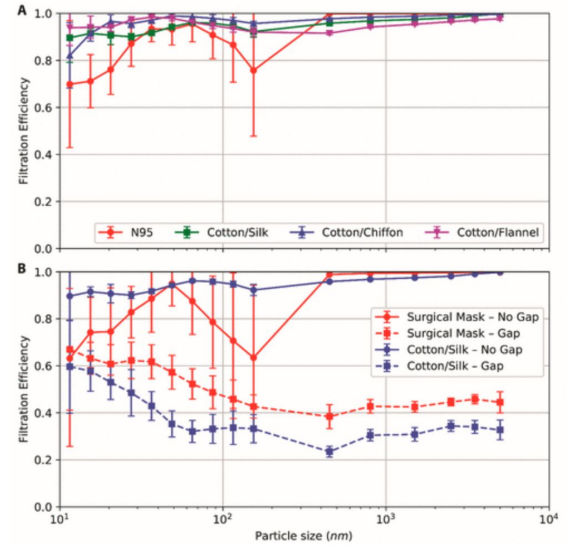


Figure 4. Filtration efficiency of hybrid fabrics at a flow rate of 1.2 CFM. (a) Plot showing the filtration efficiencies without gap for an N95 respirator and a combination of different fabrics: 1 layer of 600 threads per inch (TPI) cotton and 2 layers of silk (cotton/silk), 1 layer of 600 TPI cotton and 2 layers of chiffon (cotton/chiffon), and 1 layer of 600 TPI cotton and 1 layer of flannel (cotton/flannel). (b) Plot showing the filtration efficiencies of a surgical mask and cotton/silk with (dashed) and without a gap (solid). The gap used is ~1% of the active mask surface area. The error bars on the <300 nm measurements are higher, particularly for samples with high filtration efficiencies because of the small number of particles generated in this size range, the relatively poorer counting efficiency of the detector at <300 nm particle size, and the very small counts downstream of the sample. The sizes of the error bars for some of the data points (>300 nm) are smaller than the symbol size and hence not clearly visible.

Big data integration and analytics to prevent a potential hospital outbreak of COVID-19 in Taiwan.

Chen FM, Feng MC, Chen TC, Hsieh MH, Kuo SH, Chang HL, Yang CJ, Chen YH.
Journal of Microbiology, Immunology and Infection
2020, April 20; PMID: 32327328
Level of Evidence: Level 6 - No data cited
Type of Article: Letter to the Editor
Summary: The authors review the propensity for patients to be untruthful about recent travel history or COVID-19 exposures, which puts healthcare workers at risk of infection. To combat this, the Taiwan government has integrated data from the National Health Insurance Admin., National Immigration Agency and Taiwan CDC to provide quick and accurate immigration and contact information when patients scan their Taiwan National Health Insurance card. This, in addition to the Kaohsiung Municipal Ta-Tung Hospital policy that investigates all suspected COVID-19 patients at an outdoor quarantine station, could significantly reduce the prevalence of hospital outbreaks.

COVID-19 and the need of targeted inverse quarantine.

Standl F, Jöckel KH, Stang A.
Eur J Epidemiol.
2020 Apr 24; PMID: 32328991
Level of Evidence: 5 - Expert Opinion
Type of Article : Commentary
Summary: COVID-19 is most fatal in the elderly and comorbid population. Inverse quarantine, isolating high-risk uninfected patients, is proposed as an economically viable method of reducing mortality while achieving herd immunity more quickly and reducing the chances of aggressive viral strains evolving.

Prevention in the Hospital

Quarantine hospitals are essential for COVID-19 contention

Wang, M-W; Zhou, M-Y; Yu, P; Cheng, Y-R; Ye, L; Chen, J; Feng, Z-H
European review for medical and pharmacological sciences
2020 Apr 25; PMID: 32329814
Level of Evidence: 6 - no data cited
Type of Article: Letter
Summary:
The authors of the article discuss that public health experts worldwide should learn from the Chinese experience and response to SARS-CoV-2. They state that the home quarantine approach adopted to stop transmission does not curb the spread of the virus. Instead they believe that mandatory inpatient-quarantine through the use of quarantine hospitals played a paramount role in infection control and ultimately curbed the virus.

Transmission risk of SARS-CoV-2 to healthcare workers -observational results of a primary care hospital contact tracing

Canova V, Lederer Schläpfer H, Piso RJ, Droll A, Fenner L, Hoffmann T, Hoffmann M.
Swiss Med Wkly
2020 Apr 25; PMID: 32333603
Level of Evidence: 3 - Retrospective cohort study
Type of Article: Research

BLUF: This retrospective cohort study followed 21 healthcare workers at a primary care hospital in Switzerland who were exposed to a patient presenting for angina who later tested COVID-19 positive. All 21 workers endorsed using standard precautions only (hand hygiene, no masks) and all tested negative for COVID-19 (NP swab with RTPCR) at a follow up of seven days after exposure which led the authors to conclude that the risk of transmission of COVID-19 to healthcare workers is likely minimal in lower risk, non-droplet/aerosol-generating settings such as primary care facilities.

Abstract:
Background: The coronavirus disease (COVID)-19 epidemic is evolving rapidly. Healthcare workers are at increased risk for infection, and specific requirements for their protection are advisable to ensure the functioning of the basic healthcare system, including the availability of general practitioners (GPs). Understanding the transmission risk is particularly important for guiding evidence-based protective measures in the primary healthcare setting.
Methods: Healthcare worker contacts of an initially undiagnosed COVID-19 case, who were without personal protective equipment, in particular not wearing facemasks, were screened with nasopharyngeal swabs and polymerase chain reaction tests for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), irrespective of respiratory symptoms or fever seven days after initial contact. The details of exposure to the index case were obtained during routine contact investigation after unintentional pathogen exposure.
Results: Twenty-one healthcare workers reported contacts with the index case. Three healthcare workers reported respiratory symptoms (cough) or low-grade fever within 4 days. None of them tested positive for SARS-CoV-2 at the time of symptom onset. All 21 healthcare workers tested SARS-CoV-2 negative 7 days after initial index case contact, including the three healthcare workers with previous symptoms. Ten of the 21 healthcare workers reported a cumulative exposure time of >15 minutes. Longer cumulative contact times were associated with more individual contacts, reduced contact time per contact and activities with physical patient contact. The closest relative of the index patient tested SARS-CoV-2 positive 2 days after the index case presented at the hospital emergency department.
Conclusion: We found a low risk of SARS-CoV-2 transmission in a primary care setting. These findings are compatible with previous reports of the highest transmission probability in household settings with prolonged close contacts. The current protective measures for healthcare workers, including strict adherence to basic standard hygiene and facemasks, offer considerable protection during short periods of contact with symptomatic COVID-19 cases by diminishing the risk of direct and indirect transmission.

Effective infection prevention and control strategies in a large accredited psychiatric facility in Singapore

Poremski, Daniel; Subner, Sandra; Lam, Grace; Kin, Fong; Dev, Raveen; Mok, Yee Ming; Chua, Hong Choon; Fung, Daniel Ss
Infect Control Hosp Epidemiol
2020 Apr 23; PMID: 32321623
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter
BLUF: Authors detail their measures used for infection prevention of COVID-19 in a large psychiatric facility in Singapore.

- Architecture: 28 HEPA filtered negative pressure rooms on campus, multiple administrative buildings allow departments to split COVID-19 exposure.
- Infection prevention and control:
    - Essential services: lowered outpatient visits, used telehealth when possible.

- Preventing introduction of COVID-19: frequent staff screening, restricting access to one entrance, isolation ward for COVID-19 rule-out and positive.
- Resource management: allow units to conduct essential functions of the whole department
- Frequent communication

Abstract:
The Institute of Mental Health in Singapore continues to attempt to prevent the introduction of COVID-19, despite community transmission. Essential services are maintained and quarantine measures are currently unnecessary. To help similar organizations, strategies are listed along three themes: sustaining essential services, preventing infection, and managing human and consumable resources.

Personal Protective Equipment Recommendations Based on COVID-19 Route of Transmission.

Gupta MK, Lipner SR
J Am Acad Dermatol
2020 Apr 21; PMID: 32330629
Level of Evidence: 5- Expert opinion
Type of Article: Letter
Summary: A previous article about avoiding dermatitis in the context of increased hand hygiene expressed concern that broken skin could provide an entry point for SARS-CoV-2. The authors dispute this concern due to the lack of evidence that SARS-CoV-2 can be transmitted as a blood borne pathogen. They concur that dermatitis may create a barrier to proper hand hygiene and recommend alcohol based sanitizers as a less irritating option. Additionally, they urge careful attention to mask doffing to avoid touching and contaminating the face despite frequent facial irritation from extended mask use.

High-flow Nasal Cannula May Be No Safer Than Non-Invasive Positive Pressure Ventilation For COVID-19 Patients.

Remy KE, Lin JC, Verhoef PA
Crit Care
2020 Apr 24; PMID: 32326959
Level of Evidence: 5- Opinion
Type of Article: Letter
Summary: Three critical care physicians associated with Washington University express “great concern” over the recent Surviving Sepsis Campaign recommendation to use high-flow nasal cannulation (HFNC) over non-invasive positive pressure ventilation (NIPPV) in COVID-19 patients, due to risk of aerosolization. They argue this risk likely exists in both methods, and that previous studies suggesting HFNC were not associated with aerosolization studied bacteria- not viruses. Therefore, they recommend that airborne precautions be used for both of these non-invasive methods of ventilation until clear data emerges.

Management

Acute care

Interpretation of the 7th edition of the "diagnosis and treatment guidelines of coronavirus disease 2019 in China": Progress and challenges.

Xie, Li-Xin
Chronic Dis Transl Med
2020 Apr 23; PMID: 32328337
Level of Evidence: 5 - Expert Opinion
Type of Article: Editorial

BLUF: This editorial summarizes the changes seen in the 7th edition of the "Novel Coronavirus Pneumonia (COVID-19) Diagnosis and Treatment Guidelines in China" when compared to previous editions. These guidelines include pathological changes, lab examination and pathogen diagnosis, clinical warning signs of severe disease, glucocorticoid therapy, and a summary of treatment and rehabilitation options.

Summary:

Pathological changes in the organs of patients with COVID-19

- Lungs of COVID-19 patients exhibit pulmonary consolidation with intra-alveolar serous fluids, fibromyxoid exudates, and hyaline-membrane formation, leading to poor treatment outcomes of conventional respiratory support in some patients.
- Multiple organs are affected:
    - Reduced lymphocyte count in spleen and lymph nodes
    - Reduction in trilineage hematopoiesis in bone marrow

Laboratory Examination and pathogen Diagnosis

- Etiological examination
    - Adopt the reverse transcriptase-polymerase chain reaction and/or next generation sequencing technology to detect the presence of SARS-CoV-2 in secretions and blood/stool samples
    - Tests from lower respiratory tract are more accurate
- Serological examination
    - Peripheral blood IgM and IgG are highly useful for diagnosis, evaluation of therapeutic effect of plasma therapy, and status of patient's autoimmune function.

Clinical warning signs of severe/critical illness

- Progresive reduction of peripheral blood lymphocyte levels
- Progressive increase in peripheral inflammatory cytokine levels (IL-6, CRP)
- Progressive increase in lactate levels
- Rapid progression of lung lesions in short term

Glucocorticoid therapy:

- Implement 40-160 mg/day for short course (5-10 days) if in one of these situations and if there is no cellular immunosuppression present (abs lymphocyte count ≥ 0.6 x10^9/L)
    - Early stage of disease (within 10 days of onset)
    - Rapid disease deterioration within 24 h
    - Severe cytokine storm present (IL-6/CRP values >10x normal)

Treatment of severe/critical cases

- Emphasis of importance of lung-protective ventilation
- Indications of extracorporeal membrane oxygenation
- Continuous renal replacement therapy
- Treatment during pregnancy

- New treatments: Plasma therapy, tocilizumab, IG

Comorbidities and Rehabilitation

- Hypertension and diabetes are independent risk factors
- Refer to "COVID-19 Respiratory Rehabilitation Guidelines (2nd edition)" by Respiratory Rehabilitation Committee of Chinese Association of Rehabilitation Medicine

Mild or Moderate Covid-19.

Gandhi RT, Lynch JB, Del Rio C.
N Engl J Med
2020 Apr 24; PMID: 32329974
Level of Evidence: Level 5 - Expert Opinion
Type of Article: Review

BLUF: Patients at high risk for having COVID-19 with potential complications should receive PCR testing of a nasopharyngeal swab for SARS-CoV-2, an examination, and chest radiography. Those with moderate or severe disease should be hospitalized for further observation. There is no data to support any COVID-19-specific therapy.

Summary: COVID-19 has a range of clinical symptoms including cough, fever, malaise, myalgias, GI symptoms, and anosmia. Management depends on the severity of the disease. A physical exam should be performed to assess for tachypnea, hypoxemia, and abnormal lung findings. Laboratory tests should include a complete blood count and a comprehensive metabolic panel. Chest radiography is usually the initial imaging method. Patients with mild disease recover at home with supportive care and isolation. If new or worsening symptoms develop in a patient with mild illness, additional evaluation is warranted. Patients with moderate or severe COVID-19 are usually hospitalized for observation and supportive care. There are no proven therapies for COVID-19. Hydroxychloroquine is recommended in China but high-quality data to show if it is safe and effective is lacking. Lopinavir-Ritonavir, an HIV-1 protease inhibitor has been proposed as a treatment but it is not known if drug levels adequate to inhibit the SARS-CoV-2 protease can be achieved. Remdesivir is an RNA-dependent RNA polymerase inhibitor that has activity against SARS-CoV-2 in vitro and has shown some efficacy in one case series. Results of phase 3, randomized controlled trials are still to come. There has been concern about patients using ACE inhibitors and ARBS but the current recommendation is that patients should not stop taking these medications routinely. Health care workers should be protected from acquiring SARS-CoV-2 by using telehealth when possible and using PPE that includes an isolation gown, gloves, a face mask, and eye protection. Many uncertainties remain on the spread of COVID-19 and its management and data to inform treatment remain limited.

Successful recovery of COVID-19 pneumonia in a patient from Colombia after receiving chloroquine and clarithromycin

Millán-Oñate J, Millan W, Mendoza LA, Sánchez CG, Fernandez-Suarez H, Bonilla-Aldana DK, Rodríguez-Morales AJ
Ann Clin Microbiol Antimicrob
2020 Apr 24; PMID: 32331519
Level of Evidence: 4 – Case Report
Type of Article: Research

BLUF: This article discusses the treatment of a patient in Colombia with COVID-19 and class-II obesity. The authors to**ok serial CTs and measurements under a regimen of clarithromycin (12mg IV q4h) and ampicillin/sulbactam (3g IV q4h) on day 3, adding chloroquine (300mg PO q12h) on day 4. The patient went on to recover without complication and**

had undetectable viral load. The authors highlight these therapeutics as not inducing harmful effects, though they acknowledge the low power (n=1) of this study.

Abstract:
Background: COVID-19 pandemics is a challenge *(sic)* for public health and infectious diseases clinicians, especially for the therapeutical *(sic)* approach that is not yet adequately defined. Amid this situation, investigational agents are being used, including chloroquine. We report here the clinical features and therapeutic course of the first reported patient with **confirmed COVID-19 pneumonia** that **recovered in Colombia**, after the **use of chloroquine and clarithromycin**. Case presentation: A 34-year-old male, returning from Spain, presented with complaints of **fever, and cough, and class-II obesity**, being hospitalized *(sic)*. The respiratory viruses and bacteria tested by FilmArray® PCR were negative. Two days later, clarithromycin was started because the patient was suspected as *(sic)* community-acquired pneumonia. At the third day *(sic)*, the rRT-PCR confirmed the **SARS-CoV-2 infection**. A day later, **chloroquine was started** because of that. His chest computed tomography was performed and showed bilateral multifocal **ground-glass opacities with consolidation**, which suggested viral pneumonia as a differential diagnosis. Progressively his **clinical condition improved** and at **day 9**, patient **rRT-PCR for SARS-CoV-2 became negativ**e. The patient was discharged and isolated at home per 14 days *(sic)*.
Conclusions: Our patient improved significantly. This and other COVID-19 cases are urgently demanding results from clinical trials that support evidence-based therapeutical *(sic)* approaches to this pandemic and the clinical management of patients, especially those at critical care.

Pulmonary embolism in returning traveler with COVID-19 pneumonia.

Foch E, Allou N, Vitry T, Masse L, Allyn J, Andre M, Allou N
J Travel Med
2020 Apr 25; PMID: 32330267
Level of Evidence: 4- Case report
Type of Article: Research
Summary: A case report including lab findings and chest images of a 50 year old man with no prior medical history who tested positive for COVID-19 by RTPCR of a nasopharyngeal swab after a long plane flight. He was later found to have a pulmonary embolism. The authors suggest looking out for PE in patients with a combined history of COVID-19 and travel.

Ventilator Triage Policies During the COVID-19 Pandemic at U.S. Hospitals Associated With Members of the Association of Bioethics Program Directors.

Matheny Antommaria AH, Gibb TS, McGuire AL, Wolpe PR, Wynia MK, Applewhite MK, Caplan A, Diekema DS, Hester DM, Lehmann LS, McLeod-Sordjan R, Schiff T, Tabor HK, Wieten SE, Eberl JT; and for a Task Force of the Association of Bioethics Program Directors.
Ann Intern Med.
2020 Apr 24.; PMID: 32330224
Level of Evidence: 4 - Qualitative Cross-sectional Survey
Type of Article: Research
BLUF: A survey to 67 survey program directors from the Association of Bioethics Program Directors (ABPD) reported that many institutions (n=36) did not have approved ventilator triage policies while the hospitals that do (n=29) have heterogeneity in criterion. Suggestions for improvement of policies include implementing processes to reduce bias and to clearly specify who has the authority to activate these triage policies.

Abstract:
Background**:** The coronavirus disease 2019 pandemic has or threatens to overwhelm health care systems. Many institutions are developing ventilator triage policies.
Objective: To characterize the development of ventilator triage policies and compare policy content.
Design: Survey and mixed-methods content analysis.
Setting: North American hospitals associated with members of the Association of Bioethics Program Directors.
Participants: Program directors.
Measurements: Characteristics of institutions and policies, including triage criteria and triage committee membership.
Results: Sixty-seven program directors responded (response rate, 91.8%); 36 (53.7%) hospitals did not yet have a policy, and 7 (10.4%) hospitals' policies could not be shared. The 29 institutions providing policies were relatively evenly distributed among the 4 U.S. geographic regions (range, 5 to 9 policies per region). Among the 26 unique policies analyzed, 3 (11.3%) were produced by state health departments. The most frequently cited triage criteria were benefit (25 policies [96.2%]), need (14 [53.8%]), age (13 [50.0%]), conservation of resources (10 [38.5%]), and lottery (9 [34.6%]). Twenty-one (80.8%) policies use scoring systems, and 20 of these (95.2%) use a version of the Sequential Organ Failure Assessment score. Among the policies that specify the triage team's composition (23 [88.5%]), all require or recommend a physician member, 20 (87.0%) a nurse, 16 (69.6%) an ethicist, 8 (34.8%) a chaplain, and 8 (34.8%) a respiratory therapist. Thirteen (50.0% of all policies) require or recommend those making triage decisions not be involved in direct patient care, but only 2 (7.7%) require that their decisions be blinded to ethically irrelevant considerations.
Limitation: The results may not be generalizable to institutions without academic bioethics programs.
Conclusion: **Over one half of respondents did not have ventilator triage policies. Policies have substantial heterogeneity, and many omit guidance on fair implementation.**

Title Coronavirus Disease 2019 and Prevalence of Chronic Liver Disease: A Meta-Analysis

Mantovani A, Beatrice G, Dalbeni A.
Liver Int.
2020 Apr 4; PMID: 32329563
Level of Evidence: 4 -Meta-analysis
Type of Article: Research
BLUF: A meta-analysis of data from 11 observational studies found the overall prevalence of chronic liver disease in COVID-19 patients at baseline to be 3%, and found individuals with severe disease to have alterations of liver enzymes and coagulation properties. Although this suggests chronic liver disease not is not a major risk factor for COVID-19, more studies are needed to further evaluate mechanisms of liver damage in severe disease

Abstract:
At present, there is **scarce information regarding the global prevalence of chronic liver disease in individuals with coronavirus** disease 2019 (COVID-19) disease, which is becoming a global pandemic. The aim of this study was to **assess the overall prevalence** of **chronic** liver disease among patients with COVID-19 disease by **meta-analysing data in observational studies** and to investigate the **relationship between liver damage and COVID-19 disease**. We included 11 observational studies for a total of 2034 adult individuals (median age 49 years [IQR 45-54], 57.2% men). The overall prevalence of chronic liver disease at baseline was 3% (95% CI

2%-4%; I2 = 29.1%). Individuals with severe COVID-19 disease had relevant alterations of liver enzymes and coagulative profile, probably due to the innate immune response against the virus. Further studies are needed to better investigate the causes of liver injury in patients with COVID-19 disease and the effect of treatment for COVID-19 on the liver.

Self-reported olfactory loss associates with outpatient clinical course in Covid-19.

Yan CH, Faraji F, Prajapati DP, Ostrander BT, DeConde AS.
International Forum of Allergy and Rhinology.
2020 Apr 24; PMID: 32329222
Level of Evidence: 4 - Retrospective cohort study
Type of Article: Research

BLUF: This cohort study of 128 patients determines if using subjective reports of loss of smell is a good predictor of prognosis and can help stratify mild and moderate SARS-CoV-2 infections. The study found that "milder cases of COVID-19 may be heralded by profound anosmia and higher self-reporting, compared to the undetected or mild hyposmia associated with moderate to severe COVID-19 cases."

Abstract:
Background**:** Rapid spread of the SARS-CoV-2 virus has left many health systems around the world overwhelmed, forcing triaging of scarce medical resources. Identifying indicators of hospital admission for Covid-19 patients early in the disease course could aid the efficient allocation of medical interventions. Self-reported olfactory impairment has recently been recognized as a hallmark of Covid-19 and may be an important predictor of clinical outcome.
Methods**:** A retrospective review of all patients presenting to a San Diego Hospital system with laboratory-confirmed positive Covid-19 infection was conducted with evaluation of olfactory and gustatory function and clinical disease course. Univariable and multivariable logistic regression were performed to identify risk factors for hospital admission and anosmia.
Results**:** A total of 169 patients tested positive for Covid-19 disease between March 3 and April 8, 2020. Olfactory and gustatory data were obtained for 128/169 (75.7%) subjects of which 26/128 (20.1%) required hospitalization. Admission for Covid-19 was associated with intact sense of smell and taste, increased age, diabetes, as well as subjective and objective parameters associated with respiratory failure. On adjusted analysis, anosmia was strongly and independently associated with outpatient care (a OR 0.09 95% CI: 0.01-0.74) while positive findings of pulmonary infiltrates and/or pleural effusion on chest radiograph (a OR 8.01 95% CI: 1.12-57.49) was strongly and independently associated with admission.
Conclusions**:** Normosmia is an independent predictor of admission in Covid-19 cases. Smell loss in Covid-19 may associate with a milder clinical course.

Clinical value of immune-inflammatory parameters to assess the severity of coronavirus disease 2019

Zhu Z, Cai T, Fan L, Lou K, Hua X, Huang Z, Gao G.
Infect Dis
Sci Total Environ
2020 Apr 222; PMID: 32334118
Level of Evidence: 4 - Retrospective Cohort Study
Type of Article: Research

BLUF: In this retrospective study, the authors analyze throat and nasopharyngeal swabs, sputum samples and blood from 127 hospitalized patients with confirmed COVID-19 at Hwa Mei Hospital (China) between

January 23 and February 20, 2020. They classified patients (mild, moderate, severe or critical) based on specific clinical criteria and characterized each patient group to compare clinical features of COVID-19. The study focused on markers of inflammation and found a high level of IL-6, CRP, and hypertension were independent risk factors for assessing the severity of COVID-19.

Abstract:
Objective: To explore the clinical value of immune-inflammatory markers to assess the severity of coronavirus disease 2019 (COVID-19).
Methods: 127 consecutive hospitalized patients with confirmed COVID-19 were enrolled in this study, and classified into non-severe and severe groups. Demographics, symptoms, underlying diseases and laboratory data were collected and assessed for predictive value.
Results: Of 127 COVID-19 patients, 16 cases (12.60%) were classified into the severe group. High level of interleukin-6 (IL-6), C-reaction [*sic*] protein (CRP) and hypertension were independent risk factors for the severity of COVID-19. The risk model based on IL-6, CRP and hypertension had the highest area under the receiver operator characteristic curve (AUROC). Additionally, the baseline IL-6 was positively correlated with other immune-inflammatory parameters and the dynamic change of IL-6 in the severe cases were parallel to the amelioration of the disease.
Conclusion: **Our study showed that high level *(sic)* of IL-6, CRP and hypertension were independent risk factors for assessing the severity of COVID-19.** The risk model established upon IL-6, CRP and hypertension had the highest predictability in this study. Besides, IL-6 played a pivotal role in the severity of COVID-19 and had a potential value for monitoring the process of severe cases.

No adequate evidence indicating hypertension as an independent risk factor for COVID-19 severity.

Li G, Li H, Lu J.Li G, et al.
Clin Res Cardiol.
2020 Apr 23; PMID: 32328736
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter
BLUF: The authors conclude that a finding of hypertension being a possible high risk factor for progression of severe complication in COVID-19 from one meta-analysis was not properly investigated due to lapses in study design and data analysis.

Summary: The authors explore the findings that hypertension could be a high risk factor for COVID-19 patients to progress to severe complications in a meta-analysis study entitled: *Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in China*. They expressed that one should practice caution when interpreting results, specifics in the study design, collection, and analytics of data. The state this study was drawn from a small sample size, some articles did not seem to robustly investigate their own hypothesis, there was no explaination or adjustment for confounders, such as age or sex, which are common practice. For these reasons, they felt the link between hypertension and COVID-19 had yet to be fully investigated despite this meta-analysis.

Increased amylase and lipase in patients with COVID-19 pneumonia: don´t blame the pancreas just yet!

de-Madaria E; Siau K; Cárdenas-Jaén K
Gastroenterology.
2020 Apr 21; PMID: 32330475
Level of Evidence: 5 - Expert Opinion

Type of Article: Letter

Summary: Authors write this letter in response to a study that suggested COVID-19 patients had pancreatic injury based on elevated lipase and amylase. Based on the history and definition of pancreatic injury, and past studies showing other reasons why those enzymes can be elevated (salivary gland damage, released from the kidney), the authors encourage using imaging (CT or MRI) to diagnose pancreatic injury in COVID-19 patients instead of enzyme serum levels.

Emergency Medicine

Cardiac Arrest in the COVID-19 Era.

Christian Hassager, Susanna Price, Kurt Huber
European Heart Journal
2020, Apr 23; PMID: 32324049
Level of Evidence: 5 - Expert opinion
Type of Article: Editorial

Summary: Many survivors of out of hospital or in hospital cardiac arrest will require a stay in the ICU. With the COVID-19 pandemic impacting ICU bed availability, survival rates of cardiac arrest may decline. Additionally, the authors "encourage public access defibrillation and compression-only resuscitation of adults for lay people, and suggest that healthcare professionals always use adequate PPE whenever a COVID-19 infection may be suspected." They hope these actions will help to decrease the transmission of the virus, as they note that there is overlap between the populations that COVID-19 impacts and populations that tend to require CPR for cardiac arrest.

Critical Care

Tracheostomy in the COVID-19 pandemic.

Mattioli F, Fermi M, Ghirelli M, Molteni G, Sgarbi N, Bertellini E, Girardis M, Presutti L, Marudi A.Mattioli F, et al.
Eur Arch Otorhinolaryngol.
2020 Apr 22; PMID: 32322959
Level of Evidence: 3 - Cohort study
Type of Article: Short Communication

BLUF: Tracheostomy should be considered in COVID-19 patients suffering from ARDS to improve long-term outcomes and decrease ICU stay. It should be considered after 7 days to maximize benefit and should not be considered in those who are close to reaching invasive mechanical intervention weaning targets. Additionally, tracheostomy should not be delayed past 14 days due to inflammatory changes that may make the procedure less likely to succeed.

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.

Serial bedside lung ultrasonography in a critically ill COVID-19 patient

Ji, L; Cao, C; Lv, Q; Li, Y; Xie, M
QJM
2020 Apr 24; PMID: 32330262
Level of Evidence: 4 - Case Report
Type of Article: Research

Summary: The authors of this case report hope to encourage more beside ultrasound use for COVID-19 patients for diagnosis and resolution monitoring in hopes of reducing overall CT scan use. This patient was found to have **numerous B-lines, small consolidations, and pleural line thickening in her intercostal spaces with ultrasound**, which the authors deemed equivalent to the initial CT scan findings. After 20 days of treatment, both CT scan and ultrasound presented a degree of resolution.

Are subpleural consolidations indicators for segmental pulmonary embolism in COVID-19?

Zotzmann V, Lang CN, Bamberg F, Bode C, Staudacher DL.Zotzmann V, et al.
Intensive Care Med.
2020 Apr 23; PMID: 32328727
Level of Evidence: 5 - Expert opinion
Type of Article: Correspondence

BLUF: In patients with elevated d-dimers and subpleural consolidations on lung ultrasonography, further diagnostic workup of a potential pulmonary embolism (PE) might be advised. Thus, lung ultrasonography might be an addition rather than a replacement for computed tomography (CT).

Summary: A bedside snapshot study was conducted on all SARS-CoV-2-positive patients on mechanical ventilation and with elevated d-dimers at a tertiary hospital in Freiburg, Germany. These patients were screened for the presence of subpleural consolidations. Three out of 10 patients met the inclusion criteria. None of them suffered from coagulopathy or clinical signs of thrombosis, and all were on prophylactic heparin therapy. All patients underwent a chest contrast CT since the likelihood for PE in these patients was considered medium to high. Segmental pulmonary artery embolisms in all three patients were detected. Although incidence of PE in COVID-19 patients has to be further investigated, it might be a specific complication of COVID19.

One Ventilator For 2 Patients: Feasibility and Considerations of a Last Resort Solution in Case of Equipment Shortage

Tonetti T, Zanella A, Pizzilli G, Irvin Babcock C, Venturi S, Nava S, Pesenti A, Ranieri VM.Tonetti T, et al.
J Thorax
2020 Apr 23; PMID: 32327566
Level of Evidence: 5- Mechanism-based research
Type of Article: Research

BLUF: A group of Italian critical care physicians evaluate the feasibility of assembling a 'double circuit' system that allows mechanical ventilation of 2 patients with 1 ventilator. They conclude in-vitro feasibility and describe the method, but emphasize appropriate indications and caution of potential consequences.

Summary: A group of Italian critical care physicians assembled, tested, and confirmed the in-vitro feasibility of ventilating 2 patients with a single ventilator. This article describes their method for

assembling and implementing this system using tubing and supplies that are readily available in most intensive care settings (Figures 1 and 2). However, the authors emphasize that this "extreme" technique should only be used in emergency triage situations, and caution that potential technical, clinical, and ethical issues may arise, such as inability to monitor respiratory mechanics.

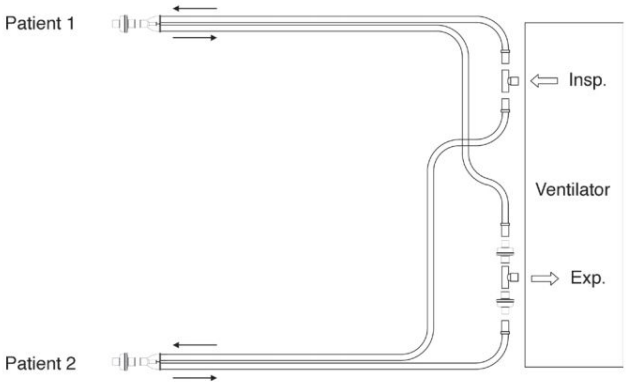


Figure 2 Circuit set-up. Arrows pointing left indicate inspiratory airflow, arrows pointing right indicate expiratory airflow. Insp., inspiratory port; Exp., expiratory port.

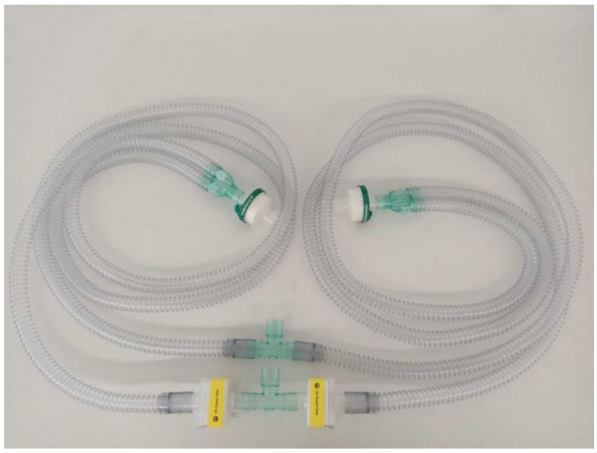


Figure 1 Assembled circuit.

[Management of COVID-19 Respiratory Distress.]

Marini JJ, Gattinoni L., et al.
JAMA.
2020 Apr 24; PMID: 32329799
Level of Evidence: 5 - Expert Opinion
Type of Article: Clinical Update

Summary: COVID-19 acute respiratory distress syndrome (CARDS) appears to have a component of vascular insult that may require a distinct treatment approach from other ARDS. CARDS may be classified along a spectrum of two conceptual models, type L or type H. Type L is defined by high compliance, lower lung weight on CT and low response to PEEP. Type H is one that appears more like traditional ARDS with extensive CT consolidations, low compliance, higher lung weight on CT and high PEEP response. The strategies for managing each type is described below. described in the table below) with distinct pathophysiologies.

Table. Time Course and Treatment Approach to Ventilation Support for Patients With CARDS

Time period	Objective	Respiratory support options	Rationale
Before intubation	Adequate gas exchange Avoid P-SILI	Supplemental oxygen, CPAP, NIV, HFNC Awake prone positioning, Target nonvigorous breathing	Powerful respiratory effort can cause reinforcing lung and vascular stress, resulting in injury
During mechanical ventilation	Avoid pulmonary deterioration and VILI vortex	Minimize PEEP, frequency and tidal volume Adjust to acceptable gas exchange Maintain fluid balance Reduce O_2 demand Consider ECMO	Minimize transpulmonary and vascular stresses
After intubation	Minimize pulmonary stress Optimize O_2 Avoid VILI vortex	Type L[a]: use lower PEEP (<10 cm H_2O) Use more liberal tidal volume (7-9 mL/kg) as needed Reduce O_2 demand Consider prone positioning	Lower tidal volumes are unnecessary Higher PEEP is ineffective, creates dead space, and adversely redirects blood flow
	Reduce and evenly distribute lung and vascular stresses Optimize O_2 Avoid VILI vortex	Type H[a]: use higher PEEP (<15 cm H_2O) Lower tidal volume (5-7 mL/kg) Reduce O_2 demand Implement prone positioning	More closely behaves and responds like typical ARDS
Weaning phase	Avoid reversion to previously worsened pulmonary state by causing VILI and worsening edema	Make transitions cautiously Avoid abrupt changes Spontaneous trials only at the very end of the weaning process	Strong spontaneous efforts raise O_2 demand, increase edema, and promote P-SILI

Abbreviations: ARDS, acute respiratory distress syndrome; CARDS, COVID-19 with ARDS; CPAP, continuous positive airway pressure; ECMO, extracorporeal membrane oxygenation; HFNC, high-flow nasal cannula; NIV, noninvasive ventilation; P-SILI, patient self-inflicted lung injury; PEEP, positive end-expiratory pressure; VILI, ventilator-induced lung injury.

[a] Type L: Scattered ground-glass infiltrates, higher compliance (>50 mL/cm H_2O), not PEEP responsive; less dyspnea. Type H: Extensive infiltrates of atelectasis and edema, lower compliance, PEEP responsive, overtly dyspneic.

Medical subspecialties

COVID-19 - does exercise prescription and maximal oxygen uptake (VO_2 max) have a role in risk-stratifying patients?

Ahmed I
Clin Med (Lond)
2020 Apr 23; PMID: 32327405
Level of Evidence: 5 - Expert opinion
Type of Article: Letter

BLUF: The author theorizes that a patient's maximal oxygen uptake (VO2 max) could be used as a supplemental representation of their overall risk of COVID-19 severity. They discuss the potential role for patients establishing a baseline VO2 max through guidelines of remote exercise tests and prescription of home exercise regimens to improve this value; and suggest that higher numbers correlate to lower risk of disease severity.

Abstract:
As the UK shields 'high risk' patients and enforces social distancing measures, patients will be at risk of significantly reducing physical activity levels. We explore the evidence base for COVID-19-specific recommendations and exercise interventions to 'precondition' patients prior to infection and appraise the role of maximal oxygen uptake (VO2 max) as a risk-stratifying triage tool. We conclude that structured exercise programmes can be used to maintain physical activity levels and prevent deconditioning and that VO2 max has the potential to be used as a clinically relevant triage tool during the COVID-19 outbreak.

Dermatology

Risk of hospitalization and death from COVID-19 infection in patients with chronic plaque psoriasis receiving biological treatment and renal transplanted recipients in maintenance immunosuppressive treatment.

Gisondi P, Zaza G, Del Giglio M, Rossi M, Iacono V, Girolomoni G.
J Am Acad Dermatol.
2020 Apr 21; PMID: 32330632
Level of Evidence: 3 – Non-Randomized cohort study
Type of Article:

BLUF: In this retrospective observational study, although psoriasis and transplant patients were older, burdened by metabolic and cardiovascular comorbidities, and immunosuppressed, there were no early indications of increased hospitalizations or deaths from COVID-19 in such patients compared to the general population.

Summary:
There is still **uncertainty as to whether biologics and immunosuppressive drugs should be interrupted for preventing severe complications of COVID-19**. Herein, the authors performed a retrospective observational study to determine whether chronic plaque psoriasis patients on biological or other immunosuppressive therapy and renal transplant patients had a higher risk of hospitalization or death from COVID-19 compared to the general population of Verona from February 20 to April 10, 2020. As of April 10, the total number of COVID-19-positive patients (including those not hospitalized or dead) in Verona was 3,199. Among 980 patients with chronic plaque psoriasis on biologics, there were no cases of hospitalization or death. Among 243 renal transplant patients, one required hospitalization for fever and pneumonia, but fully recovered. Comorbidities were more

prevalent among the study population compared to the general population of Verona; the mean age and prevalence of male gender was also higher in the study population. In spite of these differences, there was **no indication that the study population was subject to increased hospitalizations or death from COVID-19**, compared to the general population.

Dermatoethics: Self-Prescribing Plaquenil during the COVID-19 Pandemic.

Stoj VJ, Grant-Kels JM.
Int J Womens Dermatol.
2020 Apr 23; PMID: 32328511
Level of Evidence: 5 – Expert Opinion
Type of Article: Letter
Summary: The author examines the question of whether it is ethical for dermatologists to pre-emptively prescribe hydroxychloroquine for patients or for their own parents.
There are ethical concerns of non-maleficence in prescribing a medication not yet shown to be beneficial. Furthermore, stockpiling a medication and depleting supply for patients with clear indications could be considered a violation of the bioethical principles of justice and nonmaleficence.

Cardiology

Inpatient Use of Ambulatory Telemetry Monitors for COVID-19 Patients Treated with Hydroxychloroquine and/or Azithromycin

Chang D, Saleh M, Gabriels J, et al.
J American College of Cardiology
2020 Apr 21; PMID: 32330546
Level of Evidence: 4- Non-randomized case series
Type of Article: Research
Summary: In a single-center case series of 117 COVID-19 patients, electrophysiologists from North Shore University Hospital in New York conclude that Mobile Cardiac Outpatient Telemetry (MCOT) devices may be an innovative method to monitor for arrhythmias and prolonged QTc in COVID-19 patients without severe cardiac disease. This allows telemetry beds to be allocated for more critically ill patients and decreases resources required for serial electrocardiograms (ECGs) in patients receiving Hydroxychloroquine and Azithromycin.

Arrhythmias and sudden cardiac death in the COVID-19 pandemic.

Kuck KH
Herz
2020 Apr 24; PMID: 32333026; No Abstract
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter
Summary: COVID-19 was noted to cause myocardial injury in a study done in Wuhan, China - 17% of cases were found to have elevated troponin levels and 23% were found to have heart failure. Currently, no specific antiarrhythmic therapy except external defibrillation/cardioversion has been described. The only medication that may be considered, as in other life-threatening situations, is amiodarone, but not in combination with chloroquine therapy.

Hematology and Oncology

Direct oral anticoagulant plasma levels striking increase in severe COVID-19 respiratory syndrome patients treated with antiviral agents. The Cremona experience.

Testa S, Prandoni P, Paoletti O, Morandini R, Tala M, Dellanoce C, Giorgi-Pierfranceschi M, Betti M, Danzi GB, Pan A, Palareti G.
Journal of Thrombosis and Haemostasis.
2020 Apr 23; PMID: 32329231
Level of Evidence: 4 - Cohort study
Type of Article: Research

BLUF: This article details a study comparing the levels of direct oral anticoagulants (DOAC) in 32 COVID-19 patients on DOACs before and during hospitalization because of the known potential for increased serum concentration of DOACs when used with antivirals. The results showed a significant increase (6.14 x greater) in DOAC during hospitalization when compared to before hospitalization. They have concerns of bleeding in these patients and suggest potentially withholding DOAC and replacing them with alternatives.

Abstract:
Background: Antiviral drugs are administered in patients with severe COVID-19 respiratory syndrome (SARS-CoV-2), including those treated with direct oral anticoagulants (DOACs). Concomitant administration of antiviral agents has the potential to increase their plasma concentration. A series of patients managed in the Cremona Thrombosis Center were admitted at Cremona Hospital for SARS-CoV-2 and started antiviral drugs without stopping DOAC therapy. DOAC plasma levels were measured in-hospital and results compared with those recorded before hospitalization.
Methods: All consecutive patients on DOACs were candidates for administration of antiviral agents (lopinavir, ritonavir or darunavir). Plasma samples for DOAC measurement were collected 2-4 days after starting antiviral treatment, at 12 hours from the last dose intake in patients on dabigatran and apixaban, and at 24 hours in those on rivaroxaban and edoxaban. For each patient, C-trough DOAC level , expressed as ng/mL, was compared with the one measured before hospitalization.
Results: Of the 1039 patients hospitalized between February 22th and March 15th 2020 with SARS-CoV-2 and candidates for antiviral therapy, 32 were on treatment with a DOAC. DOAC was stopped in 20, and continued in the remaining 12. On average, C-trough levels were 6.14 times higher during hospitalization than in pre-hospitalization period.
Conclusion: DOAC patients treated with antiviral drugs show an alarming increase in DOAC plasma levels. In order to prevent bleeding complications, we believe that physicians should consider withholding DOACs from patients with SARS-CoV-2 and replacing them with alternative parenteral antithrombotic strategies for as long as antiviral agents are deemed necessary and until discharge.

Hospital-based use of thromboprophylaxis in patients with COVID-19.

Spyropoulos AC, Ageno W, Barnathan ES.
Lancet.
2020 Apr 21; PMID: 32330428
Level of Evidence: 5 - Expert Opinion
Type of Article: Correspondence

Summary: This correspondence was made in response to a number of case-series papers done in China during the time of the COVID-19 pandemic suggesting that higher numbers of D-dimers

correlate with higher levels of mortality and ARDS in patients with COVID-19 infection. **The suggestion made here is for thromboprophylaxis with LMWH to be strictly adhered to as numbers increase and for prospective real-time data to begin to be collected on this topic**.

Fibrinolytic abnormalities in acute respiratory distress syndrome (ARDS) and versatility of thrombolytic drugs to treat COVID-19.

Whyte CS, Morrow GB, Mitchell JL, Chowdary P, Mutch NJ.
J Thromb Haemost
2020 Apr 23; PMID: 32329246
Level of Evidence: Level 5 - Literature Review
Type of Article: Review Article

BLUF: There is evidence that fibrin deposits occur in the lungs prior to the onset of symptoms in COVID-19, leading to the possibility that targeting the fibrinolytic system with agents such as nebulized tPA could limit disease severity and improve pulmonary function.

Abstract:
The global pandemic of coronavirus disease 2019 (COVID-19) is associated with the development of acute respiratory distress syndrome (ARDS), which requires ventilation in critically ill patients. The pathophysiology of ARDS results from acute inflammation within the alveolar space and prevention of normal gas exchange. The increase in proinflammatory cytokines within the lung leads to recruitment of leukocytes, further propagating the local inflammatory response**. A consistent finding in ARDS is the deposition of fibrin in the air spaces and lung parenchyma. COVID-19 patients show elevated D-Dimers and fibrinogen**. Fibrin deposits are found in the lungs of patients due to the dysregulation of the coagulation and fibrinolytic systems. Tissue factor (TF) is exposed on damaged alveolar endothelial cells and on the surface of leukocytes promoting fibrin deposition, while significantly elevated levels of plasminogen activator inhibitor 1 (PAI-1) from lung epithelium and endothelial cells create a hypofibrinolytic state. **Prophylaxis treatment of COVID-19 patients with low molecular weight heparin (LMWH) is important to limit coagulopathy. However, to degrade pre-existing fibrin in the lung it is essential to promote local fibrinolysis. In this review, we discuss the repurposing of fibrinolytic drugs, namely tissue-type plasminogen activator (tPA), to treat COVID-19 associated ARDS.** tPA is an approved intravenous thrombolytic treatment, and the nebulizer form has been shown to be effective in plastic bronchitis and is currently in Phase II clinical trial. **Nebulizer plasminogen activators may provide a targeted approach in COVID-19 patients to degrade fibrin and improve oxygenation in critically ill patients.**

Type and dose of heparin in COVID-19.

Thachil J, Tang N, Gando S, Falanga A, Levi M, Clark C, Iba T, Cattaneo M.Thachil J, et al.
Thromb Haemost.
2020 Apr 23; PMID:32329221
Level of Evidence: 5 - Expert opinion
Type of Article: Letter

Summary: LMWH can be given to COVID-19 patients to mitigate pulmonary vessel occlusion. However, there is no demonstration that the standard prophylactic doses or that UFH is insufficient to prevent it. Thus, Thachil et al. **emphasize the importance of better defining heparin dosing in these patients and the urgent need to consider thromboprophylaxis in all patients hospitalized for COVID-19.**

Surgical Subspecialties

Colorectal surgery

General Surgery

Isolation protocol for a COVID-2019 patient requiring emergent surgical intervention: case presentation.

Firstenberg MS, Libby M, Ochs M, Hanna J, Mangino JE, Forrester J
Patient Saf Surg
2020 Apr 19; PMID: 32328170
Level of Evidence: 4 - Case Report
Type of Article: Letter

BLUF: The authors detail the steps they took to ensure appropriate COVID-19 isolation precautions from the ICU, to the OR, and back for a patient requiring emergent surgery with suspected (later confirmed) COVID-19. The authors outline and support the efficacy of the steps taken in this case based on the fact that no member of the ICU or surgical teams involved have developed symptoms or tested positive for COVID-19.

Abstract:
Background: The concerns of the highly contagious and morbid nature of Coronavirus Disease-2019 (COVID-2019) have prompted healthcare workers to implement strict droplet and contact isolation precautions. Unfortunately, some patients who may be or presumptively or confirmed as infected with COVID-2019 may also require emergent surgical procedures. As such, given the high-risk for exposure of many healthcare workers involved the complex requirements for appropriate isolation must be adhered to.
Case Presentation: We present our experience with a 77-year-old who required emergency cardiac surgery for a presumed acute aortic syndrome in the setting of a presumed, and eventually confirmed, COVID-2019 infection. We outline the necessary steps to maintain strict isolation precautions to limit potential exposure to the surgical Team.
Conclusions: We hereby provide our algorithm for emergent surgical procedures in critically-ill patients with presumptive or confirmed infection with COVID-2019. The insights from this case report can potentially be templated to other facilities in order to uphold high standards of infection prevention and patient safety in surgery during the current COVID-19 pandemic.

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

Haen, Pierre; Caruhel, Jean-Baptiste; Laversanne, Sophie; Cordier, Pierre-Yves
Oral Oncol
2020 Apr 20; PMID: 32331964
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter

Summary: Regarding tracheostomy techniques for COVID-19 patients, the authors recommend percutaneous tracheostomy versus open tracheostomy. Reasons for this include similar complication rate, no risk of contamination in the OR, and better control of expiratory flow.

Tracheostomy guidelines developed at a large academic medical center during the COVID-19 pandemic.

David AP, Russell MD, El-Sayed IH, Russell MS.David AP, et al.
Head Neck.
2020 Apr 24; PMID: 32329926
Level of Evidence: 5 - Expert Opinion
Article Type: Review

BLUF: The authors propose tracheostomy guidelines tailored to the current COVID-19 pandemic after a multidisciplinary review. These guidelines include proper practice and PPE use during pre-, post-, and perioperative care (Table 2), new technical considerations (Table 1), and multidisciplinary discussions before proceeding with a tracheostomy.

Abstract: Background: During the SARS-CoV-2 pandemic, tracheostomy may be required for COVID-19 patients requiring long term ventilation in addition to other conditions such as airway compromise from head and neck cancer. **As an aerosol generating procedure, tracheostomy increases healthcare worker exposure to COVID-19 infection. Performing surgical tracheostomy and tracheostomy care requires a strategy that mitigates these risks and maintains the quality of patient care.**
Methods: **A multidisciplinary review of institutional tracheostomy guidelines and clinical pathways.** Modifications to support clinical-decision making in the context of COVID-19 were derived by consensus and available evidence.
Results: **Modified guidelines for all phases of tracheostomy care at an academic tertiary care center in the setting of COVID-19 are presented.**
Discussion: During the various phases of the COVID-19 pandemic, clinicians must carefully consider the indications, procedural precautions, and post-operative care for tracheostomies. **We present guidelines to mitigate risk to healthcare workers while preserving the quality of care.**

Table 1: Technical and logistic considerations regarding tracheostomy

COVID-19 Status	Recommendations	Other Considerations
Positive/PUI or Unknown	Location: ICU preferred, negative pressure room PPE: N95 mask or PAPR, head covering, eye protection, gown and two pairs of gloves	• Limit number of providers in the room during the procedure • Use of paralysis recommended to prevent coughing • Clear and constant communication with anesthesia during the tracheostomy, holding ventilation when the ETT cuff is deflated and when the trachea is opened • Avoid use of laryngotracheal topical anesthesia (aerosolizing)
Negative (one test 48-72 hours prior) or Asymptomatic	Location: OR or ICU, negative pressure room PPE: N95 mask or PAPR, head covering, eye protection, gown and two pairs of gloves	

COVID-19 – coronavirus disease 2019; PUI – person under investigation; ICU – intensive care unit; PAPR – powered air-purifying respiratory; OR – operating room, ETT – endotracheal tube

Table 2: Summary of mitigation strategies at various phases of tracheostomy care.

Phase of Care	Considerations and Mitigation Strategies
Preoperative	Decrease in viral shedding: ● Testing available – De-isolation after two negative PCR tests in 24 hours ● Testing unavailable – Consider delaying tracheostomy until 21 days post-intubation
Perioperative	Location: ● ICU preferable- minimizes transport ● Negative pressure room Surgical Team: ● Minimize number of staff members during the procedure ● Use of appropriate PPE (airborne and contact precautions) Technical Considerations: ● Patient paralysis to prevent coughing ● Holding ventilation during tracheotomy until cuff inflated and circuit reconnected
Postoperative	● Droplet precautions during tracheostomy care ● Use of closed, inline suctioning ● Closed circuit with HEPA filter if on mechanical ventilatory support ● HME when off ventilatory support ● Delaying the first tracheostomy change to one month or after de-isolation occurs for COVID-19 positive patients

PCR – polymerase chain reaction; ICU – intensive care unit; PPE – personal protective equipment; HEPA – high efficiency particulate arrestance; HME – heat and moisture exchange; COVID-19 – coronavirus disease 2019

Transplant Surgery

COVID-19 in Solid Organ Transplant Recipients: Initial Report from the US Epicenter.

Pereira MR, Mohan S, Cohen DJ, Husain SA, Dube GK, Ratner LE, Arcasoy S, Aversa MM, Benvenuto LJ, Dadhani D, Kapur S, Dove LM, Brown RS, Rosenblatt RE, Samstein B, Uriel N, Farr MA, Satlin M, Small CB, Walsh T, Kodiyanplakkal RP, Miko BA, Aaron JG, Tsapepas DS, Emond JC, Verna EC
Am J Transplant.
2020 Apr 24; PMID: 32330343
Level of Evidence: 4 - Case Series
Type of Article: Research

BLUF: A case series of COVID-19 positive solid organ transplant patients conducted at two large academic medical centers in New York City during the first three weeks of outbreak found that:

- Common presenting symptoms were fever, cough, and dyspnea, although dyspnea was the only symptom significantly associated with severe clinical course
- Patients with severe disease had significantly higher respiratory rates (p = 0.01), lower O2 saturation (p = 0.01), and lower maximum temperature (p = 0.03) than those with moderate disease (Table 1)
- Advanced age, hypertension, and active cancer were associated with severe disease (Table 1)
- Fifteen (17%) reported a known exposure, and three (4%) were suspected of having a nosocomial transmission (Table 1)
- Procalcitonin was the only biomarker significantly more elevated in the severe group compared to the moderate group

- No significant conclusions were drawn on the efficacy of a particular therapeutic intervention (ie hydroxychloroquine, azithromycin, remdesivir, tocilizumab, steroids) (Table 3)
- Optimal management of immunosuppression remains largely uncertain, although immunosuppressive therapy was reduced in the majority of patients in this cohort (Table 3)

Abstract:
Solid organ transplant recipients may be at a high risk for SARS-CoV2 infection and poor associated outcomes. We herein report our **initial experience with solid organ transplant recipients with SARS-CoV2 infection at two centers during the first 3 weeks of the outbreak in New York City**. Baseline characteristics, clinical presentation, antiviral and immunosuppressive management were compared between patients with mild/moderate and severe disease (defined as ICU admission, intubation or death). **90 patients** were analyzed with a median age of 57 years. **46 were kidney recipients, 17 lung, 13 liver, 9 heart and 5 dual-organ transplants.** The most common presenting symptoms were **fever (70%), cough (59%) and dyspnea (43%)**. 22 (24%) had mild, 41 (46%) moderate and 27 (30%) severe disease. Among the **68 hospitalized patients**, **12% required non-rebreather and 35% required intubation**. 91% received hydroxychloroquine, 66% azithromycin, 3% remdesivir, 21% tocilizumab and 24% bolus steroids. **Sixteen patients died (18% overall, 24% of hospitalized, 52% of ICU) and 37 (54%) were discharged**. In this initial cohort, transplant recipients with COVID-19 appear to have more severe outcomes, although testing limitations likely led to undercounting of mild/asymptomatic cases. As this outbreak unfolds, COVID-19 has the potential to severely impact solid organ transplant recipients.

Earliest cases of coronavirus disease 2019 (COVID-19) identified in solid organ transplant recipients in the United States.

Kates OS, Fisher CE, Stankiewicz-Karita HC, Shepherd AK, Church EC, Kapnadak SG, Lease ED, Riedo FX, Rakita RM, Limaye AP.
Am J Transplant.
2020 Apr 24; PMID: 32330356
Level of Evidence: 4 - Case Reports
Type of Article: Research
BLUF: Four case reports on **solid-organ transplant recipients**, kidney, liver, lung, and heart, infected with COVID-19 are presented. All four had resolution of symptoms with at least one month of follow-up. Temporal eduction of immunosuppression and usage of antimalarials were reported in one case. In three out of the four patients, there was no fever on examination; lung auscultation may not always reveal pathology.

Abstract:
With the rapidly expanding pandemic of SARS-CoV-2, there is concern that solid organ transplant recipients will be particularly vulnerable to infection and may experience a more severe clinical course. We report **four cases of COVID-19 in solid organ transplant recipients including recipients of kidney, liver, lung, and heart transplants**. We describe each patient's medical history including transplantation history, their clinical presentation and workup, and their course from diagnosis to either hospital discharge or to improvement in symptoms. These reports demonstrate a **range of symptoms, clinical severity, and disease course** in solid organ transplant recipients with COVID-19, including two hospitalized patients and two patients managed entirely in the outpatient setting.

OBGYN

Analysis of the susceptibility to COVID-19 in pregnancy and recommendations on potential drug screening.

Zhao X, Jiang Y, Zhao Y, Xi H, Liu C, Qu F, Feng X.
Eur J Clin Microbiol Infect Dis
2020 Apr 23; PMID: 32328850
Level of Evidence: 5 - Mechanism Based Reasoning
Type of Article: Review

BLUF: A consideration of physiological factors that could put pregnant patients at a higher risk of COVID-19 infection and mortality is presented. Based on existing literature on drug safety, COVID-19 treatments with reasonable safety profiles in pregnancy are also suggested, including chloroquine, interferon, lobinavir/ritonavir, metformin, statins, and glycyrrhizic acid.

Summary: This article discusses the physiological changes that occur during pregnancy that could explain the observed increase in pregnant patients' susceptibility to respiratory viruses like influenza and SARS. These factors, which could potentially also mean pregnant patients are at a higher risk of COVID-19, include:

- Changes to the respiratory system during pregnancy that may make patients more susceptible to viral infections spread by aerosol transmission and could increase risk of hypoxic respiratory failure
- Changes in immune and endocrine systems during pregnancy may also increase risk of infection
- ACE-2 expression is upregulated in pregnancy

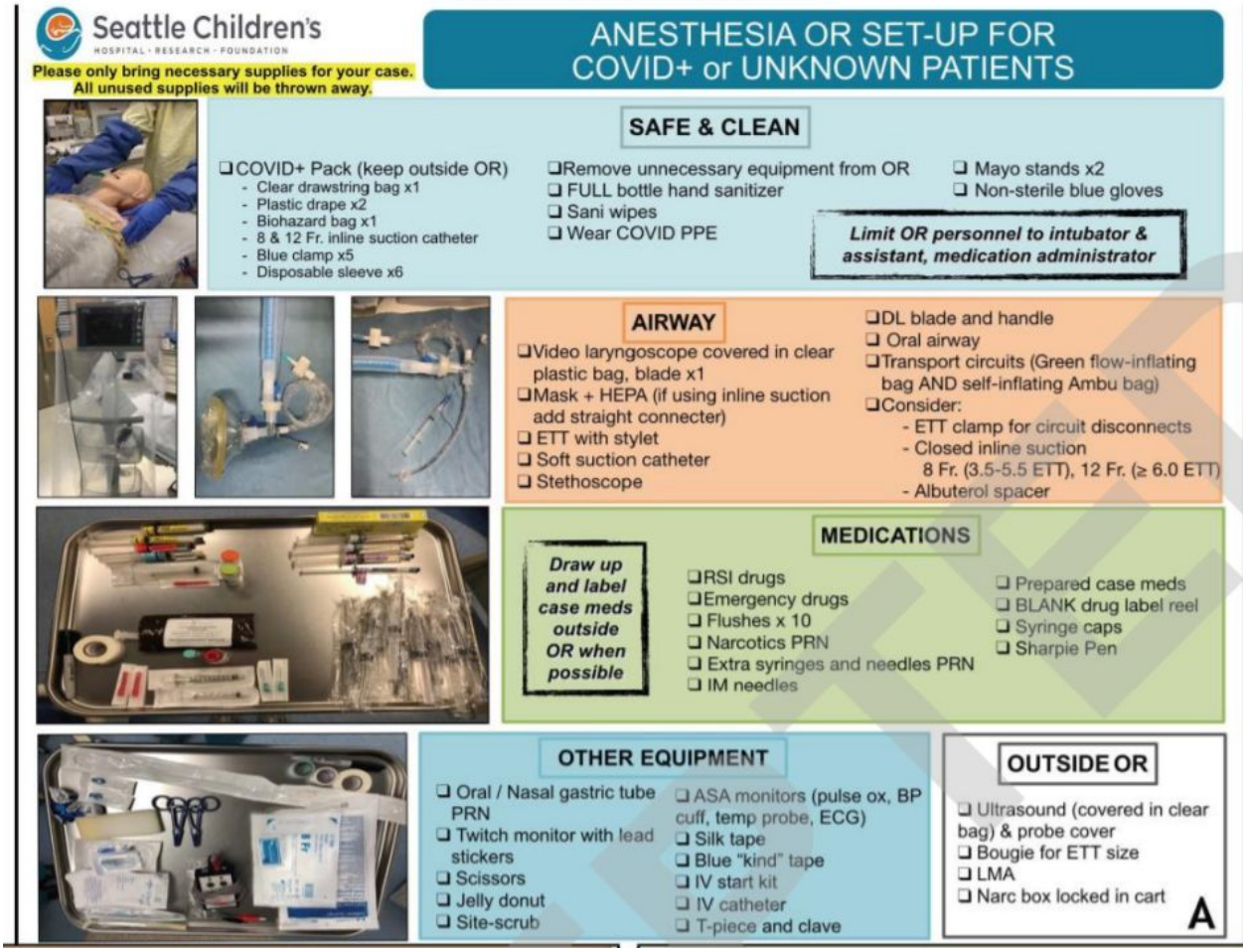
The authors also suggest potential COVID-19 drugs that may be safe for use in pregnancy, acknowledging that more research is needed in this area. Drugs and drug formulations they suggest could have a reasonable maternal/fetal safety profile include:

- Chloroquine: Classified as class C by the FDA, but several studies suggest fetal damage has not been reported with chloroquine use in pregnant patients.
- Interferon: One study of interferon use in pregnant patients showed no increased risk of miscarriages, stillbirths, preterm birth, or major malformations.
- Lobinavir/ritonavir: Recommended for COVID-19 management in pregnant patients by a group at Huazhong University of Science and Technology Union Hospital and two studies suggest there is no increased risk of preterm labor or birth defects.
- Host Directed Therapy (e.g., Metformin and Statins): This category includes therapies intended to modulate patients' immune systems and prevent overactive inflammatory responses. Metformin is commonly used to treat gestational diabetes and does not increase malformation risk in the first trimester. A small number of reports suggests that statins do not increase the risk of congenital deformities. These drugs could also be used in strategies to minimize the doses of other drugs used to treat COVID-19.
- Glycyrrhizic acid: The main bioactive ingredient in licorice. Some studies have suggested a risk of preterm delivery with high doses, but this remains debated. Does not appear to have teratogenic effects. Effects on the P450 system have been observed, so dosing of other drugs may need to be adjusted if used.
- Nanoparticle mediated drug delivery: With a nanocarrier that does not cross the placenta, this drug delivery system could theoretically be developed and used to administer drugs without fear of teratogenicity.

Pediatrics

One Size Does Not Fit All: How to Rapidly Deploy Intubation Practice Changes in a Pediatric Hospital During the COVID-19 Pandemic.

Brown S, Verma S, Lean A, Patrao F.
Anesth Analg.
2020 Apr 22; PMID: 32332294
Level of Evidence: 6 - No data given
Type of Article: Letter to the Editor
Summary: To minimize COVID-19 exposure risk during intubation, the authors developed several techniques to standardize the procedure. They created a job aide for OR set up which emphasizes the need for appropriate PPE, lists what equipment should be brought into the room vs kept ready outside, and defines specific roles during the procedure. These guidelines are appropriate for and currently being implemented in emergency departments and ICU. They also conducted live multidisciplinary simulation sessions, and streamed/recorded simulations to avoid gathering of large groups.



Geriatrics

COVID-19, osteoarthritis and women's health.

Mobasheri A.
Case Rep Womens Health.
2020 Apr 23; PMID: 32328442
Level of Evidence: 5 - Expert Opinion
Article Type: Editorial

Summary: The author discusses how universal closure of gyms and other public open spaces presents a challenge for individuals with osteoarthritis who use exercise and weight management as a core treatment. Thus, the author suggests patients with osteoarthritis to continue exercising at home, eating a healthy diet, and taking dietary supplements. Some of the exercises that are suggested include yoga, walking, Tai chi, Pilates and chair-based sessions, exercise streaming services, and Nintendo Wii Fit balancing board.

Alternative Medicine

An alternative approach to minimize the risk of coronavirus (Covid-19) and similar infections.

Ahmad A, Rehman MU, Alkharfy KM
2020 Apr 24; Eur Rev Med Pharmacol Sci.
PMID: 32329879
Level of Evidence: 5 - Expert Opinion
Type of Article: Review

BLUF: This literature review identified reports on phytochemicals with anti-viral properties. They searched key-words in pubmed “Coronavirus”, “COVID-19”, “2019-nCoV and anti-viral natural products” and restricted results to those published in 2020. Several studies were found on clinical trials of herbal therapies for viral diseases which showed preliminary results. The authors conclude more work needs to be done, including larger, randomized clinical studies.

Abstract: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a new strain that was discovered in 2019 and has not been previously identified in humans. On December 31st 2019 World Health Organization (WHO) was informed of a cluster of cases with pneumonia of unknown origin from Wuhan City, Hubei province of China. The WHO announced in February 2020 that COVID-19 is the official name of the coronavirus diseases. A total of 519,899 confirmed cases with 23,592 deaths linked to this pathogen as on March 27, 2020 have been reported. Due to increasing number of infected people across the continents and huge loss to human life, the WHO has declared the novel COVID-19 outbreak a pandemic. A pandemic is defined as the "worldwide spread" of a new disease. Currently, no COVID-19 specific treatments have been approved by the United States Food and Drug Administration (US-FDA). However, the current treatment options include hydroxychloroquine, tocilizumab, remdesivir, lopinavir-ritonavir (Kaletra®), and nitazoxanide. In recent past, some natural herbal compounds have demonstrated encouraging anti-viral properties. **This article attempted to summarize available information on the reported anti-viral activity of some natural products.**

Adjusting Practice During COVID-19

For Healthcare Professionals

COVID-19 diffusion capability is its worst, unpredictable characteristic. How to visit a patient from a distance.

Sterpetti AV.
Br J Surg.
2020 Apr 24; PMID: 32329517
Level of Evidence: 5 – Expert Opinion
Type of Article: Letter to the Editor

Summary: The author suggests the following methods for caring for patients while maintaining physical distance to prevent transmission of COVID-19.

- Patients should be seen via video conference.
- If symptoms warrant COVID-19 testing, the patients can have a swab and if positive, the patient can be taken directly by ambulance to a dedicated COVID-19 hospital.
- Via video conference, physicians can look for signs of respiratory distress or cyanosis. Chest auscultation can be performed by asking the patient or their relative to place the microphone of the phone on the different chest regions.

Hospital preparedness for COVID-19 pandemic: Experience from department of medicine at Veterans Affairs Connecticut Healthcare System.

Gupta S, Federman DG.
Postgrad Med.
2020 Apr 24; PMID: 32331509
Level of Evidence: 6 – No Data Cited
Type of Article: Perspective

Summary: The authors outline the response taken at their VA hospitals in response to COVID-19:

- Organization of an Incident Command Center (ICC) consisting of chiefs from various departments.
- Implementation of screenings at entrances, off-site testing, emergency room safeguards.
- Implementation of droplet precautions, PPE and social distancing.
- Redistributed hospital beds to prepare for inpatients with COVID-19 and restructured healthcare worker teams to provide longer resting periods between service times.
- Developed a clinical algorithm to help providers decide testing for COVID-19.

Acute care

Emergency Medicine

The role of emergency medical services in containing COVID-19

Jaffe, Eli; Strugo, Refael; Bin, Eli; Blustein, Oren; Rosenblat, Ido; Alpert, Evan Avraham; Roman Sonkin
Am J Emerg Med
2020 Apr 18; PMID: 32327247
Level of Evidence: 5 - Mechanism-Based Reasoning
Type of Article: Letter to the Editor

Summarizing Excerpt: "Maximizing EMS during a pandemic by carrying out phone triage, home testing, and drive-in testing significantly decreases visits to physicians' offices and hospitals and allows early identification of those with COVID-19. These activities contribute to the effort to contain the spread of disease."

Pulmonary embolism in returning traveler with COVID-19 pneumonia.

Foch E, Allou N, Vitry T, Masse L, Allyn J, Andre M, Allou N
J Travel Med
2020 Apr 25; PMID: 32330267
Level of Evidence: 4- Case report
Type of Article: Research

Summary: A case report including lab findings and chest images of a 50 year old man with no prior medical history who tested positive for COVID-19 by PCR of a nasopharyngeal swab after a long plane flight. He was later found to have a pulmonary embolism. The authors suggest looking out for PE in patients with a combined history of COVID-19 and travel.

World Federation for Ultrasound in Medicine and Biology Position Statement: How to Perform a Safe Ultrasound Examination and Clean Equipment in the Context of COVID-19.

World Federation for Ultrasound in Medicine and Biology Safety Committee (Jacques S. Abramowicz, Iwaki Akiyama, David Evans, J. Brian Fowlkes, Karel Marsal, Yusef Sayeed and Gail ter Haar), et al.
Ultrasound Med Biol.
2020 Apr 4; PMID: 32327199
Level of Evidence: 5 - Expert Opinion
Article Type: Review

Summary: The main guidelines for safe ultrasound examination during the COVID-19 pandemic are outlined as follows:

- **Triage of patients to routine or emergent examination**
- **Protect the patient and ultrasound providers**
    - Exclude practitioners with specific health problems from performing ultrasounds
    - Infection control training and fit testing for respirators for ultrasound practitioners
    - Respect the time of scheduled visits, widen the appointment intervals, space seats in the waiting 6 feet apart.
    - Limit the number of visitors in the examination room to a maximum of 1
    - Scan a confirmed COVID19 patient at the end of the clinic list
    - Practice hand hygiene using alcohol-based hand rub or washing hands with soap and water for at least 20 seconds.
    - Scanning should be performed with one hand on transducer while having the other hand semi-clean but in contact with the key-board. Gel application should occur with the semi-clean hand.
    - If required to scan the patient in an isolation room, medical staff should don PPE (respirator, goggles, face protective shield, surgical gown and gloves) before entry of isolation room
    - Specific PPE for when caring for a patient with confirmed or suspected COVID-19 includes: respirator or face mask, eye protection, gloves, gowns, and donning and doffing training
    - Single-use, non-sterile gel packets should be used for any external ultrasound exam with suspected or confirmed COVID-19 individuals. If these are not available, use gel bottles for external scans only.

- **Prepare and clean the ultrasound room and equipment**
    - Protective eyewear and gloves should be worn when cleaning room and equipment
    - Equipment should be cleaned using an LLD with agents recommended by the CDC and EPA.
    - Equipment covers, such as for the ultrasound scanner console, will enhance the workflow, as LLD of mechanical keyboards and console controls may become time-consuming
    - Reduce number of transducers connected to ultrasound machine to a minimum
    - Ultrasound transducers and cables should be cleaned and disinfected after each scan

Diagnostic radiology

Adapting to a new normal? 5 key operational principles for a radiology service facing the COVID-19 pandemic.

Chen RC, Tan TT, Chan LP.Chen RC, et al.
Eur Radiol.
2020 Apr 2; PMID: 32328761
Level of Evidence: 5 - Expert Opinion
Type of Article: Editorial

BLUF: Outlines five principles used by a large academic radiology division in managing the response to COVID-19 pandemic:

1. Leadership - Create a task force to evaluate daily operational capacity, to act as a single point of contact for other departments, and to rapidly disseminate key information within the division
2. Patient Risk Stratification - Initially stratified based on non-suspect/suspect/confirmed COVID-status, and now moving toward universal precautions
3. Adequate Manpower - postpone elective staff leave, segregate into multiple teams so that if one team needs to quarantine the others can continue to operate
4. Daily Operations - For non-suspect COVID-19 patients - continue standard pre-pandemic precautions of antimicrobial wipes, strict hand hygiene, and add surgical masks for staff interacting with patients. For suspected or confirmed COVID-19 patients - minimize unnecessary imaging, use portable exam equipment to minimize patient movement, for non-portable exam equipment plan and rehearse route of transport, utilize negative pressure rooms, extensive plastic wrap, antimicrobial wipes, and UV-C light
5. Workplace and Social Responsibility - provide educational materials for staff about hand hygiene and proper donning/doffing of PPE, sick workers encouraged to stay home, utilize mandatory temperature checks

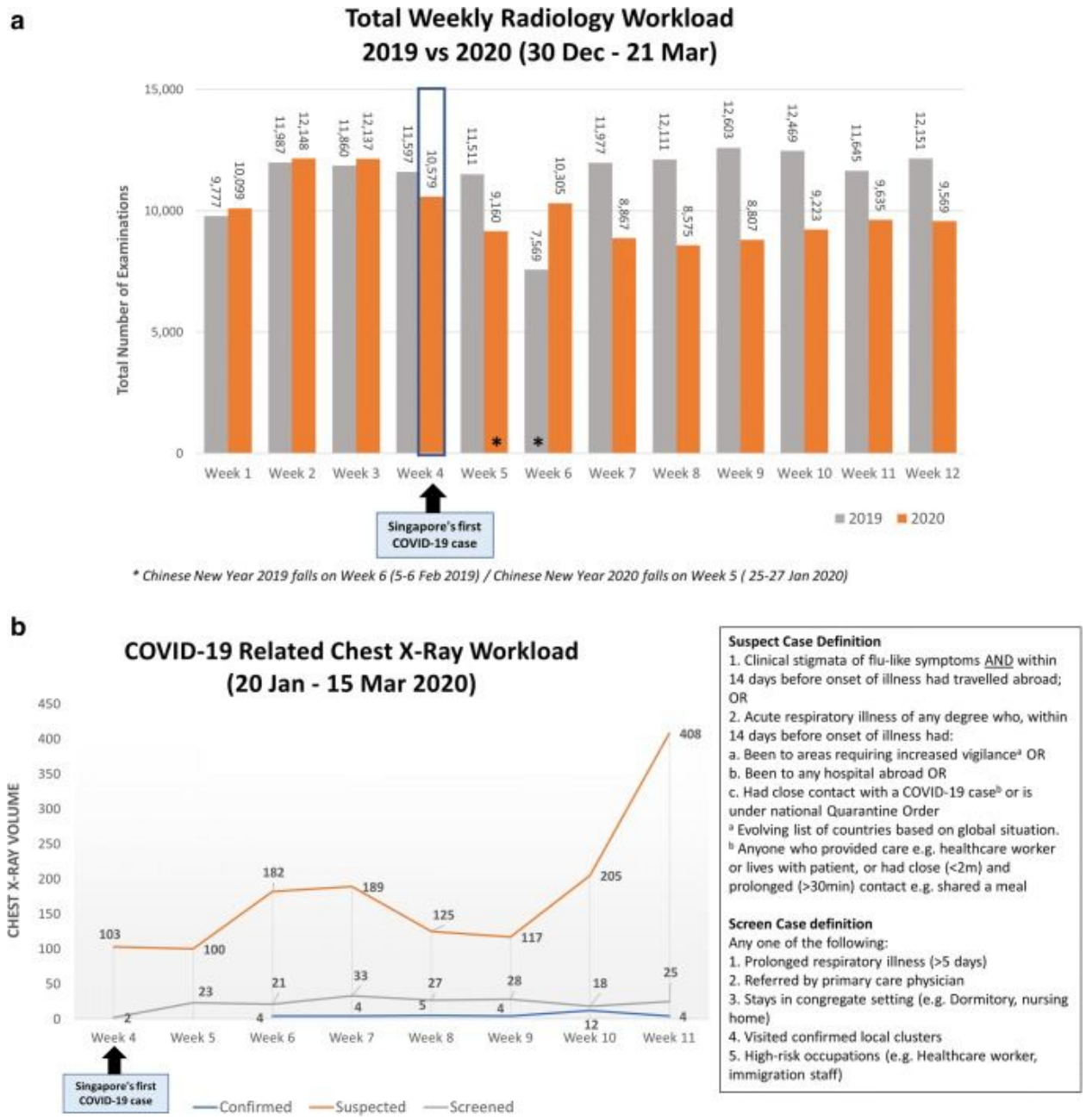


Figure 1. a Total radiology workload, 2019 vs 2020. We have made a conscious effort to reduce our workload to deal with the increased operational demands and potential surges in patient load during this outbreak period. Since our first COVID-19 case, our workload has decreased by approximately 25% compared to last year. **b** COVID-19-related chest x-ray workload, 20 January to 15 March 2020. Our COVID-19 suspect chest x-ray workload has dramatically increased, largely related to an interim change in suspect case definition from recent travel from China to any recent travel from abroad.

Diagnosing Pulmonary Thromboembolism in COVID-19: A Stepwise Clinical and Imaging Approach.

Rouhezamin MR, Haseli S
Acad Radiol
2020 Apr 17; PMID: 32331965
Level of Evidence: 5-Expert opinion
Type of Article: Letter

Summary excerpt: "Hospitalized patients with severe COVID-19 are at **high risk of PTE**. Performing CT angiography to diagnose PTE is limited by an overall **high propensity for CIN [contrast induced nephropathy]** in patients admitted with severe COVID-19. Careful, detailed evaluation of the clinical course to **identify signs and symptoms** suggestive of PTE complicating

the course of the disease, assessment with **electrocardiography and laboratory tests** suggestive of myocardial injury and stretch, followed by a **stepwise imaging approach** [color Doppler of lower extremities, followed by CT angiography in select patients] would aid in the diagnosis of PTE while reducing the risk of CIN."

Anaesthesia

Personal protective equipment (PPE) for both anesthesiologists and other airway managers: principles and practice during the COVID-19 pandemic

Lockhart, Shannon L; Duggan, Laura V; Wax, Randy S; Saadm Stephan; Grocott, Hilary P
Can J Anaesth
2020 Apr 23; PMID: 32329014
Level of Evidence: 5 - Expert Opinion
Type of Article: Commentary

BLUF: Authors recommend PPE guidelines according to degree of care and proximity to aerosol-generating procedures and advocate for a three-tried approach for reducing COVID-19 spread. **For high risk procedures, the authors specifically recommend neck cover, two pairs of gloves, and Associations for Advancement of Medical Instrumentation (AAMI) level-3 gown in addition to standard PPE for patient care of COVID-19 patients.**

Abstract:
Healthcare providers are facing a coronavirus disease pandemic. This pandemic may last for many months, stressing the Canadian healthcare system in a way that has not previously been seen. Keeping healthcare providers safe, healthy, and available to work throughout this pandemic is critical. The consistent use of appropriate personal protective equipment (PPE) will help assure its availability and healthcare provider safety. The purpose of this communique is to give both anesthesiologists and other front-line healthcare providers a framework from which to understand the principles and practices surrounding PPE decision-making. **We propose three types of PPE including: 1) PPE for droplet and contact precautions, 2) PPE for general airborne, droplet, and contact precautions, and 3) PPE for those performing or assisting with high-risk aerosol-generating medical procedures.**

Neurology

Spinal muscular atrophy care in the COVID-19 pandemic era.

Veerapandiyan A, Connolly AM, Finkel RS, Arya K, Mathews KD, Smith EC, Castro D, Butterfield RJ, Parsons JA, Servais L, Kuntz N, Rao VK, Brandsema JF, Mercuri E, Ciafaloni E
Muscle Nerve
2020 Apr 24; PMID: 32329921
Level of Evidence: 5 - Expert Opinion
Type of Article: Editorial

BLUF: Experts in spinal muscular atrophy (SMA) from the US and Europe created recommendations regarding care of SMA patients during the COVID-19 pandemic:

- SMA treatments should not be considered elective and should not be delayed or interrupted if possible.
- It is important to resume the original schedule of nusinersen after a delayed dose.
- Home blood draws and telemedicine may be clinically appropriate for monitoring after onasemnogene abeparvovex-xioi gene transfer therapy.
- Standardized physical therapy assessments to maintain insurance coverage for SMA treatments should be flexible.

- Infants with SMA identified by newborn screening (NBS) should receive urgent evaluation and rapid initiation of treatment.

Abstract:
The Corona Virus Disease 2019 (COVID-19) pandemic has resulted in reorganization of healthcare settings affecting the delivery of clinical care to patients with spinal muscular atrophy (SMA). There is a concern that **patients with SMA may be at increased risk of manifesting severe symptoms of COVID-19**. Currently approved therapies for SMA improve survival and motor function, however, their delivery requires an increased exposure to the health system and a dedicated healthcare team. In this paper, we discuss **consensus recommendations pertaining to care of SMA patients during the pandemic**. We highlight that **SMA treatments should not be perceived as elective**. Decisions regarding the delay of treatments should be made with consideration of the potential risks of COVID-19 exposure and the risk of that delay. We emphasize the **importance of collaborative treatment decisions** between the patient, family, and health care provider, considering any geographic or institution-specific policies and precautions for COVID-19.

Keeping people with epilepsy safe during the Covid-19 pandemic.

French JA, Brodie MJ, Caraballo R, Devinsky O, Ding D, Jehi L, et al.
Neurology.
2020 Apr 23; 2020.PMID: 32327490
Level of Evidence: 5 - No Evidence Provided
Type of Article: Letter

Summarizing excerpt: " The recommendations [by the American Academy of Neurology] focus on administration of as much care as possible at home to keep people with epilepsy out of health care facilities, where they are likely to encounter COVID-19 (including strategies for rescue therapy), as well as minimization of risk of seizure exacerbation through adherence, and through ensuring a regular supply of medication."

Medical subspecialties

Allergy and immunology

Handling of Allergen Immunotherapy in the COVID-19 Pandemic: An ARIA-EAACI Statement.

Ludger Klimek, Marek Jutel, Cezmi Akdis, Jean Bousquet, Mübeccel Akdis, et al.
Allergy.
2020 Apr 24; PMID: 32329930
Level of Evidence: 5 - Expert opinion
Type of Article: Letter

BLUF:
In **non-infected or recovered COVID-19** cases that were previously on AIT:
- **Continuation** of subcutaneous and/or sublingual immunotherapy is advised.

In **confirmed or suspected COVID-19** cases that were previously on AIT:
- **Interrupting** subcutaneous and/or sublingual immunotherapy is advised.

Summary: Allergen-specific immunotherapy (AIT) aims to induce tolerance in allergy patients by modulating B and T cell responses and inhibiting migration of eosinophils, basophils, and mast cells.

In COVID-19 both CD4 and CD8 T cells are exhausted, disrupting antiviral immunity. Thus, Klimek et al. conclude that active COVID-19 cases should discontinue their AIT regimen as the marked lymphopenia in these patients can contribute to the pathogenesis and severity of COVID-19.

Asthma and COVID-19.

Abrams EM, Geert W 'J, Yang CL
CMAJ
2020 Apr 24; PMID: 32332038; No Abstract
Level of Evidence: 5 - Expert Opinion
Type of Article: Management
Summary: The COVID-19 virus commonly triggers asthma exacerbations. Good asthma control - such as with oral steroids - can help prevent these exacerbations. Additionally, a metered-dose inhaler with a valved holding chamber is strongly preferred over nebulization in order to decrease the risk of aerosolization of SARS-CoV-2 and infection transmission.

Dermatology

Safety of dupilumab in severe atopic dermatitis and infection of Covid-19: two case reports.

Ferrucci S, Romagnuolo M, Angileri L, Berti E, Tavecchio S.Ferrucci S, et al.J Eur Acad Dermatol Venereol. 2020 Apr 24. doi: 10.1111/jdv.16527. Online ahead of print.J Eur Acad Dermatol Venereol. 2020.PMID: 32330323
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter
BLUF: Dupilumab is a treatment for severe atopic dermatitis (AD) and previous studies have reported the low risk (2%) of contracting viral infections, which is a concern considering the current COVID-19 pandemic. This authors emphasizes the **long term safety of dupilumab** since only 2 out of 245 patients on dupilumab developed COVID-19-induced interstitial pneumonia.

Abstract:
Dupilumab is a fully human monoclonal antibody against the alfa subunit of interleukin (IL)-4 receptor that blocks signalling from both IL-4 and IL-13, which are key type 2 cytokines in the pathophysiology of **atopic dermatitis (AD)**. It shows good efficacy with a rapid response and good safety with few side effects. In a paper of Deleuran et al. the authors showed **long term safety and efficacy of dupilumab**; they reported viral upper respiratory tract infection, cough and influenza in about 2% of patients.

Cardiology

Cardio-oncology Care in the Time of COVID-19 and the Role of Telehealth.

Parikh A, Kumar AA, Jahangir E.
JACC CardioOncol.
2020 Apr 22; PMID: 32328590
Level of Evidence: 5 - Expert Opinion
Type of Article: Comment
Summary: Telehealth has its pros and cons-it is the only viable way for providers to continuously take care of their patients, but there is an extent of de-personalization that is concurrent with this transition. This commentary by three cardio-oncologists at Vanderbilt University discuss the impacts the COVID-19 pandemic has on the future of telehealth, saying that even once the period of social

distancing is over, the entire healthcare system and delivery of care will still look very different from where it was when this all started.

Hematology and Oncology

Transition to a Virtual Multidisciplinary Tumor Board during the COVID-19 Pandemic: The University of Pittsburgh Experience.

Dharmarajan H, Anderson JL, Kim S, Sridharan S, Duvvuri U, Ferris RL, Solari MG, Clump DA 2nd, Skinner HD, Ohr JP, Zandberg DP, Branstetter B 4th, Hughes MA, Traylor KS, Seethala R, Chiosea SI, Nilsen ML, Johnson JT, Kubik MW.
Head Neck.
2020 Apr 24; PMID: 32329958
Level of Evidence: 5 - Expert Opinion
Type of Article: Comment

Abstract: Multidisciplinary conferences (MDC) are an important component of head and neck oncologic care including diagnosis, treatment, and survivorship. Virtual MDC allows for improved collaboration between providers at distant sites and proper allocation of healthcare resources in a time of crisis. When approached systematically, a virtual MDC is feasible to design and implement in a large academic medical center with multiple satellite hospitals.

Management of hepatocellular carcinoma in the time of COVID-19.

Iavarone M, Sangiovanni A, Carrafiello G, Rossi G, Lampertico P.
Annals of Oncology
2020 Apr 21; PMID: 32330540
Level of Evidence: 5 – Qualitative data
Type of Article: Letter to the Editor

BLUF: This letter goes over a modified algorithm to tackle the COVID-19 crisis by reducing the risk of patients' exposure to SARS-CoV-2 and spreading of the infection within the hospital.

Summarizing Excerpt:
"We agree that more intensive attention should be paid to patients with cancer during the COVID-19 crisis, both for reducing the risk of SARS-CoV-2 infection and ensuring appropriate cancer patient management programs. In our center, all hepatocellular carcinoma (HCC) cases are managed following EASL guidelines and the BCLC staging system based on discussion from multidisciplinary meetings. To tackle the COVID-19 crisis by reducing as low as possible the risk of patients' exposure to SARS-CoV-2 and spreading of the infection within the hospital, we modified the management algorithm… According to these modifications in our HCC management, we compared our performance between 24th February and 20th March 2020 to those in the same time-frame in 2019 (Table 1). **In summary, the HCC treatments for 42 patients were scheduled with a delay of ≥2 months in only 11 (26%) patients: 2 Thermal ablation (TA), 4 transarterial chemoembolization (TACE), 3 transarterial radioembolization (TARE), and 2 systemic therapies. TAs were performed instead of preplanned surgical resection in 3 patients.** As the pandemic evolves, our approach to HCC management will be reviewed and our procedures updated. However, we believe that many of these changes implemented today to face this crisis will remain useful in managing any future emergencies."

Lymphopenia that may develop in patients treated with temozolomide and immune control check-point inhibitor may be a high risk for mortality during the COVID-19 outbreak.

Tanriverdi O.
Med Oncol.
2020 Apr 24; PMID: 32333196
Level of Evidence: 5 - Expert Opinion
Type of Article: Commentary

BLUF: Cancer patients on anti-cancer drugs are at risk for developing lymphopenia, which would place these patients at greater risk and mortality from COVID-19. Management of cancer patients during the COVID-19 pandemic warrants further investigation.

Abstract:
As we know more about the clinical and laboratory features of COVID-19, which is now accepted as a pandemic, many questions have been raised about how to manage and monitor the treatment of cancer patients. It was determined that the **incidence of lymphopenia increased in COVID-19** and there was a **significant relationship between lymphopenia and mortality.** This can be thought of as an unresponsive problem in how to maintain anti-cancer drugs that cause lymphopenia. This article was written for a hypothetical approach in cancer patients diagnosed with COVID-19 in order to be an idea of collecting data for treatment with anti-cancer drugs that cause lymphopenia.

Potential Impact of the COVID-19 Pandemic on Financial Toxicity in Cancer Survivors

Baddour, Khalil; Kudrick, Lauren D; Neopaney, Aakriti; Sabik, Lindsay M; Peddada,
Head & neck
2020 Apr 24; PMID: 32329924
Level of Evidence: 5 – Expert Opinion
Type of Article: Correspondence

BLUF:
Cancer survivors have been disproportionately affected by rising unemployment and economic recession as a result of COVID-19, which the authors believe will lead to higher cancer mortality.

Abstract:
Background: In the context of COVID-19, cancer survivors represent a particularly vulnerable population that may be "doubly hit" both by costs of cancer treatment and financial strain imposed by the pandemic.
Methods: We performed a review of the literature pertaining to cancer, financial toxicity, and economic challenges.
Results: Multiple societies have put forth recommendations to modify delivery of cancer care in order to minimize patient exposure to the virus**.** Cancer survivors, especially patients with head and neck cancer, have been disproportionately affected by rising unemployment levels and economic recessions in the past, both of which are linked to higher cancer mortality. Patients who rely on employer-provided insurance and do not qualify for Medicaid may lose access to life-saving treatments.
Conclusions: It is essential to implement interventions and policy changes in order to mitigate the effects of this pandemic but also to ensure this becomes a non-issue during the next one.

Outpatient Medicine

Managing People with Diabetes Fasting for Ramadan During the COVID-19 Pandemic: A South Asian Health Foundation Update.

Hanif S, Ali SN, Hassanein M, Khunti K, Hanif W.
Diabetic Medicine
2020 Apr 25; PMID: 32333691
Level of Evidence: 4 – Narrative Review
Type of Article: Review

BLUF: The purpose of this review is to discuss the implications of fasting in individuals with diabetes in Ramadan during the COVID-19 pandemic. Overall, the outpatient management of diabetes in people who are fasting and develop COVID-19 include: frequent blood glucose monitoring, checking ketones every 2-4 hours, breaking the fast, ensuring adequate hydration, and following government advice for mild symptoms of COVID-19.

Abstract:
The month of Ramadan forms one of the five pillars of the Muslim faith. Adult Muslims are obligated to keep daily fasts from dawn to sunset, with exceptions. This year Ramadan is due to begin on 23 April 2020 and the longest fast in the UK will be approximately 18 hours in length. In addition, due to the often high-calorie meals eaten to break the fast, Ramadan should be seen as a cycle of fasting and feasting. Ramadan fasting can impact those with diabetes, increasing the risk of hypoglycaemia, hyperglycaemia and dehydration. This year, Ramadan will occur during the global COVID-19 pandemic. Reports show that diabetes appears to be a risk factor for more severe disease with COVID-19. In addition, the UK experience has shown diabetes and COVID-19 is associated with dehydration, starvation ketosis, diabetic ketoacidosis and hyperglycaemic hyperosmolar state. This makes fasting in Ramadan particularly challenging for those Muslims with diabetes. Here, we discuss the implications of fasting in Ramadan during the COVID-19 pandemic and make recommendations for those with diabetes who wish to fast.

Rheumatology

Patients with lupus are not protected from COVID-19.

Sawalha, Amr H
Ann Rheum Dis
2020 Apr 24; PMID: 32332075
Level of Evidence: 5 - Expert Opinion
Type of Article: Correspondence

Summary: In this correspondence, the author refutes claims that patients with lupus are protected from COVID-19 and cites evidence that indicates that those with lupus are more susceptible to viral infections. They also state that there is not enough clinical data to show that hydroxychloroquine is protective in COVID-19.

Surgical Subspecialties

Colorectal surgery

In considerations of robotic colorectal surgery within a COVID-19 pandemic.

Felsenreich DM, Gachabayov M, Dong XD, Cianchi F, Bergamaschi R.
Minerva Chir.

2020 Apr 24; PMID: 32329322
Level of Evidence: 5 – Expert Opinion
Type of Article: Editorial

Summary: The authors provide recommendations for robotic colorectal surgery based on the idea that we ought to distinguish epicenters and non-epicenters in order to offer a nuanced approach to the potential benefits and drawbacks of robotic surgery.

- Almost normal scenario: routine elective robotic colorectal activity may be maintained.
- Low level alert scenario: only patients with malignant colorectal diseases should be operated electively using robotic technique.
- Medium level alert scenario: only rectal cancer patients are operated electively robotically if capacity in ICU allows it.
- High level alert scenario: No robotic colorectal operations should be carried out.

General Surgery

Tracheostomy Protocols during COVID-19 Pandemic

Heyd, CP; Desiato, VM; Nguyen, SA; O'Rourke, AK; Clemmens, CS; Awad, MI; Worley, ML; Day, TA
Head Neck
2020 Apr 24; PMID: 32329922
Level of Evidence: 5 - Literature Review
Type of Article: Guideline

BLUF: Authors review current tracheostomy use in the COVID-19 pandemic and make recommendations on the current guidelines based on literature review up until March 31st.

- General
  - postpone elective cases for COVID-19 patients
  - test all tracheostomy patients for COVID-19 prior to surgery
  - educate and rehearse with staff
  - avoid tracheostomy in unstable patients
- Location
  - In the ICU or OR, negative pressure when possible. Reduce transportation.
- Personnel
  - Reduce to essential staff, additional can be outside the room
  - Most experienced staff should perform the procedure
  - Consider designated tracheostomy team
- Equipment
  - Proper Personal protective equipment (PPE)
  - PPE should be readily nearby the staff
  - Have surgical tracheostomy tray nearby
  - Use viral filter when possible
  - Closed suction system
- Intraoperative Techniques
  - Limit suction and electric cautery
  - Complete paralysis
  - Preoxygenate 5 minutes prior at 100%
- Emergency Tracheostomy in COVID-19 positive or unknown
  - Follow guidelines above as much as possible
  - Consider likelihood of survival if endotracheal intubation cannot be performed
- Tracheostomy management in COVID-19 positive patients
  - General: have the patient clean and care for themselves as much as possible

- Delay tracheostomy change procedure until the patient isn't positive anymore
- Ventilated: avoid disconnecting from ventilator, clamp distal to viral filter
- Non-ventilated: simple facemask, viral filter on tracheostomy tube, keep tube cuffs inflated.

Abstract:
Background: The COVID-19 pandemic has resulted in the implementation of rapidly changing protocols and guidelines related to the indications and perioperative precautions and protocols for tracheotomy. The purpose of this study was to evaluate current guidelines for tracheostomy during the COVID-19 pandemic to provide a framework for health systems to prepare as the science evolves over the upcoming months and years.
Methods: Literature review was performed. Articles reporting clinical practice guidelines for tracheostomy in the context of COVID-19 were included.
Results: A total of thirteen tracheotomy guidelines were identified. Two were available via PubMed, five in society or organization websites, and six identified via health system websites or other sources. Five were from Otolaryngology-Head and Neck Surgery specialties, six from Anesthesiology and one from Pulmonary/Critical Care. All (100%) studies recommended postponing elective OR cases in COVID-19 positive patients, while seven recommended reducing team members to only essential staff and three recommended forming a designated tracheostomy team. Recommendations with supporting references are summarized in the manuscript.
Conclusions: Tracheostomy guidelines during the COVID-19 pandemic vary by physician groups and specialty, hospital systems, and supply-chain/resource availability. This summary is provided as a point-in-time current state of the guidelines for tracheotomy management in April, 2020 and is expected to change in coming weeks and months as the COVID-19 pandemic, virus testing and antibody testing evolves.

COVID-19 and emergency surgery.

Hogan A.
Br J Surg.
2020 Apr 24; PMID: 32329524
Level of Evidence: 5 – Expert Opinion
Type of Article: Letter to the Editor

Summary: The author makes a case for a recommendation that every patient scheduled for emergency surgical intervention be offered either a thorax CT or RT-PCR screening for COVID-19 prior to intervention, given that the presence of COVID-19 seems to have an adverse impact on perioperative outcomes.

Neurosurgery

Management of Traumatic Spinal Fracture in the Coronavirus Disease 2019 Situation.

Sornsa-Ard T, Niramitsantiphong A, Liawrungrueang W
Asian Spine J
2020 Apr 24; PMID: 32326671
Level of Evidence: 5 - Expert Opinion
Type of Article: Editorial

BLUF: Orthopedics in Thailand provide recommendations and an algorithm (Figure 1) for traumatic spine fracture patient care including:

- Use screening criteria for conscious and stable patients, and provide patients with surgical masks

- In patients who are unconscious and/or unstable and require intubation or a ventilator, surgeons should use full PPE and infection control measures
- Discuss with local COVID-19 regarding the best place for care
- Emergent operative procedure may be performed without waiting for the results of COVID-19 rapid testing or PCR as long as surgeons wear PPE and the patient is placed in a post-operative isolation room or ward

ABSTRACT:
The coronavirus outbreak was labeled a pandemic by the World Health Organization in 2020. Patients who require spine surgery should receive coronavirus disease 2019 (COVID-19) screening to prevent nosocomial cross-infection before surgery. However, **spine fracture and spinal injury are critical and serious**, and there are no standard protocols for management. This article aims to **propose a treatment algorithm for the management of traumatic spine fracture during the COVID-19 pandemic.**

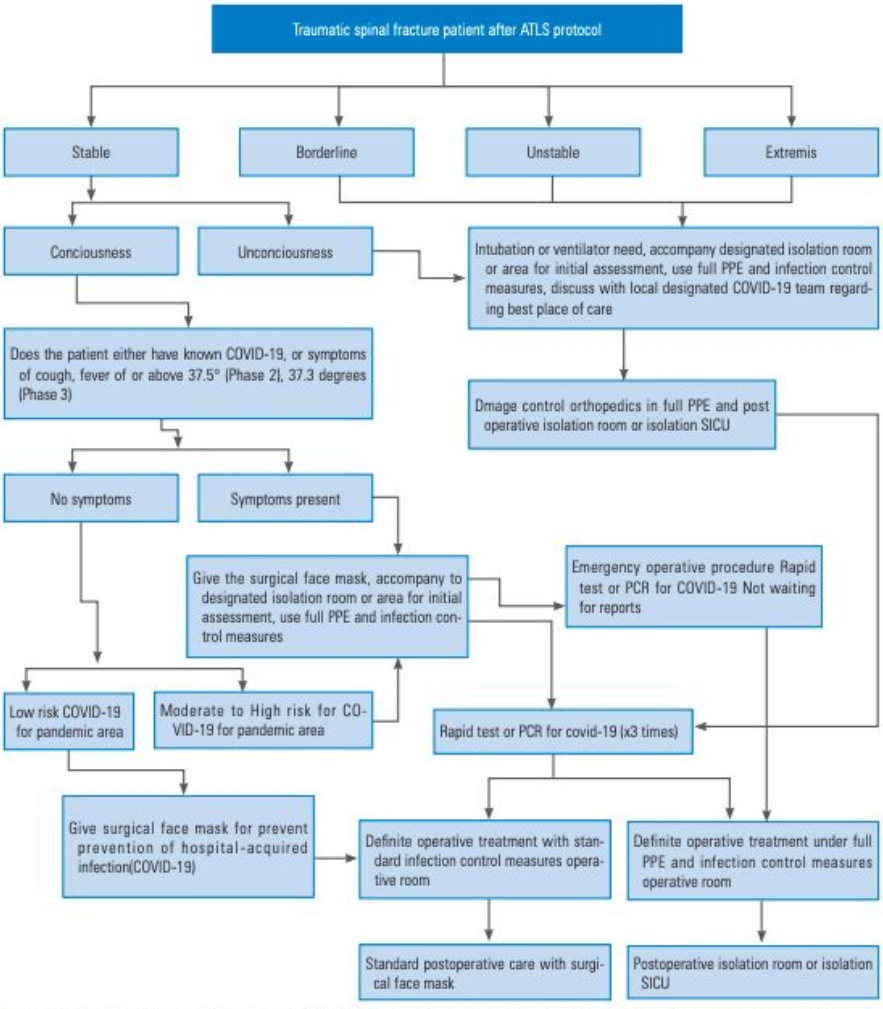


Fig. 1. The authors preferred algorithm to assess COVID-19 risk in patients with a traumatic spine fracture. ATLS, Advanced Trauma Life Support; PPE, personal protective equipment; COVID-19, coronavirus disease 2019; SICU, surgical intensive care unit; PCR, polymerase chain reaction.

Otolaryngology

COVID-19 and hearing difficulties.

Trecca EMC, Gelardi M, Cassano M.
Am J Otolaryngol

2020 Apr 19; PMID: 32327217
Level of Evidence: Level 4 - Case Series
Type of Article: Letter to the Editor
BLUF: The authors present preliminary data on 59 patients with mild to profound hearing loss in Southern Italy who classified the difficulties they experienced during an Emergency Department visit after COVID-19 in relation to their hearing impairment. Eight had no difficulties, 15 had mild, 22 had moderate, and 14 had severe difficulties.
Summary: COVID-19 is having a negative impact on mental health and extra attention should be paid to those with impairments, such as hearing loss, who are living in an extra condition of isolation. Additionally, information and resources regarding COVID-19 is not always available to this community and the use of face masks reduces acoustic transmission and prevents lip reading. The authors report preliminary data from a series of patients at Foggie University Hospital in Southern Italy including 59 patients with mild to profound grades of hearing impairment who were referred from the Emergency Department for urgent ORL consultations. Patients were asked to classify the difficulties experienced during their visit after the COVID-19 outbreak in regards to their hearing impairment. 8 subjects had no difficulties, 15 had mild difficulties, 22 had moderate difficulties, and 14 had severe difficulties.

What ENT doctors should know about COVID-19 contagion risks.

Meccariello G, Gallo O.
Head Neck.
2020 Apr 24, PMID: 32329539
Level of Evidence: 5 - Expert Opinion
Article Type: Commentary
Summary: Otolaryngologists are at an increased risk of exposure to COVID-19 even with routine procedures. It is recommended to wear proper PPE and to implement a screening process for asymptomatic patients to reduce the risk of contagion and spread.

Orthopaedic Surgery

Geospatial Mapping of Orthopaedic Surgeons Age 60 and Over and Confirmed Cases of COVID-19.

Jella TK, Acuña AJ, Samuel LT, Jella TK, Mroz TE, Kamath AF
J Bone Joint Surg Am
2020 Apr 23; PMID: 32332218
Level of Evidence: 5 - Geospatial Mapping
Type of Article: Research
BLUF: The authors of this article compared AAMC-gathered physician demographic information with ESRI-geospatial COVID-19 distribution data and found that the states in the US with the highest numbers of COVID-19 infections have high percentages of orthopedic surgeons >60 years of age and thus at higher risk of severe COVID-19 infection (See attached Figures). They propose solutions to those at risk such as temporarily shifting to telemedicine, distancing from their inpatient colleagues within a practice and assuming less hands-on leadership roles such as resident teaching.

Abstract:
Background: Although elective surgical procedures in the United States have been suspended because of the coronavirus disease 2019 (COVID-19) pandemic, orthopaedic surgeons are being recruited to serve patients with COVID-19 in addition to providing orthopaedic acute care. Older individuals are deemed to be at higher risk for poor outcomes with COVID-19. Although previous studies have shown

a high proportion of older providers nationwide across medical specialties, we are not aware of any previous study that has analyzed the age distribution among the orthopaedic workforce. Therefore, the purposes of the present study were (1) to determine the geographic distribution of U.S. orthopaedic surgeons by age, (2) to compare the distribution with other surgical specialties, and (3) to compare this distribution with the spread of COVID-19.

Methods: Demographic statistics from the most recent State Physician Workforce Data Reports published by the Association of American Medical Colleges were extracted to identify the 2018 statewide proportion of practicing orthopaedic surgeons ≥60 years of age as well as age-related demographic data for all surgical specialties. Geospatial data on the distribution of COVID-19 cases were obtained from the Environmental Systems Research Institute. State boundary files were taken from the U.S. Census Bureau. Orthopaedic workforce age data were utilized to group states into quintiles.

Results: States with the highest quintile of orthopaedic surgeons ≥60 years of age included states most severely affected by COVID-19: New York, New Jersey, California, and Florida. For all states, the median number of providers ≥60 years of age was 105.5 (interquartile range [IQR], 45.5 to 182.5). The median proportion of orthopaedic surgeons ≥60 years of age was higher than that of all other surgical subspecialties, apart from thoracic surgery.

Conclusions: To our knowledge, the present report provides the first age-focused view of the orthopaedic workforce during the COVID-19 pandemic. States in the highest quintile of orthopaedic surgeons ≥60 years old are also among the most overwhelmed by COVID-19. As important orthopaedic acute care continues in addition to COVID-19 frontline service, special considerations may be needed for at-risk staff. Appropriate health system measures and workforce-management strategies should protect the subset of those who are most potentially vulnerable.

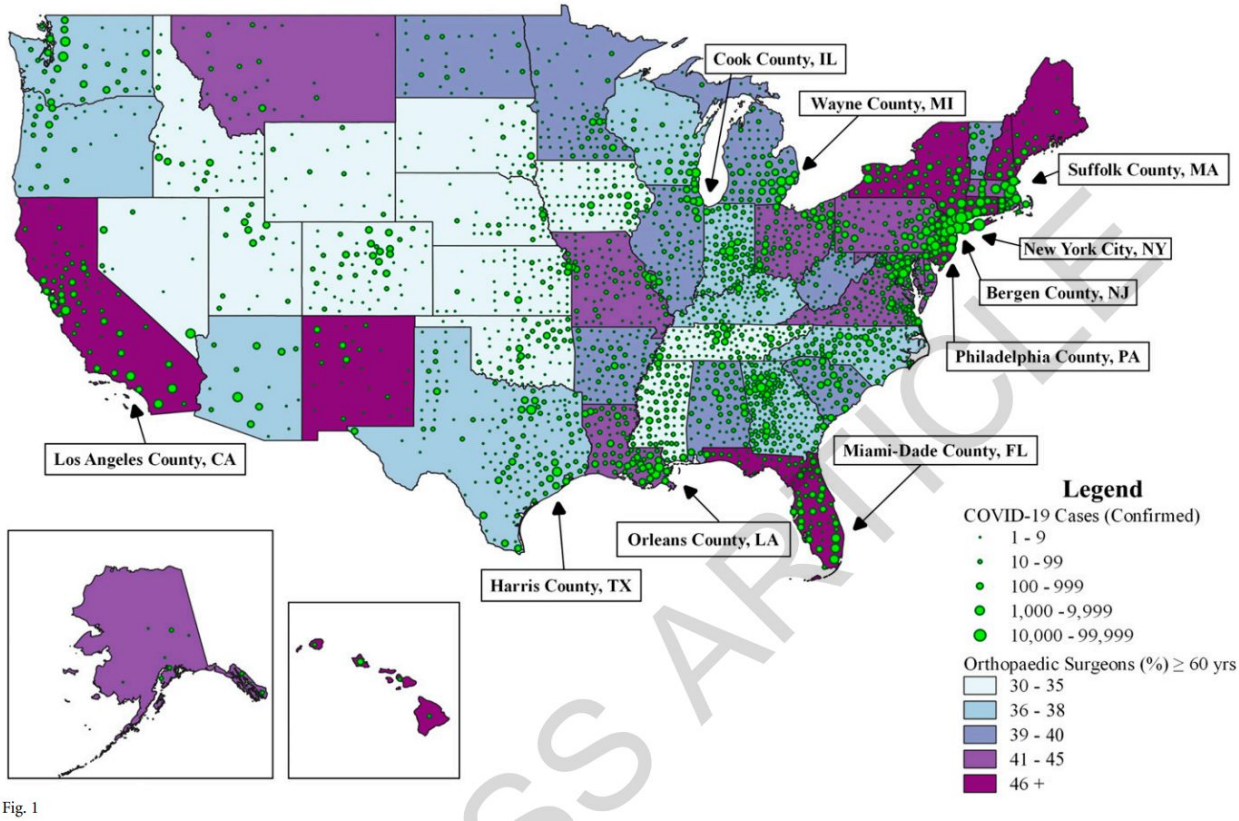


Fig. 1

Map demonstrating the proportion of orthopaedic surgeons ‡60 years of age in the workforce, overlain on the distribution of confirmed COVID-19 cases as of April 8, 2020. Hawaii and Alaska were repositioned for this visualization and are not shown to scale. The green dots represent clusters of confirmed COVID-19 cases, with size adjustments proportional to the number of cases in each cluster. Labeled counties and cities have the highest proportion of COVID-19 cases in their states as of April 8, 2020

TABLE I Orthopaedic Workforce Characteristics for the Top 10 States Impacted by COVID-19*

State	No. of Confirmed COVID-19 Cases	No. of Orthopaedic Surgeons ≥60 Years of Age (% of Total No. of Orthopaedic Surgeons in State)	Total No. of Orthopaedic Surgeons in State	Total State Population ≥60 Years of Age (% of Total State Population)
New York	140,386	546 (47.6%)	1,148	4,480,458 (22.9%)
New Jersey	44,416	264 (47.5%)	556	2,022,272 (22.7%)
Michigan	18,970	204 (39.5%)	516	2,421,416 (24.2%)
California	17,625	1,092 (48.0%)	2,274	7,963,713 (20.2%)
Louisiana	16,284	132 (43.0%)	307	1,019,862 (21.9%)
Massachusetts	15,202	211 (44.4%)	475	1,588,116 (23.0%)
Pennsylvania	14,956	347 (45.8%)	758	3,227,151 (25.2%)
Florida	14,747	545 (46.6%)	1,170	5,765,648 (27.2%)
Illinois	13,553	250 (39.4%)	634	2,804,799 (22.0%)
Texas	9,211	508 (38.8%)	1,309	5,139,025 (18.0%)

*COVID-19 case numbers are accurate as of April 8, 2020. Orthopaedic surgeon demographic data are taken from the 2019 AAMC State Physician Workforce Data Reports and are accurate as of December 31, 2018. State population demographics are taken from 2018 U.S. Census Bureau data (https://www.census.gov/newsroom/press-kits/2018/pop-estimates-national-state.html).

Transplant Surgery

The Swiss approach to the COVID-19 outbreak.

Moeckli B, Peloso A, Oldani G, Orci LA, Banz V, Dutkowski P, Toso C, Berney T.
Am J Transplant
2020 Apr 24; PMID: 32330352
Level of Evidence: Level 5 - Expert Opinion
Type of Article: Letter to the Editor

BLUF: The number of transplants in Switzerland has decreased which will likely increase waitlist mortality. The authors advocate for resuming transplant activity in a stepwise fashion once the pandemic plateaus. The authors also advocate for broad testing of donors and recipients for SARS-CoV-2.

Summary: In response to COVID-19 Switzerland has taken a stepwise approach to transplants which goes as follows: 1) Stop live donor transplantations; 2) Stop pancreas and islet transplants; 3) Stop deceased donor kidney transplants ;4) A tailored approach to urgent status transplants; 5) Only urgent transplants to be performed; 6) Stop all transplants. In hotspots like Geneva, all transplants have been stopped and less affected centers have continued activity at level 4. Between February and March 2020 the number of kidney transplants has gone down and wait times have increased which will likely increase waitlist mortality. For this reason once the pandemic has reached a plateau it is essential to have a staged resumption of transplant activity.The authors also advocate for serological testing of waitlisted patients and molecular testing of patients for SARS-CoV-2 immediately before transplantation.

Urology

Managing Urology Consultations during COVID-19 Pandemic: Application of a Structured Care Pathway.

Borchert A, Baumgarten L, Dalela D, Jamil M, Budzyn J, Kovacevic N, Yaguchi G, Palma-Zamora I, Perkins S, Bazzi M, Wong P, Sood A, Peabody J, Rogers CG, Dabaja A, Atiemo H.
Urology.
2020 Apr 21; PMID: 32330531
Level of Evidence: 3- Nonrandomized controlled cohort

Type of Article: Research

BLUF: A risk-stratified triage pathway for inpatient urology consultations was implemented and evaluated during a three-week period (3/16/2020 – 4/2/2020) and found that out of 53 inpatient consultations, COVID-19 associated consultations represented 18/53 (34%) of all consultations, and of these, 8/18 (44.4%) were managed successfully via telemedicine alone. No team members developed COVID-19 infection.Therefore, most urology consultations can be managed in a patient and physician safety-conscious manner.

Abstract

Objectives**:** To describe and evaluate a risk-stratified triage pathway for inpatient urology consultations during the SARS-CoV-2 (COVID-19) pandemic. This pathway seeks to outline a urology patient care strategy that reduces the transmission risk to both healthcare providers and patients, reduces the healthcare burden, and maintains appropriate patient care.

Methods**:** Consultations to the urology service during a three-week period (March 16 to April 2, 2020) were triaged and managed via one of three pathways: Standard, Telemedicine, or High-Risk. Standard consults were in-person consults with non- COVID-19 patients, High-Risk consults were in-person consults with COVID-19 positive/suspected patients, and Telemedicine consults were telephonic consults for low-acuity urologic issues in either group of patients. Patient demographics, consultation parameters and consultation outcomes were compared to consultations from the month of March 2019. Categorical variables were compared using Chi-square test and continuous variables using Mann-Whitney U test. A p-value <0.05 was considered significant.

Results**:** Between March 16 and April 2, 2020, 53 inpatient consultations were performed. By following our triage pathway, a total of 19/53 consultations (35.8%) were performed via Telemedicine with no in-person exposure, 10/53 consultations (18.9%) were High-Risk, in which we strictly controlled the urology team member in-person contact, and the remainder, 24/53 consultations (45.2%), were performed as Standard in-person encounters. COVID-19 associated consultations represented 18/53 (34.0%) of all consultations during this period, and of these, 8/18 (44.4%) were managed successfully via Telemedicine alone. No team member developed COVID-19 infection.

Conclusions**:** During the COVID-19 pandemic, most urology consultations can be managed in a patient and physician safety-conscious manner, by implementing a novel triage pathway.

OBGYN

A systematic scoping review of COVID-19 during pregnancy and childbirth.

Farida Elshafeey, Rana Magdi, Nader Hindi, Mohamed Elshebiny, Nourhan Farrag, et al.

Int J Gynaecol Obstet.

2020 Apr 24; PMID: 32330287

Level of Evidence: 1 - Systematic review

Type of Article: Systematic review

BLUF: A systematic review of 33 articles and 385 COVID-19 positive pregnant women concluded that COVID-19 infection during pregnancy has clinical presentation and severity similar to non-pregnant adults showing a minimal association with poor maternal or perinatal outcomes.

Abstract:

Background: Clinical presentation and outcomes of COVID-19 infection during pregnancy remain limited and fragmented.

Objectives: To summarize the existing literature on COVID-19 infection during pregnancy and childbirth, particularly concerning clinical presentation and outcomes.

Search strategy: A systematic search of LitCovid, EBSCO MEDLINE, CENTRAL, CINAHL, Web of Science, and Scopus electronic databases. The references of relevant studies were also searched.
Selection criteria: Identified titles and abstracts were screened to select original reports and cross-checked for overlap of cases.
Data collection and analysis: A descriptive summary organized by aspects of clinical presentations (symptoms, imaging, and laboratory) and outcomes (maternal and perinatal).
Main results: We identified 33 studies reporting 385 pregnant women with COVID-19 infection: 368 (95.6%) mild; 14 (3.6%) severe; and 3 (0.8%) critical. Seventeen women were admitted to intensive care, including six who were mechanically ventilated and one maternal mortality. A total of 252 women gave birth, comprising 175 (69.4%) cesarean and 77 (30.6%) vaginal births. Outcomes for 256 newborns included four RT-PCR positive neonates, two stillbirths, and one neonatal death.
Conclusion: COVID-19 infection during pregnancy probably has a clinical presentation and severity resembling that in non-pregnant adults. It is probably not associated with poor maternal or perinatal outcomes.

Rapid Deployment of a Drive-Through Prenatal Care Model in Response to the Coronavirus Disease 2019 (COVID-19) Pandemic.

Turrentine M, Ramirez M, Monga M, Gandhi M, Swaim L, Tyer-Viola L, Birsinger M, Belfort M.
Obstetrics and Gynecology.
2020 Apr 24; PMID: 32332322
Level of Evidence: 5 - Mechanism based evidence
Type of Article: Opinion

BLUF: In this article, the authors devise a drive-through model to provide prenatal care during the COVID-19 pandemic. They argue that "Drive-through care visits reduce person-to-person interaction and contact with potential fomites, reducing the risk of coronavirus disease 2019 (COVID-19) infection while simultaneously providing needed prenatal care."

Abstract: Coronavirus disease 2019 (COVID-19) has been declared a public health emergency for the entire United States. Providing access to prenatal health care while limiting exposure of both obstetric health care professionals and patients to COVID-19 is challenging. Although reductions in the frequency of prenatal visits and implementation of telehealth interventions provide some options, there still remains a need for patient-health care professional visits. A drive-through prenatal care model was developed in which pregnant women would remain in their automobiles while being assessed by the health care professional, thus reducing potential patient, health care professional, and staff exposure to COVID-19. **Drive-through prenatal visits would include key elements that some institutions cannot perform by telehealth encounters, such as blood pressure measurements for evaluation for hypertensive disorders of pregnancy, fetal heart rate assessment, and selected ultrasound-based measurements or observations, as well as face-to-face patient-health care professional interaction, thereby reducing patient anxiety resulting from the reduction in the number of planned clinic visits with an obstetric health care professional as well as fear of virus exposure in the clinic setting.** We describe the rapid development of a drive-through prenatal care model that is projected to reduce the number of in-person clinic visits by 33% per patient compared with the traditional prenatal care paradigm, using equipment and supplies that most obstetric clinics in the United States can access.

Be aware of misdiagnosis---A 21-Year-Old Primipara with Suspected COVID-19.

Fang H, Xingfei P, Yingwei Q, Dunjin C
Int J Gynaecol Obstet

2020 Apr 24; PMID: 32330289
Level of Evidence: 5-Case report
Type of Article: Brief Communication
Summary: A case report of a 21 year old pregnant female in China initially diagnosed with HELLP and pneumonia, suspected of having COVID-19, and eventually diagnosed with H1N1 influenza and Staph Aureus pneumonia.

Considerations for scaling down fetal echocardiograms during the COVID-19 pandemic.

Cardinal MP, Poder TG, Roy-Lacroix ME, Cavallé-Garrido T, Vaujois L, Dallaire F; FREQUENCY study investigators.Cardinal MP, et al.
Can J Cardiol.
2020 Apr 21; PMID: 32330534
Level of Evidence: 5 - Expert Opinion
Article Type: Letter to the Editor
BLUF: This letter highlights evidence that reducing fetal echocardiograms during the COVID-19 pandemic could be done if necessary for patients with a normal 2nd trimester scan without increasing the number of undetected severe congenital heart disease (CHD).

Summary: The authors assess the feasibility of reducing fetal echocardiograms (FE) through presenting the preliminary results of the FREQUENCY study, a retrospective analysis of the performance of prenatal congenital heart disease (CHD) screening in Quebec (Table 1). Based on these findings, the authors estimate that "in the presence of a normal 2nd trimester ultrasound, not performing FE for maternal diabetes, family history of CHD, maternal medication, and increased nuchal translucency would reduce the number of FE by >40%." "From the perspective of the overall population of Quebec, not performing a FE when the 2nd trimester ultrasound is normal would increase the overall number of undetected significant CHD by <0.8 per 10,000 pregnancies." The authors conclude that, if needed, scaling down the number of fetal echocardiograms in patients with a normal 2nd trimester ultrasound could be done without a significant increase in undetected severe CHD.

Table

Indication	Nb of FE (% of all pregnancies referred for a FE)	Moderate to severe CHD		Severe CHD	
		Number	Number needed to screen	Number	Number needed to screen
All FE indications	30,396 (100%)	1,073	28	796	38
FE on fetuses with normal 2nd trimester U/S	12,266 (40%)	55	222	34	361
Family history of CHD	5,646 (19%)	27	209	15	376
Maternal diabetes	4,031 (13%)	19	212	12	336
Medication	853 (3%)	2	426	2	426
Increased nuchal translucency	1,736 (6%)	7	248	5	347
Abnormal cardiac views at the 2nd trimester U/S	3,460 (11%)	694	5	553	6
Suboptimal cardiac images	630 (2%)	31	20	13	48
FE performed before the 2nd trimester scan*	4,387 (14%)	104	42	69	64
Extracardiac malformations	2,740 (9%)	47	58	27	101
All other indications	6,914 (23%)	143	48	100	69

CHD: congenital heart disease, FE: fetal echocardiography
*These FE were referred for high risk pregnancies but were performed before the 2nd trimester scan for various logistical reasons. These were excluded from the analysis as he results of the FE were known to the physicians performing the 2nd trimester scan.

Successful Treatment of Preterm Labor in Association with Acute COVID-19 Infection.

Browne PC, Linfert JB, Perez-Jorge E.Browne PC, et al.
Am J Perinatol.
2020 Apr 24; PMID: 32330970
Level of Evidence: Level 4 - Case study
Type of Article: Research

BLUF: A case report in one female with multiple risk factors for preterm labor and confirmed COVID-19 indicates a 'standard therapy' with IV magnesium sulfate, steroids, and antibiotic prophylaxis for GBS may be safe and effective in terminating preterm previable uterine contractions.

Summary: A case report describing the successful treatment of preterm labor in an 33 y/o African American G1 female, GBS+, pregnant with dichorionic diamniotic twins, and with a h/o asthma and migraine headaches. She developed premature uterine contractions at 23 weeks, 9 days after diagnosis with an acute illness, strongly suspected, and later confirmed to be COVID-19. Her uterine contractions were resolved with 'standard therapy' described above and at the time of the case report the patient was at 27 weeks and had experienced no further contractions

Oncology

Surgical management of bone and soft tissue sarcomas and skeletal metastases during the COVID-19 pandemic.

Cardoso P, Rodrigues-Pinto R.
Eur J Surg Oncol.
2020 Apr 18; PMID: 32331984
Level of Evidence: 5 – Expert Opinion
Type of Article: Letter to the Editor

Summary: The author prioritizes the urgency of various sarcomas and metastases and provides the following recommendations:

- Sarcomas for which surgery is the first or unique curative treatment: high priority even in case of severe resource constraints, especially if delayed treatment may ultimately preclude a limb salvage procedure.
- Sarcoma surgery after neoadjuvant chemotherapy: high priority, independently of the health system constraints.
- Recurrent resectable sarcomas without metastases: high priority, independently of the pandemic level.
- Resectable primitive or recurrent sarcomas with resectable pulmonary metastases: medium priority, consider palliative radio and chemotherapy depending on severity of health system constraint.
- Resectable primitive or recurrent sarcomas with non-resectable pulmonary metastases but expecting a longer survival with combined systemic therapy: medium/low priority, should not be operated in cases of severe or even moderate health system constraints
- Solitary and resectable bone metastases from renal cell carcinoma: medium priority, can be delayed for a short period of time
- Impending or established pathologic fractures of the appendicular skeleton: priority based on morbidity and mortality indicated by fracture location and pattern
- Impending or establish pathologic fractures of the spine: High priority to prevent permanent neurologic impairment

Skin cancer triage and management during COVID-19 pandemic.

Tagliaferri L, Di Stefani A, Schinzari G, Fionda B, Rossi E, Del Regno L, Gentileschi S, Federico F, Valentini V, Tortora G, Peris K
J Eur Acad Dermatol Venereol.
2020 Apr 25; PMID: 32333832
Level of Evidence: 5 - Expert opinion
Type of Article: Letter

Summarizing excerpt: "The worldwide medical community is striving to pursue the most appropriate clinical choices in the worst event of pandemic of the modern times, with over 1 million patients affected by COVID-19 (i.e., swab positive patients with or without symptoms) reported so far. In this context, the aim of the ideal management of cancer patients is to achieve the best possible balance between the two different issues to be considered, which include the risk of cancer progression and the risk of infectious disease."

Ophthalmology

Guidance for anti-VEGF intravitreal injections during the COVID-19 pandemic.

Korobelnik, Jean-Francois; Loewenstein, Anat; Eldem, Bora; Joussen, Antonia M; Koh, Adrian; Lambrou, George N; Lanzetta, Paolo; Li, Xiaoxin; Lovestam-Adrian, Monica; Navarro, Rafael; Okada, Annabelle A; Pearce, Ian; Rodriguez, Francisco J; Wong, David T; Wu, Lihteh
Graefes Arch Clin Exp Ophthalmol
2020 Apr 23; PMID: 32328757
Level of Evidence: 5 - Expert Opinion
Type of Article: Review

BLUF: The 14-member Vision Academy's Steering Committee of International retinal disease experts released recommendations for managing patients with retinal disease who are receiving anti-VEGF intravitreal injections during the COVID-19 pandemic after reviewing existing guidelines and documents. The recommend:

- PPE use
- Adherence to scrupulous hygiene and disinfection protocols
- Pre-screening to identify symptomatic patients
- Reducing waiting room crowding

Abstract:
Purpose: There is an urgent need to address how to best provide ophthalmic care for patients with retinal disease receiving intravitreal injections with anti-vascular endothelial growth factor agents during the ongoing global COVID-19 pandemic. This article provides guidance for ophthalmologists on how to deliver the best possible care for patients while minimizing the risk of infection.
Methods: The Vision Academy's Steering Committee of international retinal disease experts convened to discuss key considerations for managing patients with retinal disease during the COVID-19 pandemic. After reviewing the existing literature on the issue, members put forward recommendations that were systematically refined and voted on to develop this guidance.
Results: The considerations focus on the implementation of steps to minimize the exposure of patients and healthcare staff to COVID-19. These include the use of personal protective equipment, adherence to scrupulous hygiene and disinfection protocols, pre-screening to identify symptomatic patients, and reducing the number of people in waiting rooms. Other important measures include triaging of patients to identify those at the greatest risk of irreversible vision loss and prioritization of

treatment visits over monitoring visits where possible. In order to limit patient exposure, ophthalmologists should refrain from using treatment regimens that require frequent monitoring. Conclusion: Management of patients with retinal disease receiving intravitreal injections during the COVID-19 pandemic will require adjustment to regular clinical practice to minimize the risk of exposure of patients and healthcare staff, and to prioritize those with the greatest medical need. The safety of patients and healthcare staff should be of paramount importance in all decision-making.

Palliative Care

Characteristics and Palliative Care Needs of COVID-19 Patients Receiving Comfort Directed Care

Sun, He; Lee, Jihae; Meyer, Benjamin J; Myers, Ellen L; Nishikawa, Mia S; Tischler, Jonah L; Blinderman, Craig D
J Am Geriatr Soc
2020 Apr 24; PMID: 32329525
Level of Evidence: 4 - Case Series
Type of Article: Letter

Summary: Authors of this case series report upon the characteristics and palliative care needs of 30 patients who were admitted to the Palliative Care Unit (PCU) of Columbia University Irving Medical Center/New York Presbyterian Hospital for severe COVID-19 which they passed from. **Delirium and dyspnea were the most common symptoms which responded to low doses of narcotics and benzodiazepines.** This study also highlighted the need for Chaplain and spiritual support given the degree of isolation from family and loved ones.

Pediatrics

Updated diagnosis, treatment and prevention of COVID-19 in children: experts' consensus statement (condensed version of the second edition).

Shen KL, Yang YH, Jiang RM, Wang TY, Zhao DC, Jiang Y, Lu XX, Jin RM, Zheng YJ, Xu BP, Xie ZD, Liu ZS, Li XW, Lin LK, Shang YX, Shu SN, Bai Y, Lu M, Lu G, Deng JK, Luo WJ, Xiong LJ, Liu M, Cui YX, Ye LP, Li JF, Shao JB, Gao LW, Wang YY, Wang XF; China National Clinical Research Center for Respiratory Diseases; National Center for Children's Health, Beijing, China; Group of Respirology, Chinese Pediatric Society, Chinese Medical Association; Chinese Medical Doctor Association Committee on Respirology Pediatrics; China Medicine Education Association Committee on Pediatrics; Chinese Research Hospital Association Committee on Pediatrics; China Non-government Medical Institutions Association Committee on Pediatrics; China Association of Traditional Chinese Medicine, Committee on Children's Health and Medicine Research; China News of Drug Information Association, Committee on Children's Safety Medication; Global Pediatric Pulmonology Alliance.
World Journal of Pediatrics.
2020 Apr 24; PMID: 32333248.
Level of Evidence: 5 - Literature Review and Expert Consensus
Type of Article: Review

BLUF: This article provides comprehensive clinical information regarding risk factors, clinical presentation, diagnosis, treatment, and prevention for children with SARS-CoV-2.

Summarizing excerpt:
"High-risk children: According to the current accumulated experiences in managing confirmed COVID-19 pediatric patients and experiences from diagnosis and treatment of community-acquired pneumonia in children, children who meet any of the following criteria are at high-risk to become severe or critical cases:

1. Patients with a contact history of cases with severe COVID-19.
2. Patients with underlying diseases, such as congenital heart, lung and airway diseases, chronic heart and kidney diseases, malnutrition, tumors, diabetes, immunodeficiency or hypoimmunity, hereditary metabolic diseases, etc.
3. Patients who are under long-term medication of immunosuppressants.
4. Infants under 3 months.

Early warning indicators for severe or critical diseases are as followings:

1. Increased respiratory rate (RR): > 50 times/min (2–12 months), > 40 times/min (1–5 years), > 30 times/min (> 5 years) (after ruling out the effects of fever and crying).
2. Persistent high fever for 3–5 days, a disease course longer than 1 week, and no improvements in symptoms or signs or progressive exacerbation.
3. With poor mental response, lethargy, etc.
4. Significantly reduced and/or progressively decreased peripheral blood lymphocytes.
5. Progressively increased enzymatic indexes, such as myocardial enzymes, liver enzymes, lactate dehydrogenase.
6. Unexplainable metabolic acidosis.
7. Significantly increased D-dimer, IL-6, IL-10, and ferritin levels.
8. SpO2 ≤ 95% under the resting state.
9. Extrapulmonary complications.
10. Co-infected with other viruses and/or bacteria."

For full list of recommendations, please see original paper.

Abstract:
In the early February, 2020, we called up an experts' committee with more than 30 Chinese experts from 11 national medical academic organizations to formulate the first edition of consensus statement on diagnosis, treatment and prevention of coronavirus disease 2019 (COVID-19) in children, which has been published in this journal. With accumulated experiences in the diagnosis and treatment of COVID-19 in children, we have updated the consensus statement and released the second edition recently. The current version in English is a condensed version of the second edition of consensus statement on diagnosis, treatment and prevention of COVID-19 in children. In the current version, diagnosis and treatment criteria have been optimized, and early identification of severe and critical cases is highlighted. The early warning indicators for severe pediatric cases have been summarized which is utmost important for clinical practice. This version of experts consensus will be valuable for better prevention, diagnosis and treatment of COVID-19 in children worldwide.

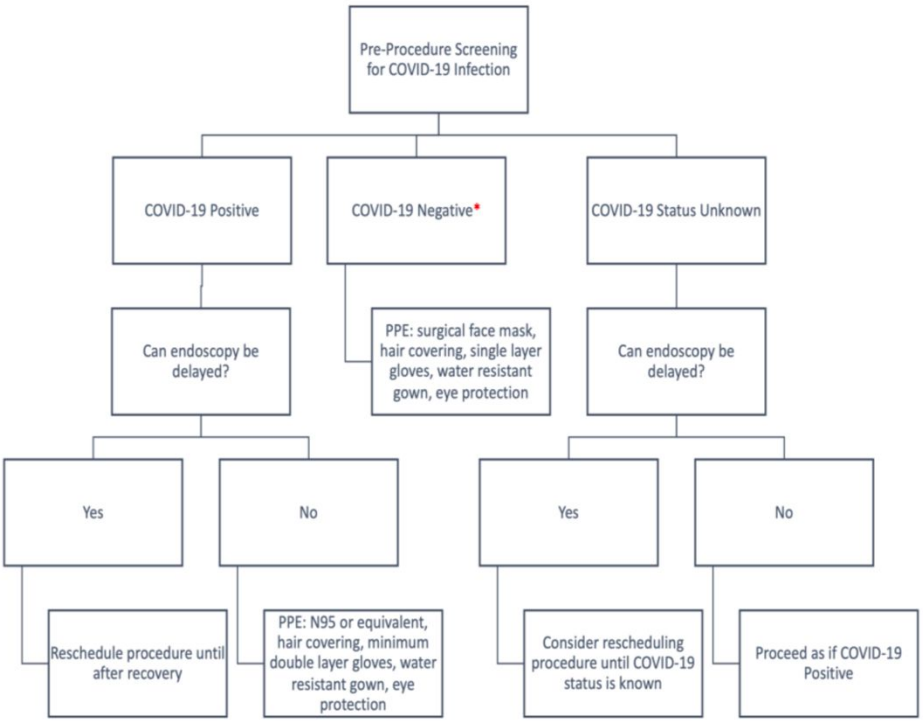
Addendum to: Risk Stratification and PPE Use in Pediatric Endoscopy During the COVID-19 Outbreak: A Single-Center Protocol.

Say DS, de Lorimier A, Lammers CR, Natale J, Lakshminrusimha S, Wiedeman J, Partridge E.
J Pediatr Gastroenterol Nutr.
2020 Apr 22; PMID: 32332323
Level of Evidence: 5 - Expert Opinion
Type of Article: Guidelines

Summary: The authors highlight amendments to their institution's protocol outlined in a previous publication.

- We continue to perform outpatient endoscopic procedures that are deemed "essential" (defined as procedures that, if delayed more than 8 to 12 weeks, could lead to harm or injury).

- All patients are screened for COVID-19 infection within 24 hours of the patient's scheduled procedure.
- Given the possibility of significant logistic difficulties, procedures may be rescheduled or proceed as "COVID-19 status unknown".
- All endoscopic procedures are performed in negative pressure rooms.
- PPE is utilized based on the algorithm below.



Managing Asthma during COVID-19: An Example for Other Chronic Conditions in Children and Adolescents.

Abrams EM, Szefler SJ.
Journal of Pediatrics.
2020 Apr 21; PMID: 32330469
Level of Evidence: 5 - Expert Opinion
Type of Article: Opinion

Summary: Asthma has been shown to increase COVID-19 morbidity and mortality in adults but the risks for children with asthma are unclear. Due to this uncertainty, the authors recommend that "Children and adolescents with asthma should remain on their current asthma medications and practice physical distancing, regular handwashing, and aeroallergen avoidance. **Treatment of asthma exacerbations should include oral corticosteroids if required. Nebulized medications are not recommended at this time due to increased risk of viral transmission.**"

Covid-19 and child disabilities: whom to protect and how.

Trabacca, Antonio; Russo, Luigi

European Journal of Physical Rehabilitation Medicine
2020 Apr 24; PMID: 32329591
Level of Evidence: 5- expert opinion
Type of Article: Letter to the Editor
Summary: In this letter, the author discusses the challenges that children and adolescents with disabilities and their families face in this pandemic due to the restriction of rehabilitation services. There is a need for consideration to be given to this issue, including exploring services such as home-based rehabilitation, telerehabilitation, and telehealth, as possible solutions.

Geriatrics

Development of a telehealth geriatric assessment model in response to the COVID-19 pandemic.

DiGiovanni G, Mousaw K, Lloyd T, Dukelow N, Fitzgerald B, D'Aurizio H, Loh KP, Mohile S, Ramsdale E, Maggiore R, Zittel J, Kadambi S, Magnuson A
J Geriatr Oncol
2020 Apr 17; PMID: 32327321
Level of Evidence: 5- Expert opinion
Type of Article: Guideline
Summary: A geriatric oncology team presents their adaptation of a geriatric assessment to telehealth. The day prior to appointments, a nurse navigator conducts a phone visit to go through relevant screenings. The day of the appointment a HIPAA-compliant teleconferencing platform allows multiple providers in different locations and specialties to come together for a single appointment with the patient and any family members (who can also be physically distant). This paper discusses specific screening and assessment tools chosen for use in this context and considerations such as using voice only appointments to reduce the technologic burden on the patient.

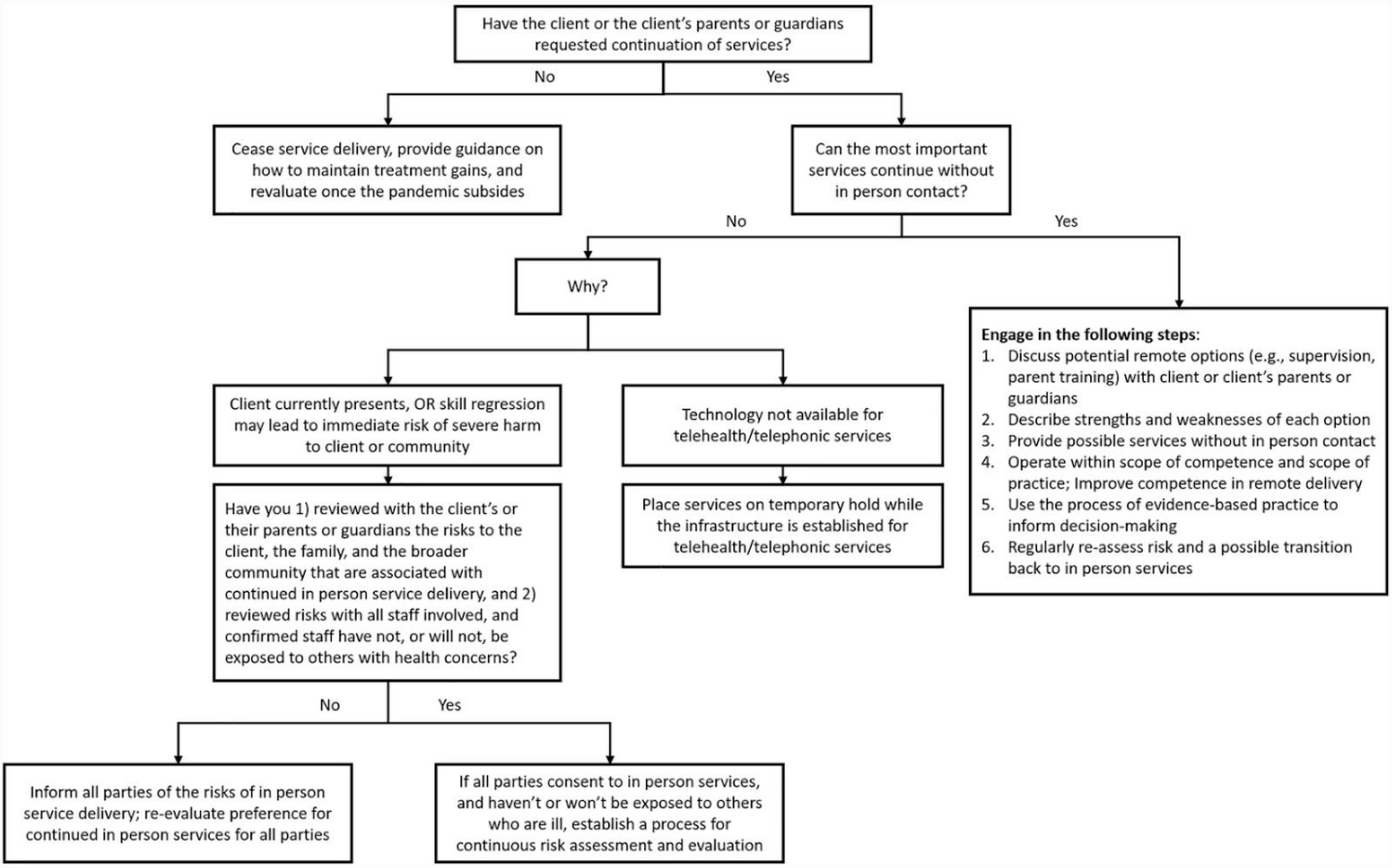
Psychiatry

A Proposed Process for Risk Mitigation During the COVID-19 Pandemic.

Cox DJ, Plavnick JB, Brodhead MT.
Behav Anal Pract
2020 Apr 23, PMID: 32328220
Level of Evidence: 5 - Expert opinion
Type of Article: Discussion and Review
BLUF: The authors argue against universal decisions to continue or postpone applied behavior analysis (ABA) services to patients with autism spectrum disorder and other behavioral difficulties. They instead recommend a case-by-base decision framework or transition to telehealth and other remote service delivery methods to mitigate risk during the COVID-19 pandemic.

Abstract:
Recent executive orders have led some applied behavior analysis (ABA) providers to interpret themselves as "essential personnel" during the COVID-19 pandemic. In this article, we argue against a blanket interpretation that being labeled "essential personnel" means that all in-person ABA services for all clients should continue during the COVID-19 pandemic. We believe this argument holds even if ABA providers are not in a jurisdiction currently under an active shelter-at-home or related order. First, we provide a brief description of risks associated with continued in-person ABA service delivery, as well as risks associated with the temporary suspension of services or the transition to remote ABA service delivery. For many clients, continued in-person service delivery carries a significant risk of severe harm to the client, family and caregivers, staff, and a currently overburdened health care

system. In these situations, ABA providers should temporarily suspend services or transition to telehealth or other forms of remote service delivery until information from federal, state, and local health care experts deems in-person contact safe. In rare cases, temporary suspension of services or a transition to remote service delivery may place the client or others at risk of significant harm. In these situations, in-person services should likely continue, and ongoing assessment and risk mitigation are essential.



A proposed process for risk mitigation during the COVID-19 pandemic

Figure: The author's proposed case-by-case decision framework to decide whether to continue or postpone ABA service delivery

R&D: Diagnosis & Treatments

Current Diagnostics

Guidance for evaluating and testing patients for COVID-19.

Blumberg E.
Am J Transplant.
2020 May; PMID: 32333516
Level of Evidence: 5 – Expert Opinion
Type of Article: Guidelines

Summary: The following are the latest CDC guidance for evaluating and testing patients for COVID-19:

- Priority 1 – focus on the hospital
  - Hospitalized patients
  - Healthcare workers
- Priority 2 – focus on symptomatic individuals at highest risk for complications
  - Patients in long-term care facilities
  - Patients ≥65 years of age
  - Patients with underlying conditions
  - First responders
- Priority 3 – focus on decreasing symptomatic infections in the community
  - Critical infrastructure workers with symptoms
  - Individuals who do not meet any of the above categories with symptoms
  - Healthcare facility workers and first responders

Individuals with mild symptoms in communities experiencing high numbers of COVID-19 hospitalizations

Rapid point-of-care testing for SARS-CoV-2 in a community screening setting shows low sensitivity.

Döhla M, Boesecke C, Schulte B, Diegmann C, Sib E, Richter E, Eschbach-Bludau M, Aldabbagh S, Marx B, Eis-Hübinger AM, Schmithausen RM, Streeck H
Public Health
2020 Apr 13; PMID: 32325421
Level of Evidence: 3 - Randomized cohort
Type of Article: Short Communication

BLUF: The authors tested 39 randomly selected patients (and 10 serum samples from previously diagnosed patients) from a COVID-19 screening center in Germany with both the SARS-CoV-2 rapid test (company not specified) and the RT-PCR test (Altona Diagnostics). They found that 22 patients were confirmed positive by RT-PCR but only 11 patients had a positive serological test. However three of these were deemed false positives when compared with the RT-PCR test. Therefore they determine that the rapid tests are inferior to the RT-PCR tests and should not be relied upon alone.

Abstract:
Objective:With the current SARS-CoV2 outbreak, countless tests need to be performed on potential symptomatic individuals, contacts and travellers. The gold standard is a quantitative polymerase chain reaction (qPCR)ebased system taking several hours to confirm positivity. For effective public health containment measures, this time span is too long. We therefore evaluated a rapid test in a high-prevalence community setting. Study design: Thirty-nine randomly selected individuals at a COVID-19 screening centre were simultaneously tested via qPCR and a rapid test. Ten previously diagnosed individuals with known SARS-CoV-2infection were also analysed. Methods: The evaluated

rapid test is an IgG/IgM based test for SARS-CoV-2 with a time to result of 20 min. Two drops of blood are needed for the test performance. Results: **Of 49 individuals, 22 tested positive by repeated qPCR. In contrast, the rapid test detected only eight of those positive correctly (sensitivity: 36.4%). Of the 27 qPCR-negative individuals, 24 were detected correctly (specificity: 88.9%)**.Conclusion:Given the low sensitivity, **we recommend not to rely on an antibody-based rapid test public health measures such as community screenings.**

Characteristics of Patients with Coronavirus Disease (COVID-19) Confirmed using an IgM-IgG Antibody Test.

Xie J, Ding C, Li J, Wang Y, Guo H, Lu Z, Wang J, Zheng C, Jin T, Gao Y, He H.Xie J, et al.
J Med Virol.
2020 Apr 24; PMID: 32330303
Level of Evidence: 4- Case series
Type of Article: Research

BLUF: Among 56 patients tested for COVID-19, only 16 (28%) had a positive real-time PCR, whereas 49 (87.5%) and 56 (100%) were positive for IgM and IgG antibodies, respectively. This data indicates the potential utility of antibody testing in diagnosis of early COVID-19.

Abstract:
Coronavirus disease (COVID-19), caused by a novel betacoronavirus, SARS-CoV-2, has rapidly developed into a pandemic since it was first reported in December 2019. Nucleic acid testing is the standard method for the diagnosis of viral infections. However, this method reportedly has a low positivity rate. To increase the sensitivity of COVID-19 diagnoses, we developed an IgM-IgG combined assay and tested it in patients with suspected SARS-CoV-2 infection. In total, 56 patients were enrolled in this study and SARS-CoV-2 was detected by using both IgM-IgG antibody and nucleic acid tests. Clinical and laboratory data were collected and analyzed. Our findings suggest that patients who develop severe illness might experience longer virus exposure times and develop a more severe inflammatory response. The IgM-IgG test is an accurate and sensitive diagnostic method. A combination of nucleic acid and IgM-IgG testing is a more sensitive and accurate approach for diagnosis and early treatment of COVID-19.

No. (%)				
	IgM		IgG	
Nucleic acid detection	+	-	+	-
Negative 40 (71.43%)	34 (85%)	6 (15%)	40 (100%)	0
Positive 16 (28.57%)	15 (93.75%)	1 (6.25%)	16 (100%)	0
Total	49 (87.5%)	7 (12.5%)	56 (100%)	0

The data are presented as No. (%). No. is the number of patients with available data.

Table 1. Comparison of IgM-IgG antibodies with nucleic acid test

Connecting clusters of COVID-19: an epidemiological and serological investigation.

Yong SEF, Anderson DE, Wei WE, Pang J, Chia WN, Tan CW, Teoh YL, Rajendram P, Toh MPHS, Poh C, Koh VTJ, Lum J, Suhaimi NM, Chia PY, Chen MI, Vasoo S, Ong B, Leo YS, Wang L, Lee VJM
Lancet Infect Dis
2020 Apr 21; PMID: 32330439
Level of Evidence: 3 - Cluster Study
Type of Article: Research

BLUF: The authors of this study stress the importance of serological (Elisa IgG) testing for COVID-19 in addition to PCR testing in regard to disease containment efforts by explaining how three geographical clusters of 28 locally transmitted COVID-19 cases were linked in a similar region in Singapore. They demonstrate how the individual in question (A2, see image below) had a negative PCR test, but subsequent positive serological test (Elisa IgG) which ultimately linked this individual to all three clusters.

Abstract:
Background: Elucidation of the chain of disease transmission and identification of the source of coronavirus disease 2019 (COVID-19) infections are crucial for effective disease containment. We describe an epidemiological investigation that, with use of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) serological assays, established links between three clusters of COVID-19.
Methods: In Singapore, active case-finding and contact tracing were undertaken for all COVID-19 cases. Diagnosis for acute disease was confirmed with RT-PCR testing. When epidemiological information suggested that people might have been nodes of disease transmission but had recovered from illness, SARS-CoV-2 IgG serology testing was used to establish past infection.
Findings: Three clusters of COVID-19, comprising 28 locally transmitted cases, were identified in Singapore; these clusters were from two churches (Church A and Church B) and a family gathering. The clusters in Church A and Church B were linked by an individual from Church A (A2), who transmitted SARS-CoV-2 infection to the primary case from Church B (F1) at a family gathering they both attended on Jan 25, 2020. All cases were confirmed by RT-PCR testing because they had active disease, except for A2, who at the time of testing had recovered from their illness and tested negative. This individual was eventually diagnosed with past infection by serological testing. ELISA assays showed an optical density of more than 1·4 for SARS-CoV-2 nucleoprotein and receptor binding domain antigens in titres up to 1/400, and viral neutralisation was noted in titres up to 1/320.
Interpretation: Development and application of a serological assay has helped to establish connections between COVID-19 clusters in Singapore. Serological testing can have a crucial role in identifying convalescent cases or people with milder disease who might have been missed by other surveillance methods.

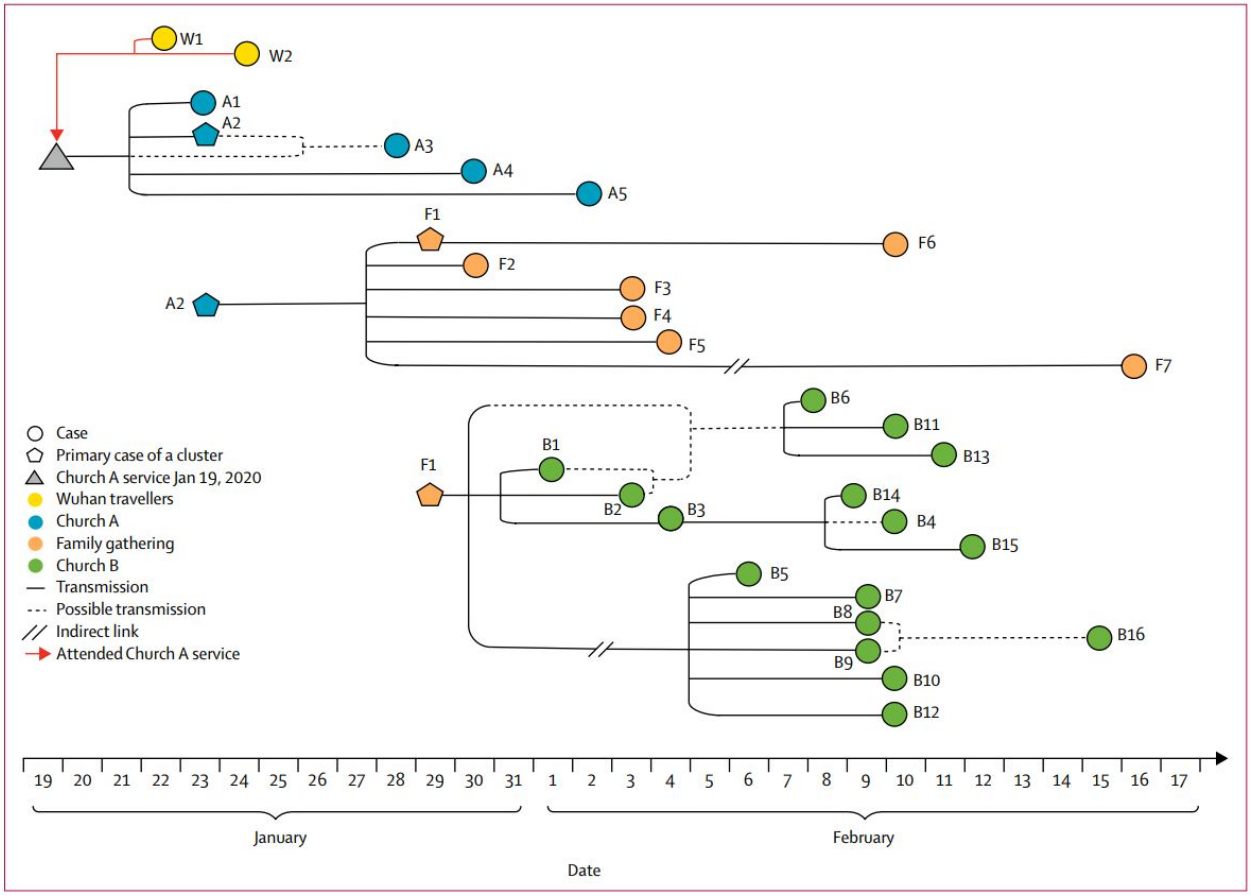


Figure 1: Transmission map of COVID-19 Map shows how COVID-19 was linked to two travellers from Wuhan, China, and two church clusters and a family gathering in Singapore. COVID-19=coronavirus disease 2019.

Diagnostic accuracy of an automated chemiluminescent immunoassay for anti-SARS-CoV-2 IgM and IgG antibodies: an Italian experience.

Infantino M, Grossi V, Lari B, Bambi R, Perri A, Manneschi M, Terenzi G, et al.

J Med Virol.

2020 Apr 24; PMID: 32330291

Level of Evidence: 3 - Nonrandomized control study

Type of Article: Prospective nonrandomized control study

BLUF: This prospective study assessed which antibodies are optimally effective in determining the laboratory diagnosis of COVID-19. The **highest sensitivity and specificity was reached at a cutoff of 10.0 AU/mL for IgM (PPV 81.5%, NPV 88.1%) and of 7.1 for IgG (PPV 100%, NPV 92.8)**. At the cutoff value of 10 AU/mL, **sensitivity was 73.3% and 76.7%** and **specificity was 92.2% and 100%** for IgM and IgG antibodies, respectively.

Abstract:

Background: A pandemic of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been spreading throughout the world. Though molecular diagnostic tests are the gold standard for COVID-19, serological testing is emerging as a potential surveillance tool, in addition to its complementary role in COVID-19 diagnostics. Indubitably quantitative serological testing provides greater advantages than qualitative tests but today there is

still little known about serological diagnostics and what the most appropriate role quantitative tests might play.
Methods: Sixty-one COVID-19 patients and 64 patients from a control group were tested by iFlash1800 CLIA analyzer for anti-SARS CoV-2 antibodies IgM and IgG. All COVID-19 patients were hospitalized in San Giovanni di Dio Hospital (Florence, Italy) and had a positive oro/nasopharyngeal swab RT-PCR result.
Results: **The highest sensitivity with a very good specificity performance was reached at a cutoff value of 10.0 AU/mL for IgM and of 7.1 for IgG antibodies,** hence near to the manufacturer's cutoff values of 10 AU/mL for both isotypes. **The ROC performance curves showed area under the curve (AUC) values of 0.918 and 0.980 for anti-SARS CoV-2 antibodies IgM and IgG, respectively.**
Conclusions: iFlash1800 CLIA analyzer has shown highly accurate results for the anti-SARS-CoV-2 antibodies profile and can be considered an excellent tool for COVID-19 diagnostics.

COVID-19: a meta-analysis of diagnostic test accuracy of commercial assays registered in Brazil.

Castro R, Luz PM, Wakimoto MD, Veloso VG, Grinsztejn B, Perazzo H
Braz J Infect Dis
2020 Apr 18; PMID: 32330437
Level of Evidence: 4 - Meta analysis of Manufacturer Data
Type of Article: Research
BLUF: A meta analysis of specificity, sensitivity and other metrics of currently available COVID-19 tests in Brazil including viral antigen, RNA, IgM and IgG. The analysis relies on data provided by test manufacturers as peer reviewed publications are currently lacking. Also, the authors acknowledge the studies reviewed do not provide patient characteristics or time of sample collection after symptomatic onset, and they call for more evidence-based validation of diagnostic tests. They study found that the pooled sensitivity of tests using the detection of COVID-19 IgM antibodies in blood was lower compared to antigen/molecular assay detection in nasopharyngeal/oropharyngeal swabs (82% [95%CI 76–87] vs 97% [95%CI 85–99]).

Abstract:
The accuracy of commercially available tests for COVID-19 in Brazil remains unclear. We aimed to perform a meta-analysis to describe the accuracy of available tests to detect COVID-19 in Brazil. We searched at the Brazilian Health Regulatory Agency (ANVISA) online platform to describe the pooled sensitivity (Se), specificity (Sp), diagnostic odds ratio (DOR) and summary receiver operating characteristic curves (SROC) for detection of IgM/IgG antibodies and for tests using naso/oropharyngeal swabs in the random-effects models. We identified 16 tests registered, mostly rapid-tests. Pooled diagnostic accuracy measures [95%CI] were: (i) for IgM antibodies Se=82% [76-87]; Sp=97% [96-98]; DOR=168 [92-305] and SROC=0.98 [0.96-0.99]; (ii) for IgG antibodies Se=97% [90-99]; Sp=98% [97-99]; DOR=1994 [385-10334] and SROC=0.99 [0.98-1.00]; and (iii) for detection of SARS-CoV-2 by antigen or molecular assays in naso/oropharyngeal swabs Se=97% [85-99]; Sp=99% [77-100]; DOR=2649 [30-233056] and SROC=0.99 [0.98-1.00]. These tests can be helpful for emergency testing during the COVID-19 pandemic in Brazil. However, it is important to highlight the high rate of false negative results from tests which detect SARS-CoV-2 IgM antibodies in the initial course of the disease and the scarce evidence-based validation results published in Brazil.

Future studies addressing the diagnostic performance of tests for COVID-19 in the Brazilian population are urgently needed.

Point of care and intensive care lung ultrasound: A reference guide for practitioners during COVID-19.

Moore S, Gardiner E.
Radiography (Lond).
2020 Apr 17; PMID: 32327383
Level of Evidence: Level 5 - Expert opinion
Type of Article: Guidance

BLUF: Ultrasound has high sensitivity for many markers of COVID-19 disease process and lung condition, but very poor specificity in relation to the virus. Therefore ultrasound should not be used as a diagnostic tool for COVID-19 but is an excellent tool for point-of-care and ICU (ITU) settings.

Abstract

Objectives: Current events with the recent COVID-19 outbreak are necessitating steep learning curves for the NHS workforce. Ultrasound, although not used in the diagnosis of COVID-19 may be utilised by practitioners at the point of care (POC) or on the intensive care units (ITUs) where rapid assessment of the lung condition may be required. **The aim of this article was to review current literature surrounding the use of lung ultrasound in relation to COVID-19 and provide Sonographers with a quick and digestible reference guide for lung pathologies.**

Key findings: Ultrasound is being used in Italy and China to help review lung condition during the COVID-19 outbreak however not strictly as a diagnostic tool as Computed Tomography (CT) of the chest and chest radiographs are currently gold standard. Ultrasound is highly sensitive in the detection of multiple lung pathologies which can be demonstrated in conjunction with COVID-19 however to date there are no specific, nor pathognomonic findings which relate to COVID-19 on ultrasound.

Conclusion: **Lung ultrasound is highly sensitive and can quickly and accurately review lung condition** creating potential to assess for changes or resolution over time, especially in the ITU and POC setting. **However it should not be used as a diagnostic tool for COVID-19 due to low specificity in relation to the virus.**

Implications for practice: The adoption of lung ultrasound to monitor lung condition during the COVID-19 outbreak may **reduce the need for serial exposure to ionising radiation** on the wards and in turn reduce the number of radiographers required to attend infected wards and bays, protecting both patients and the workforce.

Point-of-Care Lung Ultrasound Findings in Patients with Novel Coronavirus Disease (COVID-19) Pneumonia.

Yasukawa K, Minami T.
Am J Trop Med Hyg.
2020 Apr 24; PMID: 32333544
Level of Evidence: Level 4 - cohort study
Type of Article: Research

BLUF: In this small retrospective study, all 10 COVID-19 patients had characteristic glass rockets with or without the Birolleau variant (white lung) on ultrasound, as well as thick irregular pleural lines and confluent B lines. There are many advantages to using point-of-care ultrasound to diagnose and monitor COVID-19, but more robust studies are necessary.

Abstract: Patients with novel coronavirus disease (COVID-19) typically present with bilateral multilobar ground-glass opacification with a peripheral distribution. The utility of point-of-care ultrasound has been suggested, but detailed descriptions of lung ultrasound findings are not available. We evaluated lung ultrasound findings in 10 patients admitted to the internal medicine ward with COVID-19. **All of the patients had characteristic glass rockets with or without the Birolleau variant (white lung). Thick irregular pleural lines and confluent B lines were also present in all of the patients**. Five of the 10 patients had small subpleural consolidations. Point-of-care lung ultrasound has multiple advantages, including lack of radiation exposure and repeatability. **Also, lung ultrasound has been shown to be more sensitive than a chest radiograph in detecting alveolar-interstitial syndrome.** The utilization of lung ultrasound may also reduce exposure of healthcare workers to severe acute respiratory syndrome-coronavirus-2 and may mitigate the shortage of personal protective equipment. Further studies are needed to evaluate the utility of lung ultrasound in the diagnosis and management of COVID-19.

Who should perform the rhinopharyngeal swab in COVID-19 positive patients?

De Virgilio A, Pellini R, Mercante G, Ferreli F, Petruzzi G, Spriano G
Head Neck
2020 Apr 24; PMID: 32329138
Level of Evidence: 5- Expert opinion
Type of Article: Letter
Summary: The authors cite the high false negative rates of nasopharyngeal swabs and even higher false negative rate of oropharyngeal swabs at detecting SARS-CoV-2 to argue that **ENT support and the use of endoscopes could improve our detection of the virus**. They worry that the high prevalence of nasal septal deviation may be impacting the ability to truly reach the nasopharynx without expert support.

Coronavirus (COVID-19) Assessments and the Importance of Calculating the Probability of Illness.

Stovitz SD.Stovitz SD.
Med Sci Educ.
2020 Apr 22; PMID: 32328341
Level of Evidence: 5 - Expert Opinion
Type of Article: Commentary
Summary: Calculations of NPV and PPV based on sensitivity and specificity will be useful in guiding clinicians' decisions for COVID-19 patients-e.g. when to quarantine. Increases in the sensitivity of COVID-19 virus screening tools and the changing prevalence of COVID-19 will affect these calculations.

Clinical Pathway for Early Diagnosis of COVID-19: Updates from Experience to Evidence-Based Practice.

Xu G, Yang Y, Du Y, Peng F, Hu P, Wang R, Yin M, Li T, Tu L, Sun J, Jiang T et al.
Clin Rev Allergy Immunol.
2020 Apr 24; .PMID: 32328954
Level of Evidence: 5 - No Evidence Provided
Type of Article: Review
BLUF: The authors of this article stress the importance of developing a diagnostic strategy to establish control of the virus. The authors highlight the hallmark features of COVID-19 include high

fever, cough, fatigue, and progression to ARDS. Lab findings include high D-dimer, procalcitonin, CRP levels, lymphopenia and eosinopenia. Finally, imaging generally shows ground glass opacities.

Abstract: The COVID-19 pandemic is a significant global event in the history of infectious diseases. The SARS-CoV-2 appears to have originated from bats but is now easily transmissible among humans, primarily through droplet or direct contact. Clinical features of COVID-19 include high fever, cough, and fatigue which may progress to ARDS. Respiratory failure can occur rapidly after this. The primary laboratory findings include lymphopenia and eosinopenia. Elevated D-dimer, procalcitonin, and CRP levels may correlate with disease severity. Imaging findings include ground-glass opacities and patchy consolidation on CT scan. Mortality is higher in patients with hypertension, cardiac disease, diabetes mellitus, cancer, and COPD. Elderly patients are more susceptible to severe disease and death, while children seem to have lower rates of infection and lower mortality. Diagnostic criteria and the identification of persons under investigation have evolved as more data has emerged. However, the approach to diagnosis is still very variable from region to region, country to country, and even among different hospitals in the same city. The importance of a clinical pathway to implement the most effective and relevant diagnostic strategy is of critical importance to establish the control of this virus that is responsible for more and more deaths each day.

Developments in diagnostics

Highly sensitive detection of SARS-CoV-2 RNA by multiplex rRT-PCR for molecular diagnosis of COVID-19 by clinical laboratories.

Ishige T, Murata S, Taniguchi T, Miyabe A, Kitamura K, Kawasaki K, Nishimura M, Igari H, Matsushita K
Clin Chim Acta
2020 Apr 23; PMID: 32335089
Level of Evidence: 3 - Case-control
Type of Article: Letter to the editor

BLUF: Authors describe their multiplex rRT-PCR test for COVID-19 allowing for the detection of two SARS-CoV-2 genes (E and N) as well as the human ABL1 gene as an internal control. They test their multiplex rRT-PCR method on only 24 clinical samples but indicate that their test is at least as good as the current rRT-PCR test and suggest it is highly sensitive.

Abstract:
Background: The detection of SARS-CoV-2 RNA by real-time reverse transcription–polymerase chain reaction (rRT-PCR) is used to confirm the clinical diagnosis of COVID-19 by molecular diagnostic laboratories. We developed a multiplex rRT-PCR methodology for the detection of SARS-CoV-2 RNA.
Methods:Three genes were used for multiplex rRT-PCR: the *Sarbecovirus* specific E gene, the SARS-CoV-2 specific N gene, and the human *ABL1* gene as an internal control.
Results: Good correlation of Cq values was observed between the simplex and multiplex rRT-PCR methodologies. Low copies (<25 copies/reaction) of SARS-CoV-2 RNA were detected by the novel multiplex rRT-PCR method.
Conclusion: The proposed multiplex rRT-PCR methodology will enable highly sensitive detection of SARS-CoV-2 RNA, reducing reagent use and cost, and time required by clinical laboratory technicians.

Reliability and usefulness of a rapid IgM-IgG antibody test for the diagnosis of SARS-CoV-2 infection: a preliminary report.

Spicuzza L, Montineri A, Manuele R, Crimi C, Pistorio MP, Campisi R, Vancheri C, Crimi N
J Infect

2020 Apr 23; PMID: 32335175
Level of Evidence: 3 - Non-randomized case-control
Type of Article: Letter to the editor

Summary: The authors examine 30 patients in Italy [put into two groups: confirmed (n =23) or suspected (n =7) cases] and seven healthy controls (Azienda UO Policlinico-San Marco, Catania) and use the 2019-nCoV IgG/IgM Antibody Rapid Test Kit (Beijing Diagreat Biotechnologies Co., Ltd), which is a rapid serological test. Their "preliminary data suggest that the rapid IgG/IgM test is reliable in evidencing seroconversion as long as the testing is not performed <6 days before symptoms onset." They suggest that this test could be used in conjunction with standard RT-PCR testing and chest CT scans but is not suitable for detecting all cases, particularly early during the infection with patients are unlikely to have seroconverted.

Early chest computed tomography to diagnose COVID-19 from suspected patients: A multicenter retrospective study.

Miao C, Jin M, Miao L, Yang X, Huang P, Xiong H, Huang P, Zhao Q, Du J, Hong J.
Am J Emerg Med.
2020 Apr 19; PMID: 32327245
Level of Evidence: 4 - Retrospective Cohort Study
Type of Article: Research

BLUF: A multicenter retrospective study conducted at three tertiary hospitals of two provinces in China during 1/12/20 – 2/13/20 found that combination of CT findings of ground-glass opacities (GGO) with numerous other features were highly specific to COVID-19 patients, compared to those of patients without COVID-19. Thus, suggesting these GGO combinations could be useful in the identification and differential diagnosis of COVID-19.

Abstract:
Objective: The purpose of this study was to distinguish the imaging features of COVID-19 from those of other infectious pulmonary diseases and evaluate the diagnostic value of chest CT for suspected COVID-19 patients.
Methods: Adult patients suspected of COVID-19 aged N18 years who underwent chest CT scans and reverse- transcription polymerase chain reaction (RT-PCR) tests within 14 days of symptom onset were enrolled. The enrolled patients were confirmed and grouped according to the results of the RT-PCR tests. The basic demographics, single chest CT features, and combined chest CT features were analyzed for the confirmed and nonconfirmed *(sic)* groups.
Results: A total of 130 patients were enrolled, with 54 testing positive and 76 testing negative. The typical CT imaging features of the positive group were ground glass opacities (GGOs), the crazy-paving pattern and air bronchogram. The lesions were mostly distributed bilaterally and close to the lower lungs or the pleura. When features were combined, GGOs with bilateral pulmonary distribution and GGOs with pleural distribution were more common among the positive patients, found in 31 (57.4%) and 30 patients (55.6%), respectively. The combinations were almost all statistically significant (P<.05), except for the combination of GGOs with consolidation. Most combinations presented relatively low sensitivity but extremely high specificity. The average specificity of these combinations was approximately 90%.
Conclusions: The combinations with GGOs could be useful in the identification and differential diagnosis of COVID-19, alerting clinicians to isolate patients for prompt treatment and repeat RT-PCR tests until the end of incubation.

Table 4
Combined CT imaging features between positive group and negative group.

Combined features	Positive group n = 54	Negative group n = 76	*P*
GGO + Consolidation	11(20.4%)	8(10.5%)	0.12
GGO+ Crazy-paving pattern	16(29.6%)	3(3.9%)	<0.01
GGO + Air bronchogram	14(15.9%)	4(5.3%)	<0.01
GGO + Bilateral pulmonary distribution	31(57.4%)	15(19.7%)	<0.01
GGO + Bilateral lower pulmonary distribution	21(38.9%)	8(10.5%)	<0.01
GGO + Peripleural distribution	30(55.6%)	16(21.1%)	<0.01
GGO + Bilateral lower pulmonary distribution+Peripleural distribution	17(31.5%)	5(6.6%)	<0.01
GGO + Bilateral pulmonary distribution+Peripleural distribution	26(48.1%)	8(10.5%)	<0.01
GGO + Crazy-paving pattern+Peripleural distribution	12(22.2%)	3(3.9%)	<0.01
GGO + Air bronchogram +Peripleural distribution	11(20.4%)	2(2.6%)	<0.01
GGO + Crazy-paving pattern+Bilateral lower pulmonary distribution	11(20.4%)	1(1.3%)	<0.01
GGO + Air bronchogram+Bilateral lower pulmonary distribution	8(14.8%)	1(1.3%)	<0.01
GGO + Bilateral pulmonary distribution+Crazy-paving Pattern+ Pleural distribution	12(22.2%)	2(2.6%)	<0.01
GGO + bilateral pulmonary distribution+Air bronchogram+ Peripleural distribution	10(18.5%)	1(1.3%)	<0.01
GGO + Bilateral lower pulmonary distribution+Crazy-paving pattern+Peripleural distribution	9(16.7%)	1(1.3%)	<0.01
GGO + Bilateral lower pulmonary distribution+Air bronchogram +Peripleural distribution	6(11.1%)	1(1.3%)	0.02

GGO, ground glass opacity.

Table 5
The diagnostic value of combined CT imaging features between positive group and negative group.

Combined features	Sensitivity	Specificity
GGO+ Crazy-paving pattern	0.30	0.96
GGO + Air bronchogram	0.26	0.95
GGO + Bilateral pulmonary distribution	0.57	0.81
GGO + Bilateral lower pulmonary distribution	0.39	0.89
GGO + Peripleural distribution	0.57	0.79
GGO + Bilateral lower pulmonary distribution+Peripleural distribution	0.31	0.93
GGO + Bilateral pulmonary distribution+Peripleural distribution	0.48	0.89
GGO + Crazy-paving pattern+Peripleural distribution	0.22	0.96
GGO + Air bronchogram +Peripleural distribution	0.20	0.97
GGO + Crazy-paving pattern+Bilateral lower pulmonary distribution	0.20	0.99
GGO + Air bronchogram+Bilateral lower pulmonary distribution	0.15	0.99
GGO + Bilateral pulmonary distribution+Crazy-paving Pattern+ Peripleural distribution	0.22	0.97
GGO + bilateral pulmonary distribution+Air bronchogram+ Peripleural distribution	0.19	0.99
GGO + Bilateral lower pulmonary distribution+Crazy-paving pattern+Peripleural distribution	0.17	0.99
GGO + Bilateral lower pulmonary distribution+Air bronchogram +Peripleural distribution	0.11	0.99

GGO, ground glass opacity.

Rapid and sensitive detection of anti-SARS-CoV-2 IgG using lanthanide-doped nanoparticles-based lateral flow immunoassay

Zhenhua Chen, Zhigao Zhang, Xiangming Zhai, Yongyin Li, Li Lin, Hui Zhao, Lun Bian, Peng Li, Lei Yu, Yingsong Wu, Guanfeng Lin
Anal Chem
2020 Apr 23; PMID: 32323974
Level of Evidence: 5 - Mechanism Based Reasoning
Type of Article: Research

BLUF: Researchers detail a new immunodiagnostic method for COVID-19, testing their assay against 51 normal samples (detected negative), seven positive samples (detected positive), and 12 that were clinically suspicious for COVID-19 and were negative in RT-PCR (detected positive but is postulated that RT-PCR labeled these as false negatives), samples obtained from Guangzhou province in China. These results lead them to believe this assay can allow for sensitive detection of anti-SARS-CoV-2 IgG.

Abstract:
The outbreak of 2019 coronavirus disease (COVID-19) has been a challenge for hospital laboratories because of the huge number of samples that must be tested for the presence of the causative pathogen, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Simple and rapid immunodiagnostic methods are urgently needed to identify positive cases. Here we report the development of a rapid and sensitive lateral flow immunoassay (LFIA) that uses lanthanide-doped polystyrene nanoparticles (LNPs) to detect anti-SARV-CoV-2 IgG in human serum. A recombinant nucleocapsid phosphoprotein of SARS-CoV-2 was dispensed onto a nitrocellulose membrane to capture specific IgG. Mouse anti-human IgG antibody was labeled with self-assembled LNPs that served as a fluorescent reporter. A 100-μl aliquot of serum samples (1:1000 dilution) was used for this assay and the whole detection process took 10 min. The results of the validation experiment met the requirements for clinical diagnostic reagents. A value of 0.0666 was defined as the cutoff value by assaying 51 normal samples. We tested 7 samples that were positive by reverse-transcription (RT-)PCR and 12 that were negative but clinically suspicious for the presence of anti-SARS-CoV-2 IgG. One of the negative samples was determined to be SARS-CoV-2 IgG positive, while the results for the other samples were consistent with those obtained by RT-PCR. **Thus, this assay can achieve rapid and sensitive detection of anti-SARS-CoV-2 IgG in human serum and allow positive identification in suspicious cases; it can also be useful for monitoring the progression COVID-19 and evaluating patients' response to treatment.**

RT-LAMP for rapid diagnosis of coronavirus SARS-CoV-2.

Huang WE, Lim B, Hsu C, Xiong D, Wu W, Yu Y, Jia H, Wang Y, Zeng Y, Ji M, Chang H, Zhang X, Wang H, Cui Z
Microb Biotechnol.
2020 Apr 25; PMID: 32333644
Level of Evidence: 5 - Mechanism-based reasoning
Type of Article: Research
BLUF: The authors tested a reverse transcription-loop-mediated isothermal amplification (RT-LAMP) to detect SARS-CoV-2 in 30 minutes, with sensitivity to 80 copies of viral RNA per ml in a sample. The test results were consistent with conventional RT-qPCR and the authors demonstrated that a one-step process without RNA extraction is feasible.

Abstract: The pandemic coronavirus SARS-CoV-2 in the world has caused a large infected population suffering from COVID-19. To curb the spreading of the virus, WHO urgently demanded an extension of screening and testing; thus, a rapid and simple diagnostic method is needed. We applied a reverse transcription-loop-mediated isothermal amplification (RT-LAMP) to **achieve the detection of SARS-CoV-2 in 30 min**. We designed four sets of LAMP primers (6 primers in each set), targeting the viral RNA of SARS-CoV-2 in the regions of orf1ab, S gene and N gene. A colorimetric change was used to report the results, which enables the outcome of viral RNA amplification to be read by the naked eye without the need of expensive or dedicated instrument. The **sensitivity can be 80 copies of viral RNA per ml** in a sample. We validated the RT-LAMP method in a hospital in China, employing 16 clinic samples with 8 positives and 8 negatives. The testing results are consistent with the conventional RT-qPCR. In addition, we also show that one-step process without RNA extraction is feasible to achieve RNA amplification directly from a sample. This **rapid, simple and sensitive RT-LAMP method paves a way for a large screening** at public domain and hospitals, particularly regional hospitals and medical centres in rural areas.

Salivary diagnostics in COVID-19: Future research implications.

Vinayachandran D, Saravanakarthikeyan B.
J Dent Sci.
2020 Apr 23; PMID: 32328218
Level of Evidence: 5 - Expert Opinion
Type of Article: Commentary
Summary: SARS-CoV-2 can be detected in saliva samples from COVID-19 patients; thus, it is recommended that research be aimed towards developing noninvasive **diagnostic modalities using saliva**. Animal studies have shown that **ACE2 epithelial cells**, which are abundant in the oral mucosa, are the initial target of SARS-CoV; ACE2 cells should be investigated for their potential to harbor **latent COVID-19 infection**.

Continuous temperature monitoring by a wearable device for early detection of febrile events in the SARS-CoV-2 outbreak in Taiwan, 2020.

Chung YT, Yeh CY, Shu YC, Chuang KT, Chen CC, Kao HY, Ko WC, Chen PL, Ko NY.Chung YT, et al.
J Microbiol Immunol Infect.
2020 Apr 13; PMID: 32331981
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter
Summarizing Statement: "The HEARThermo, as **a wearable physiological monitor**...provides real-time data and decision support for healthcare providers and public health agencies. Our data suggest the application [of] the innovative wearable device in **continuous monitoring of body temperature with heart rate variation may be a solution in provision of early detection and point-of-care for suspected cases,** in response to the COVID-19 pandemic."

COVID-19 rapid antibody cassette point of care tests: practical considerations

Tomasik P, Krótki F, Jońca M, Anyszek T.
Pol Arch Intern Med.
2020 Apr 24; .PMID: 32329979
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter
Summary: Many companies are currently producing **rapid antibody cassette point of care (POC) testing** for COVID-19, which are cheaper than molecular diagnostics, although there are disclaimers that the tests should be **used as adjuvants**, rather than the sole predictor, for diagnosis. A limitation is that the test cannot detect early or mid-phase infection. POC testing may be useful in **epidemiological monitoring of immunocompetent status and viral reservoirs.**

The important role of serology for COVID-19 control.

Winter AK, Hegde ST
Lancet Infect Dis.
2020 Apr 21; PMID: 32330441
Level of Evidence: 5 - expert opinion
Type of Article: Comment
Summarizing Excerpt: "Serological assays are currently being developed for widespread use. Yet, several challenges remain: first, assessing the sensitivity and specificity of tests, particularly for determining disease during the acute phase of infection; second, verifying the test is not detecting

cross-reactivity with other viral pathogens that result in false-positive results; third, understanding antibody kinetics over time to distinguish thresholds of immunity, because we do not know how long immunity to this novel coronavirus might last; and finally, ensuring the test is reliable for distribution and is cost-efficient."

Screening FMT donors during the COVID-19 pandemic: a protocol for stool SARS-CoV-2 viral quantification.

Ng SC, Chan FKL, Chan PKS
Lancet Gastroenterol Hepatol
2020 Apr 22; PMID: 32333844
Level of Evidence: 3- Case-Control Study
Type of Article: Letter

Summary: The authors put forth their own screening protocol to test for SARS-CoV-2 prior to fecal microbiota transplants (FMT) that uses a questionnaire and a RT-PCR test (with an estimated turnaround time of 3 hours) to identify high risk fecal donors. To validate the assay they used stool samples obtained from either confirmed SARS-CoV-2 cases (81 total samples, 21 total patients) or healthy controls (114 total samples, 114 total patients) returning from high risk areas. All 21 PCR confirmed cases also tested positive in their stool samples, while none of the stool samples from healthy controls were positive for SARS-CoV-2. They suggest that donor fecal samples should be tested multiple times prior to FMT.

Developments in Treatments

Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection: A Randomized Clinical Trial.

Borba MGS, Val FFA, Sampaio VS, Alexandre MAA, Melo GC, Brito M, Mourão MPG, Brito-Sousa JD, Baía-da-Silva D, Guerra MVF, Hajjar LA, Pinto RC, Balieiro AAS, Pacheco AGF, Santos JDO Jr, Naveca FG, Xavier MS, Siqueira AM, Schwarzbold A, Croda J, Nogueira ML, Romero GAS, Bassat Q, Fontes CJ, Albuquerque BC, Daniel-Ribeiro CT, Monteiro WM, Lacerda MVG; CloroCovid-19 Team.
JAMA Netw Open.
2020 Apr 24; PMID: 32330277
Level of Evidence: 2 – Randomized Controlled Trial with blinding
Type of Article: Research

BLUF: This parallel, double-masked clinical trial conducted from 3/23/2020 – 4/5/2020 at a hospital in Manaus, Western Brazilian Amazon investigated safety and lethality outcomes in 81 patients with suspected COVID-19 and severe acute respiratory syndrome who were either treated with high dose or low dose chloroquine diphosphate. They found elevated CK (7/14 [50.0%] vs 6/19 [31.6%]) and QTcF prolongation (7/37 [18.9%] vs 4/36 [11.1%]) more frequently in the high-dosage group than the low-dosage group. Lethality was higher in the high-dosage (16/41 [39.0%]) than the low-dosage group (6/40 [15.0%]). Therefore, dosages of CQ as high as 12g given for 10 days should no longer be used for the treatment of severe COVID-19.

Abstract:
Importance: There is no specific antiviral therapy recommended for coronavirus disease 2019 (COVID-19). In vitro studies indicate that the antiviral effect of chloroquine diphosphate (CQ) requires a high concentration of the drug.
Objective: To evaluate the safety and efficacy of 2 CQ dosages in patients with severe COVID-19.
Design, Setting, and Participant: This parallel, double-masked, randomized, phase IIb clinical trial with 81 adult patients who were hospitalized with severe acute respiratory syndrome coronavirus 2

(SARS-CoV-2) infection was conducted from March 23 to April 5, 2020, at a tertiary care facility in Manaus, Brazilian Amazon.
Interventions: Patients were allocated to receive high-dosage CQ (ie, 600 mg CQ twice daily for 10 days) or low-dosage CQ (ie, 450 mg twice daily on day 1 and once daily for 4 days).
Main Outcomes and Measures: Primary outcome was reduction in lethality by at least 50% in the high-dosage group compared with the low-dosage group. Data presented here refer primarily to safety and lethality outcomes during treatment on day 13. Secondary end points included participant clinical status, laboratory examinations, and electrocardiogram results. Outcomes will be presented to day 28. Viral respiratory secretion RNA detection was performed on days 0 and 4.
Results: Out of a predefined sample size of 440 patients, 81 were enrolled (41 [50.6%] to high-dosage group and 40 [49.4%] to low-dosage group). Enrolled patients had a mean (SD) age of 51.1 (13.9) years, and most (60 [75.3%]) were men. Older age (mean [SD] age, 54.7 [13.7] years vs 47.4 [13.3] years) and more heart disease (5 of 28 [17.9%] vs 0) were seen in the high-dose group. Viral RNA was detected in 31 of 40 (77.5%) and 31 of 41 (75.6%) patients in the low-dosage and high-dosage groups, respectively. Lethality until day 13 was 39.0% in the high-dosage group (16 of 41) and 15.0% in the low-dosage group (6 of 40). The high-dosage group presented more instance of QTc interval greater than 500 milliseconds (7 of 37 [18.9%]) compared with the low-dosage group (4 of 36 [11.1%]). Respiratory secretion at day 4 was negative in only 6 of 27 patients (22.2%).
Conclusions and Relevance: The preliminary findings of this study suggest that the higher CQ dosage should not be recommended for critically ill patients with COVID-19 because of its potential safety hazards, especially when taken concurrently with azithromycin and oseltamivir. These findings cannot be extrapolated to patients with nonsevere COVID-19.

Table 2. Safety Outcomes in the Intention-to-Treat Population Until Day 13[a]

	No/ total No. (%)					
	All patients			COVID-19 confirmed cases		
Variable	Total	Low-dosage group[b]	High-dosage group[c]	Total	Low-dosage group[b]	High-dosage group[c]
Hemoglobin decreased[d]	11/42 (26.2)	4/18 (22.2)	7/24 (19.2)	7/29 (24.1)	3/11 (27.3)	4/18 (22.2)
Creatinine increased[e]	16/38 (42.1)	7/15 (46.7)	9/23 (39.1)	13/27 (48.1)	5/9 (55.6)	8/18 (44.4)
CK increased	13/33 (39.4)	6/19 (31.6)	7/14 (50.0)	9/24 (37.5)	3/15 (20.0)	6/9 (66.7)
CKMB increased	10/26 (38.4)	3/13 (23.1)	7/13 (53.8)	7/22 (31.8)	3/13 (23.1)	4/9 (44.4)
QTcF >500 ms[f]	11/73 (15.1)	4/36 (11.1)	7/37 (18.9)	8/57 (14.0)	1/27 (3.6)	7/29 (24.1)
Ventricular tachycardia	2/73 (2.7)	0/36	2/37 (2.7)	2/62 (3.2)	0/31	2/31 (6.5)

Abbreviation: CK, creatine phosphokinase; CKMB, creatinine phosphokinase-MB; COVID-19, coronavirus disease 2019; QTcF, QT interval corrected by the Fridericia method.

[a] Not all patients completed day 13 visit before this article was finalized.

[b] Low-dosage group received chloroquine for 5 days (450 mg twice daily on the first day and 450 mg once daily for 4 days).

[c] High-dosage group received chloroquine for 10 days (600 mg twice daily for 10 days).

[d] Decreases in hemoglobin level of more than 3 g/dL or 30% or greater from baseline are shown.

[e] Increases in creatinine serum levels of 30% or more from baseline are shown.

[f] Serious adverse events related to the trial regimen were prolongation of the QTcF.

An invited commentary on: "Evidence Based Management Guideline for the COVID-19 Pandemic - Review article".

Akay, Serhat; Akay, Huriye
International Journal of Surgery
2020 Apr 21; PMID: 32330658
Level of Evidence: 5 - Expert Opinion
Type of Article: Invited Commentary
Summary: This is a commentary on the well-written comprehensive up-to-date evidence-based review of current practice to implement in this pandemic published by Maria Nicole et. al. **On the topic of passive immunization using convalescent plasma from recovered patients, the authors note that this recommendation was based on low-quality, uncontrolled studies and there is a need for randomized controlled trials prior to reaching a conclusion.**

[COVID-19 research has overall low methodological quality thus far: case in point for chloroquine/hydroxychloroquine.]

Alexander PE, Debono VB, Mammen MJ, Iorio A, Aryal K, Deng D, Brocard E, Alhazzani W.
J Clin Epidemiol.
2020 Apr 21; PMID: 32330521
Level of Evidence: 5 - Expert Opinion
Type of Article: Commentary

Summary: This commentary critically appraised the quality of six COVID-19 research papers found through literature search (2019 – 4/3/2020) and found that all were classified as high risk of biased estimates of effect (Table 1). Most studies lack randomization and blinding/masking, as well as standard steps taken to minimize confounding. Overall, results are tempered by selection bias and residual confounding bias.

Table 1: Human hydroxychloroquine (HCQ) COVID-19 studies published as of April 6th 2020[5-10]

Study author, year, study design, location (reference #)	Sample size; mean/median age; % male	Intervention; comparator	Reported outcomes	Critical appraisal
RCTs				
Chen, 2020, RCT, China (5)	30; 15 HCQ, 15 control; 48.5 mean; 70%	HCQ 400 mg per day for 5 days plus SoC, control received SoC	Negative conversion rate	Small sample size, small events, unclear reporting of methods, unclear/absent randomization, concealment, blinding, sub-optimal outcomes, sparse reporting on methods
Chen, 2020, RCT, China (6)	62; 31 HCQ; 31 control; mean 44.7 (SD 15.3); 46.8%	5-day HCQ (400 mg/d), control received SoC	Time to clinical recovery (TTCR), clinical characteristics, and radiological results, adverse events	RCT, small sample size, small number of events, unclear reporting of methods, sub-optimal methods, sub-optimal outcomes, sparse reporting on methods
Huang, 2020, RCT, China (7)	22; 44.0 mean (36.5 to 57.5); 59.1%	twice-daily oral of 500mg Chloroquine (n=10) versus 400/100mg Lopinavir/Ritonavir (n=12) for 10 days	Disease progression by RT-PCR, lung pathology with CT, fever, respiratory rate, oxygen saturation and adverse events	RCT, small sample size, small events, unclear reporting of methods, unclear/absent randomization, concealment, blinding, sub-optimal outcomes, sparse reporting on methods
Observational studies				
Gautret, 2020, open-label non-randomized observational study, France (8)	42; 26 HCQ, 16 control; 45.1 ± 22.0 (mean/SD); 41.7%	HCQ 600 mg daily 6 d n=26 (AZ added depending on clinical presentation), control n=16 (6 lost in f/up due to cessation of treatment, 1 died, 3 to ICU)	Virologic cure, length of hospital stay, mortality, adverse events	Observational, small sample, > 20% attrition in intervention arm, control group taken from different care center, heterogenous allocation of co-treatments, decisions based on clinician judgement, unadjusted analysis, sparse reporting on methods; considered hypothesis generating
Gautret, 2020, case-series observational, France (9)	80; 52.5 median, 52.5%	200 mg of HCQ three times per day for ten days combined with AZ (500 mg on D1 followed by 250 mg per day for the next four days)	Need for oxygen therapy; transfer to the ICU after at least three days of treatment, contagiousness (PCR and culture) and length of stay ID ward	Observational study, no control arm; small sample size, small number of events, unadjusted analysis, no matching, stratification, restriction, sparse reporting on methods; considered hypothesis generating
Molina, 2020, consecutive case-series observational, France (10)	11; 58.7 mean, 64%	HCQ 600 mg/d for 10 days and AZ 500 mg Day 1 and 250 mg days 2 to 5	Virologic cure (positive tests)	Observational study, no control arm; small sample size, small number of events, unadjusted analysis; considered hypothesis generating

AZ- Azithromycin; CT - computed tomography scan; HCQ – Hydroxychloroquine; ICU – Intensive Care Unit; ID – Infectious Disease; RCT – Randomized Controlled Trial; RT-PCR - Reverse transcription polymerase chain reaction

[Pharmacological Therapeutics Targeting RNA-Dependent RNA Polymerase, Proteinase and Spike Protein: From Mechanistic Studies to Clinical Trials for COVID-19.]

Huang J, Song W, Huang H, Sun Q.
J Clin Med
2020 Apr 15; PMID: 32326602
Level of Evidence: 1 -Systematic Review
Type of Article: Review

BLUF: This review discusses current treatment mechanisms for COVID-19 and their efficacy including targeting RNA-dependent RNA polymerase (RdRp, important for virus replication) by remdesivir which will be studied in a phase 3 randomized, double-blind, placebo-controlled study. Additionally, proteinase inhibitors including ribavirin, lopinavir-ritonavir, and favipiravir have been used to treat SARS or MERS and may have potential in treating SARS-CoV-2 because there is more than 90% sequence similarity between SARS-CoV and SARS-CoV-2. NHC and hydroxychloroquine have also shown some efficacy against SARS-CoV-2. The authors also discuss S protein as a target for vaccines as it plays an important role in eliciting a T cell response.

Abstract
An outbreak of novel coronavirus-related pneumonia COVID-19, that was identified in December 2019, has expanded rapidly, with cases now confirmed in more than 211 countries or areas. This constant transmission of a novel coronavirus and its ability to spread from human to human have prompted scientists to develop new approaches for treatment of COVID-19. A recent study has shown that remdesivir and chloroquine effectively inhibit the replication and infection of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2, 2019-nCov) in vitro. In the United States, one case of COVID-19 was successfully treated with compassionate use of remdesivir in January of 2020. In addition, a clinically proven protease inhibitor, camostat mesylate, has been demonstrated to inhibit Calu-3 infection with SARS-CoV-2 and prevent SARS-2-spike protein (S protein)-mediated entry into primary human lung cells. Here, **we systemically discuss the pharmacological therapeutics targeting RNA-dependent RNA polymerase (RdRp), proteinase and S protein for treatment of SARS-CoV-2 infection**. **This review should shed light on the fundamental rationale behind inhibition of SARS-CoV-2 enzymes RdRp as new therapeutic approaches for management of patients with COVID-19.** In addition, we will discuss the viability and challenges in targeting RdRp and proteinase, and application of natural product quinoline and its analog chloroquine for treatment of coronavirus infection. Finally, determining the structural-functional relationships of the S protein of SARS-CoV-2 will provide new insights into inhibition of interactions between S protein and angiotensin-converting enzyme 2 (ACE2) and enable us to develop novel therapeutic approaches for novel coronavirus SARS-CoV-2.

Lopinavir/ritonavir did not shorten the duration of SARS CoV-2 shedding in patients with mild pneumonia in Taiwan.

Cheng CY, Lee YL, Chen CP, Lin YC, Liu CE, Liao CH, Cheng SH.
J Microbiol Immunol Infect
2020 Apr 21; PMID: 32331982
Level of Evidence: 3- Case series
Type of Article: Short communication
BLUF: Here the authors describe and compare five confirmed COVID-19 patients in Taiwan. Two patients received lopinavir (200 mg)/ritonavir (50 mg) and three patients received only supportive care. Comparing the CT values from RT-PCR analysis of oropharyngeal swabs and sputum samples, the authors find no significant difference in viremia between the groups, indicating that this specific formulation and combination of lopinavir/ritonavir did not improve disease outcome.

Abstract:
An increase of Ct values was 0.9 per day in 2 cases of COVID-19 treated with lopinavir/ritonavir (LPV/r), an increase was 1.0 per day in 3 cases without LPV/r through illness day 1-10, indicating that LPV/r did not shorten the duration of SARS CoV-2 shedding.

Eculizumab treatment in patients with COVID-19: preliminary results from real life ASL Napoli 2 Nord experience

Diurno, F; Numis, FG; Porta, G; Cirillo, F; Maddaluno, S; Ragozzino, A; De Negri, P; Di Gennaro, C; Pagano, A; Allegorico, E; Bressy, L; Bosso, G; Ferrara, A; Serra, C; Montisci, A; D'Amico, M; Schiano Lo Morello, S; Di Costanzo, G; Tucci, AG; Marchetti, P; Di Vincenzo, U; Sorrentino, I; Casciotta, A; Fusco, M; Buonerba, C; Berretta, M; Ceccarelli, M; Nunnari, G; Diessa, Y; Cicala, S; Facchini, G.
Eur Rev Med Pharmacol Sci
2020 Apr 24; PMID: 32329881
Level of Evidence: 4 - Case Series
Type of Article: Research

BLUF: Authors present a case series of 4 patients diagnosed with severe COVID-19 with either pneumonia or ARDS. These patients were treated with Eculizumab and a drop in inflammatory markers was found. All patients survived. The authors support off-label use of eculizumab for severe COVID-19. However, it is important to note other drugs like anticoagulants, antivirals, etc. were also administered for treatment among these patients.

Abstract:
OBJECTIVE: SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2)-related pneumonia, referred to as COVID-19 (Coronavirus Disease 19), is a public health emergency as it carries high morbidity, mortality, and has no approved specific pharmacological treatments. In this case series, we aimed to report preliminary data obtained with anti-complement C5 therapy with eculizumab in COVID-19 patients admitted to intensive care unit (ICU) of ASL Napoli 2 Nord.
PATIENTS AND METHODS: This is a case series of patients with a confirmed diagnosis of SARS-CoV2 infection and severe pneumonia or ARDS who were treated with up to 4 infusions of eculizumab as an off-label agent. Patients were also treated with anticoagulant therapy with Enoxaparin 4000 IU/day via subcutaneous injection, antiviral therapy with Lopinavir 800 mg/day + Ritonavir 200 mg/day, hydroxychloroquine 400 mg/ day, ceftriaxone 2 g/day IV, vitamine C 6 g/day for 4 days, and were on Non-Invasive Ventilation (NIV).
RESULTS: **We treated four COVID-19 patients admitted to the intensive care unit because of severe pneumonia or ARDS. All patients successfully recovered after treatment with eculizumab. Eculizumab induced a drop in inflammatory markers.** Mean C Reactive Protein levels dropped from 14.6 mg/dl to 3.5 mg/dl and the mean duration of the disease was 12.8 days.
CONCLUSIONS: Eculizumab has the potential to be a key player in treatment of severe cases of COVID-19. Our results support eculizumab use as an off-label treatment of COVID-19, pending confirmation from the ongoing SOLID-C19 trial.

Current pharmacological treatments for COVID-19: what's next?

Scavone C, Brusco S, Bertini M, Sportiello L, Rafaniello C, Zoccoli A, Berrino L, Racagni G, Rossi F, Capuano A.
British Journal of Pharmacology.
2020 Apr 24; PMID: 32329520
Level of Evidence: 5 - Literature Review
Type of Article: Review

BLUF: This article outlines the current pharmacological properties and available clinical data with regards to SARS-CoV-2 treatment including antiviral, immune-modulatory, and anti-inflammatory agents. Although preliminary trials have shown lopinavir/ritonavir, remdesivir, favipiravir and tocilizumab to be somewhat helpful for treating COVID-19 patients, it is important to recognize that

adequate clinical trials have not firmly concluded the effectiveness of these medications and frequent monitoring of patients on these treatments should be done.

Abstract:
Starting from December 2019 the novel SARS-Cov-2 has spread all over the world, being recognized as the causing agent of COVID-19. Since nowadays no specific drug therapies *(sic)* neither vaccines are available for the treatment of COVID-19, drug repositioning may offer a strategy to efficiently control the clinical course of the disease and the spread of the outbreak. In this paper we aim to describe the main pharmacological properties, including data on mechanism of action, safety concerns and drug-drug interactions, of drugs currently administered in patients with COVID-19, focusing on antivirals and drugs with immune-modulatory and/or anti-inflammatory properties. Where available, data from clinical trials involving patients with COVID-19 were reported. Several studies have been registered worldwide and a number of drugs were repurposed to face the new health emergency of COVID-19. For many of these drugs, including lopinavir/ritonavir, remdesivir, favipiravir and tocilizumab, preliminary clinical trials seem to support their benefit in improving patients' clinical conditions. However, adequate clinical trials are necessary to reach any firm conclusion on the efficacy and safety profiles of these compounds. Even though drug repurposing is necessary, it requires caution. Too many drugs that are currently tested in patients with COVID-19 have peculiar safety profiles. In conclusion, while waiting for the development of effective preventive measures, such as vaccines, many clinical trials on drugs belonging to different therapeutic classes are currently underway. It is conceivable that very soon their results will help us in defining the best way to treat COVID-19 and reducing its symptoms and complications.

Translating IL-6 biology into effective treatments.

Choy EH, De Benedetti F, Takeuchi T, Hashizume M, John MR, Kishimoto T.Choy EH, et al.
Nat Rev Rheumatol.
2020 Apr 23; PMID: 32327746
Level of Evidence: 5 - Expert opinion
Type of Article: Review
Summary: This review discusses the history of research into IL-6 biology and the development of therapies that target IL-6 signalling, with an emphasis on rheumatic diseases. Choy et al. briefly reference the use of tocilizumab in a trial on COVID-19 pneumonia without any further information.

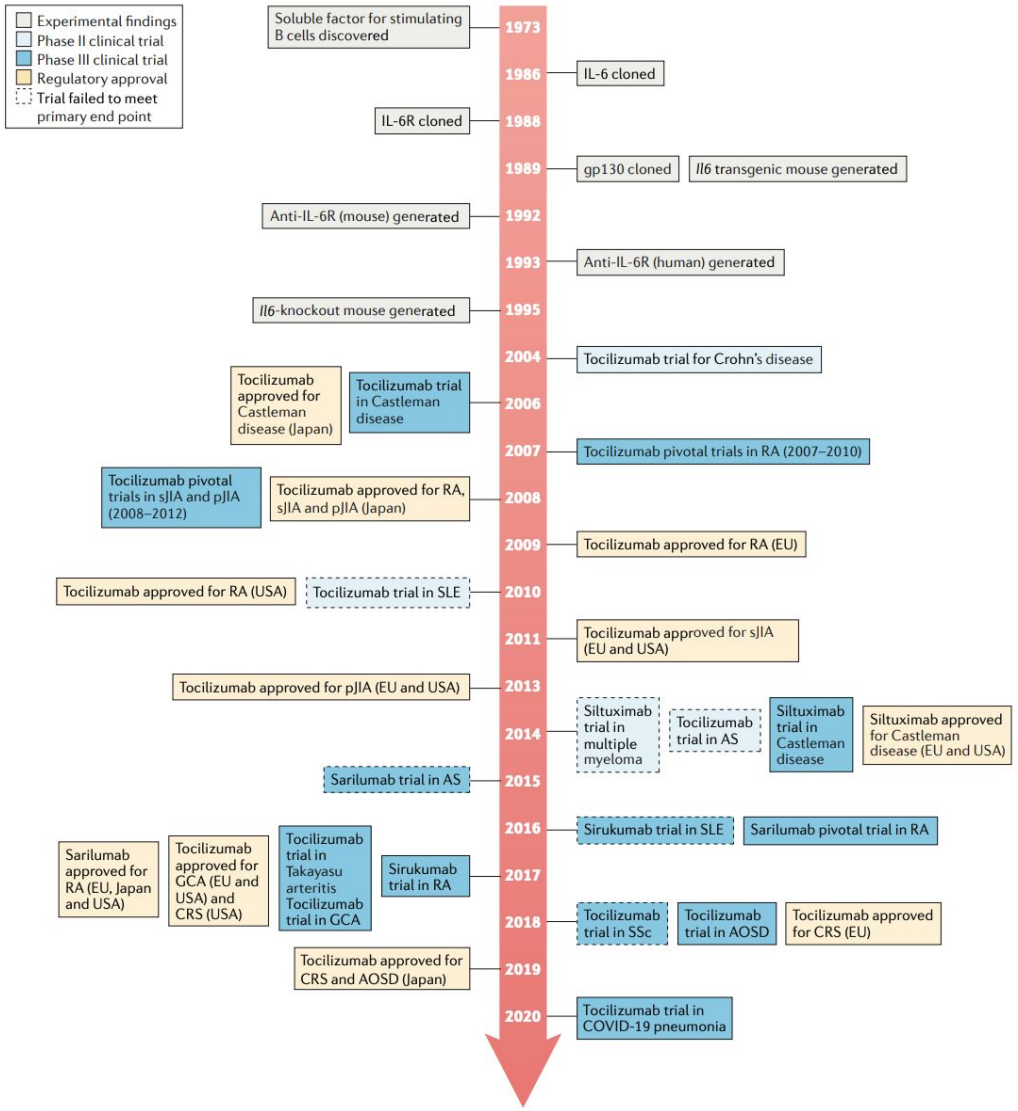


Fig. 1 | **Timeline of the discovery of IL-6 and IL-6-targeted therapies.** The timeline shows progress in the field of IL-6 pathway inhibition following the initial identification of a B cell stimulation factor in 1973, and the more definitive biochemical and molecular studies carried out in the 1980s and 1990s, to clinical trials and approvals in various diseases in the 2000s and up to the present day. AOSD, adult-onset Still's disease; AS, ankylosing spondylitis; CRS, cytokine release syndrome; GCA, giant cell arteritis; gp130, glycoprotein 130; IL-6R, IL-6 receptor; pJIA, polyarticular course juvenile idiopathic arthritis; RA, rheumatoid arthritis; sJIA, systemic juvenile idiopathic arthritis; SLE, systemic lupus erythematosus; SSc, systemic sclerosis.

Pharmacological Therapeutics Targeting RNA-Dependent RNA Polymerase, Proteinase and Spike Protein: From Mechanistic Studies to Clinical Trials for COVID-19.

Huang J, Song W, Huang H, Sun Q.
J Clin Med
2020 Apr 15; PMID: 32326602
Level of Evidence: 1 -Systematic Review
Type of Article: Review

BLUF: This review discusses current treatment mechanisms for COVID-19 and their efficacy including targeting RNA-dependent RNA polymerase (RdRp, important for virus replication) by remdesivir which will be studied in a phase 3 randomized, double-blind, placebo-controlled study. Additionally, proteinase inhibitors including ribavirin, lopinavir-ritonavir, and favipiravir have been used to treat SARS or MERS and may have potential in treating SARS-CoV-2 because there is more than 90% sequence similarity between SARS-CoV and SARS-CoV-2. NHC and hydroxychloroquine have also shown some efficacy against SARS-CoV-2. The authors also discuss S protein as a target for vaccines as it plays an important role in eliciting a T cell response.

Abstract:
An outbreak of novel coronavirus-related pneumonia COVID-19, that was identified in December 2019, has expanded rapidly, with cases now confirmed in more than 211 countries or areas. This constant transmission of a novel coronavirus and its ability to spread from human to human have prompted scientists to develop new approaches for treatment of COVID-19. A recent study has shown that remdesivir and chloroquine effectively inhibit the replication and infection of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2, 2019-nCov) in vitro. In the United States, one case of COVID-19 was successfully treated with compassionate use of remdesivir in January of 2020. In addition, a clinically proven protease inhibitor, camostat mesylate, has been demonstrated to inhibit Calu-3 infection with SARS-CoV-2 and prevent SARS-2-spike protein (S protein)-mediated entry into primary human lung cells. Here, **we systemically discuss the pharmacological therapeutics targeting RNA-dependent RNA polymerase (RdRp), proteinase and S protein for treatment of SARS-CoV-2 infection**. **This review should shed light on the fundamental rationale behind inhibition of SARS-CoV-2 enzymes RdRp as new therapeutic approaches for management of patients with COVID-19.** In addition, we will discuss the viability and challenges in targeting RdRp and proteinase, and application of natural product quinoline and its analog chloroquine for treatment of coronavirus infection. Finally, determining the structural-functional relationships of the S protein of SARS-CoV-2 will provide new insights into inhibition of interactions between S protein and angiotensin-converting enzyme 2 (ACE2) and enable us to develop novel therapeutic approaches for novel coronavirus SARS-CoV-2.

Safety signals for QT prolongation or Torsades de Pointes associated with azithromycin with or without chloroquine or hydroxychloroquine.

Sarayani A, Cicali B, Henriksen CH, Brown JD
2020 Apr 19; Res Social Adm Pharm.
PMID: 32327397
Level of Evidence: 4 - Cross sectional
Type of Article: Research
BLUF: Cross-sectional study on the reported number of events of QT prolongation or torsades caused by hydroxychloroquine/chloroquine (HCQ/CQ) and azithromycin both alone and in combination. This study analyzed reports from FDA's Adverse Event Reporting System between 1969 - 2019 and calculated proportional reporting ratios and 95% confidence intervals. Amoxicillin was used as a control. Azithromycin alone was associated with a potential risk for QT prolongation/torsades, while HCQ/CQ was not. Results for the combination of drugs did not reach threshold to show a safety risk, likely due to low number of reports as suggested by a large confidence interval (1.80 - 7.87). HCQ/CQ appears relatively safe in terms of QT prolongation/torsades, but further evidence is needed to assess it's combined risk with azithromycin.

Abstract:

Background: Combinations of hydroxychloroquine (HCQ) and azithromycin have been promoted as treatments for COVID-19 based on small, uncontrolled clinical trials that have not assessed potential risks. Risks of treatment include QT segment prolongation, Torsades de Pointes (TdP), and death. This comparative pharmacovigilance analysis evaluated the risk of these events.
Methods: Data from the U.S. Food and Drug Administration's Adverse Event Reporting System (FAERS) (>13 million total reports) were used. Queries extracted reports based on exposures of HCQ/chloroquine (CQ) alone, azithromycin alone, HCQ/CQ + azithromycin, amoxicillin alone, HCQ/CQ + amoxicillin alone. Amoxicillin served as a control. Events of interest included death and TdP/QT prolongation as well as accidents/injuries and depression as control events. **Proportional Reporting Ratios (PRR) and 95% confidence intervals (CI) were calculated where a lower limit of the of 95% CI (Lower95CI) value of ≥2.0 is interpreted as a potential safety signal**.
Results: Lower95CIs for HCQ/CQ alone showed no potential safety signals for TdP/QT prolongation, death, or any of the control events included. **The PRRs and 95% CIs for TdP/QT prolongation was 1.43 (1.29-2.59) with HCQ/CQ use alone and 4.10 (3.80-4.42) for azithromycin alone.** For the combined HCQ/CQ + azithromycin group, the PRR and 95% CI was 3.77 (1.80-7.87). For the control of amoxicillin, there were no safety signals when used alone or in combination with HCQ/CQ.
Conclusions: **HCQ/CQ use was not associated with a safety signal in this analysis of FAERS data**. However, azithromycin used alone was associated with TdP/QT prolongation events and should be used with caution.

Ticagrelor Can Be an Important Agent in the Treatment of Severe COVID-19 Patients with Myocardial Infarction.

Akşit E, Kırılmaz B, Gazi E, Aydın F.Akşit E
Balkan Med J
2020 April 22; PMID: 32326691
Level of Evidence: 5 Expert Opinion
Type of Article: Letter
BLUF: The authors propose Ticagrelor as a treatment option for patients with concomitant COVID-19 and MI due to its pleiotropic effects that include reducing proinflammatory factors, platelet reactivation, thromboinflammatory markers as well as providing antibacterial activity.

Summary: COVID-19 pneumonia is one of the adverse outcomes from the Coronavirus disease that coexists with myocardial infarction. COVID-19 is known to induce inflammatory responses within the body that elevate levels of TNF-a and IL-6, variants risk factors for pneumonia-induced septic shock in intensive care patients. The authors propose for the use of Ticagrelor, an ADP receptor inhibitor, to treat concomitant COVID-19 pneumonia and MI. Reasons for using Ticagrelor includes reduction of proinflammatory factors, platelet reactivation, and thromboinflammatory markers in patients with pneumonia. In addition, Ticagrelor at a conventional dose has antibacterial effects that will be beneficial to COVID-19 patients developing superinfections during their treatments. Considering all of the pleiotropic effects of Ticagrelor, it can contribute to the survival of patients with MI coexisting with COVID-19.

Vaccines for SARS-CoV-2: Lessons from Other Coronavirus Strains

Padron-Regalado, Eriko
Infect Dis Ther
2020 Apr 23; PMID: 32328978

Level of Evidence: 5 - Literature Review
Type of Article: Research
BLUF: This is a review of the vaccination efforts of other coronavirus strains SARS (severe respiratory syndrome) and MERS (Middle East respiratory syndrome) in hopes of providing information for current COVID-19 vaccine development. The author also discusses the short-term immunogenicity provided after infection with these strains, and the possibility of adverse side effects seen in their respective vaccine development.

Abstract:
The emergence of the strain of coronavirus SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) and its impact on global health have made imperative the development of effective and safe vaccines for this lethal strain. SARS-CoV-2 now adds to the list of coronavirus diseases that have threatened global health, along with the SARS (severe acute respiratory syndrome) and MERS (Middle East respiratory syndrome) coronaviruses that emerged in 2002/2003 and 2012, respectively. As of April 2020, no vaccine is commercially available for these coronavirus strains. Nevertheless, the knowledge obtained from the vaccine development efforts for MERS and SARS can be of high value for COVID-19 (coronavirus disease 2019). **Here, we review the past and ongoing vaccine development efforts for clinically relevant coronavirus strains with the intention that this information helps in the development of effective and safe vaccines for COVID-19.** In addition, information from naturally exposed individuals and animal models to coronavirus strains is described for the same purpose of helping into the development of effective vaccines against COVID-19.

Photobiomodulation and Antiviral Photodynamic Therapy as a Possible Novel Approach in COVID-19 Management.

Fekrazad R.Fekrazad R.
Photobiomodul Photomed Laser Surg.
2020 Apr 23; PMID: 32326830
Level of Evidence: 5 - Expert Opinion
Type of Article: Editorial
Summary: Photobiomodulation (PBM) using photon laser therapy can possibly be used to induce regeneration in lungs afflicted with acute respiratory disease Syndrome (ARDS) from COVID-19. Irradiating photosensitizer nanoparticles through antimicrobial photodynamic therapy (aPDT) to destroy the virus found in the lungs is another proposed therapy.

Discovery of Potential Multi-Target-Directed Ligands by Targeting Host-specific SARS-CoV-2 Structurally Conserved Main Protease[$].

Joshi, Rakesh S; Jagdale, Shounak S; Bansode, Sneha B; Shankar, Shiva S; Tellis, Meenakshi B; Pandya, Vaibhav K; Chugh, Anita; Giri, Ashok P; Kulkarni, Mahesh J
Journal of Biomolecular Structure and Dynamics
2020 Apr 24; PMID: 32329408
Level of Evidence: 5 - Mechanism-Based Reasoning
Type of Article: Research
BLUF: The Mpro protease, which plays a critical role in SARS-CoV-2 viral replication and maturation, was analyzed through phylogenetic and Sequence Similarity Network analysis and established to be a good target for inhibition. Screening of ~7100 molecules against Mpro was completed, yielding several that could be lead molecules (Table 1 below) for multi-targeted drug development against SARS-CoV-2.

Abstract: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has resulted in the current COVID-19 pandemic. Worldwide this disease has infected over 2.5 million individuals with a mortality rate ranging from 5 to 10%. There are several efforts are going on in the drug discovery to control the SARS-CoV-2 viral infection. The **main protease (MPro) plays a critical role in viral replication and maturation, thus can serve as the primary drug target**. To understand the structural evolution of MPro, we have performed phylogenetic and Sequence Similarity Network analysis, that depicted divergence of Coronaviridae MPro in five clusters specific to viral hosts. This clustering was corroborated with the comparison of MPro structures. Furthermore, it has been observed that backbone and binding site conformations are conserved despite variation in some of the residues. These attributes can be exploited to repurpose available viral protease inhibitors against SARS-CoV-2 MPro. In agreement with this, we performed screening of ~7100 molecules including active ingredients present in the **Ayurvedic anti-tussive medicines, anti-viral phytochemicals and synthetic anti-virals** against SARS-CoV-2 MPro as the primary target. We identified several natural molecules like **δ-viniferin, myricitrin, taiwanhomoflavone A, lactucopicrin 15-oxalate, nympholide A, afzelin, biorobin, hesperidin and phyllaemblicin B** that strongly binds to SARS-CoV-2 MPro. Intrestingly *(sic)*, these molecules also showed strong binding with other potential targets of SARS-CoV-2 infection like viral receptor human angiotensin-converting enzyme 2 (hACE-2) and RNA dependent RNA polymerase (RdRp). We anticipate that our approach for identification of multi-target-directed ligand will provide new avenues for drug discovery against SARS-CoV-2 infection.

Can early and high intravenous dose of vitamin C prevent and treat coronavirus disease 2019 (COVID-19)?

Cheng RZ.Cheng RZ.
Med Drug Discov.
2020 Mar; PMID: 32328576
Level of Evidence: 5 - Expert opinion
Type of Evidence: Editorial

BLUF: The author discusses preliminary research supporting his opinion that the antioxidant properties of high dose Vitamin C may lend to its use in modulating the ROS mediated pathways for lung injury in COVID-19 patients.

Summary: The author discusses the use of high dose Vitamin C (HD VC) for COVID-19 related ARDS and cytokine storm. Articles of note included **two studies which showed HD VC reduced ICU stays and mortality in patients with and without influenza**. Another study showed **reduced lung injury in ventilated patients.** Specific to COVID-19, a **Chinese study of 15 moderately to severely ill COVID-19 patients given HD VC demonstrated improved oxygenation** with **eventual recovery** and discharge. The author believes **these studies support his opinion that HD VC may safely attenuate lung injury in COVID-19.** Limitations to the research presented and evidence related to safety and potential adverse effects was not discussed.

Complement as a target in COVID-19?

Risitano AM, Mastellos DC, Huber-Lang M, Yancopoulou D, Garlanda C, Ciceri F, Lambris JD.Risitano AM, et al.
Nat Rev Immunol.
2020 Apr 23; PMID: 32327719
Level of Evidence: 5 - Expert Opinion
Type of Article: Comment

BLUF: There is evidence to suggest that innate immune system dysfunction, including complement, is key to the pathophysiology of inflammation and acute respiratory distress syndrome in COVID-19 patients. The authors encourage further research into the role of complement and the possible therapeutic use of complement inhibitors.

Summary Excerpt:
"The deterioration of lung function [in COVID-19] has been attributed to a maladaptive immune response rather than increased viral loads... Complement is an integral component of the innate immune response to viruses and an instigator of pro- inflammatory responses. **A recent study of SARS-CoV, which is closely related to SARS-CoV-2, found that activation of complement component C3 exacerbates disease in SARS-CoV-associated ARDS. C3-deficient mice infected with SARS-CoV exhibited less respiratory dysfunction, despite equivalent viral loads in the lungs, and this was associated with decreased lung infiltration of neutrophils and inflammatory monocytes and lower levels of cytokines and chemokines in both the lungs and sera**... A recent preprint study reported that lung biopsy samples from patients with severe COVID-19 showed widespread complement activation, characterized by C3a generation and C3-fragment deposition. A prominent increase of serum C5a levels was also observed. Importantly, treatment of patients with an anti-C5a antibody led to immediate clinical improvement, as measured by increased lung oxygenation and decreased systemic inflammation."

Does the Direct Renin Inhibitor Have a Role to Play in Attenuating Severity of the Outbreak Coronavirus Disease 2019 (COVID-19)?

Lin CW, Huang YY
Ther Adv Endocrinol Metab
2020 Apr 16; PMID: 32328234
Level of Evidence: 5 – Expert Opinion
Type of Article: Letter
Summary: The authors weigh the **benefits and drawbacks of RAS** (renin-aldosterone system) **inhibition** in the context of **COVID-19**. They note that SARS-CoV-2 invades lung epithelia via ACE-2, a key RAS mediator. Since **ACE-2 inhibitors** might potentiate infection by **inducing similar effects on RAS proteins as SARS-CoV-2**, the authors suggest looking into **upstream inhibition of renin** to **reduce invasion and RAS effects** that contribute to poor prognosis.

COVID-19 Drug Discovery Using Intensive Approaches

Asai A, Konno M, Ozaki M, Otsuka C, Vecchione A, Arai T, Kitagawa T, Ofusa K, Yabumoto M, Hirotsu T, Taniguchi M, Eguch H, Doki Y, Ishii H
Int J Mol Sci
2020 Apr 18; PMID: 32325767
Level of Evidence: 5 – Mechanism-based Reasoning
Type of Article: Review
BLUF: The authors **review current drugs** that may be used to target SARS-CoV-2 and their **mechanisms of action**. Potential therapies of interest include **antivirals** (favipiravir, remdesivir, and ritonavir) and **chloroquine phosphate**, an antimalarial lacking clinical consensus. The authors also delve into SARS-CoV-2 specific mechanisms, like **ACE-2**, **dipeptidyl peptidase 4 (DPP4)**, **aminopeptidase N (APN)**, and virus-specific **RNA modifications** as **potential drug discovery routes**, acknowledging widespread efforts directed at treating COVID-19.

Abstract:
Since the infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was reported in China during December 2019, the coronavirus disease 2019 (COVID-19) has spread on a global scale, causing the World Health Organization (WHO) to issue a warning. While novel vaccines and drugs that target SARS-CoV-2 are under development, this review provides **information on therapeutics** which are **under clinical trials** or are **proposed to antagonize SARS-CoV-2**. Based on the information gained from the responses to other RNA coronaviruses, including the strains that cause severe acute respiratory syndrome (SARS)-coronaviruses and Middle East respiratory syndrome (MERS), **drug repurposing might be a viable strategy**. Since several antiviral therapies can inhibit viral replication cycles or relieve symptoms, **mechanisms unique to RNA viruses will be important for the clinical development** of antivirals against SARS-CoV-2. Given that several currently marketed drugs may be efficient therapeutic agents for severe COVID-19 cases, they **may be beneficial for future viral pandemics** and other infections caused by RNA viruses when standard treatments are unavailable.

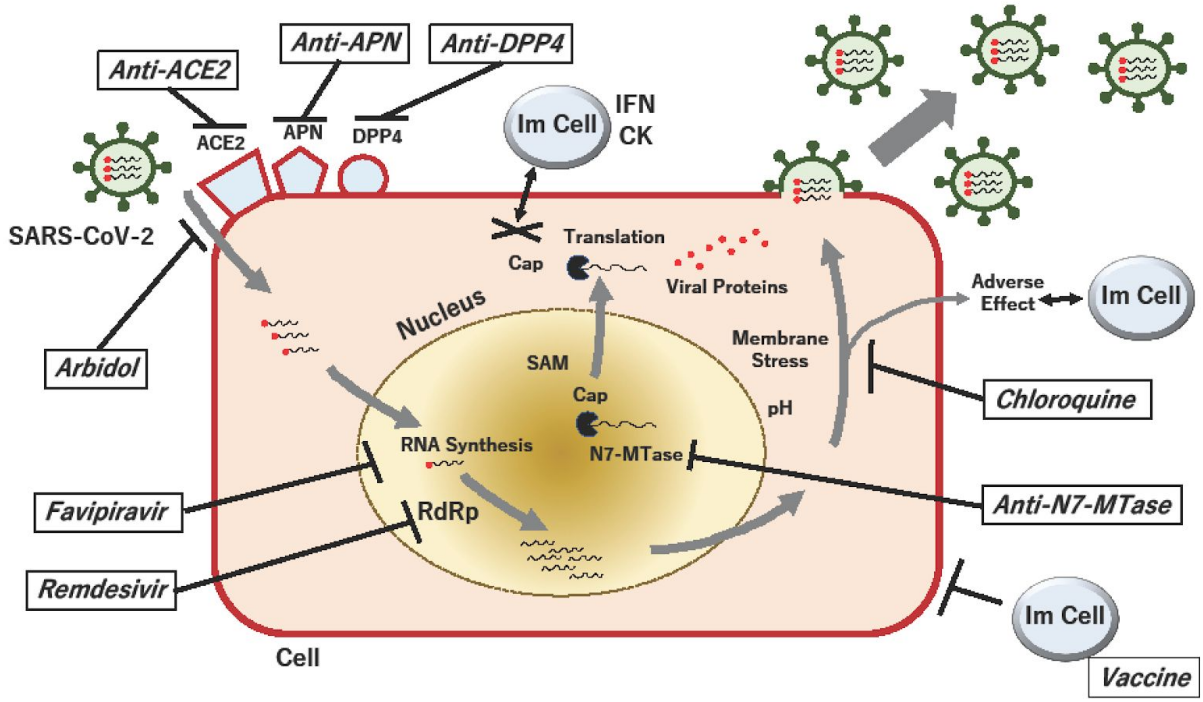


Figure 1. Proposed acting points of anti-SARS-CoV-2 in the replication cycle of the virus. When SARS-CoV-2 particles bind to their receptors, such as angiotensin-converting enzyme 2 (ACE2), aminopeptidase N (APN; CD13) and dipeptidyl peptidase 4 (DPP4; CD26), viral RNA is passed to the host cell, and RNA-dependent RNA polymerase (RdRp) produces viral RNAs. During RNA methylation, the RNA cap is formed, which protects against the host innate immune response, which involves the secretion of interferons (IFNs) and cytokines (CKs). The viral (guanine-N7)-methyltransferase (N7-MTase) plays a critical role in RNA capping, using the methyl donor S-adenosyl-methionine (SAM). The process of viral RNA synthesis and the translation of proteins is associated with pH-dependent membrane stress, which can elicit adverse effects against immune and non-immune cells. If the viral replication cycle is not inhibited and infected cells are not eradicated, packed viruses will be disseminated to other cells in the host. Proposed drugs and their possible acting points against COVID-19 are shown by bold lines.

COVID-19: lambda interferon against viral load and hyperinflammation.

Andreakos, Evangelos; Tsiodras, Sotirios
EMBO Mol Med
2020 Apr 25; PMID: 32333818
Level of Evidence: 5 - Mechanism-based Reasoning
Type of Article: Research

BLUF: These authors make a case that IFNλ can be utilized as an early intervention in high-risk COVID-19 patients due to its ability to induce viral resistance and prevent the cytokine storm in addition to its favorable safety profile.

Abstract: Coronavirus Disease 2019 (COVID-19), triggered by the betacoronavirus SARS-CoV-2, has become one of the worst pandemics of our time that has already caused more than 183.470 deaths$ [CAN YOU PLEASE MAKE IT A FOOTNOTE? $ JHU data-23/04/2020, https://www.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6].. Effective therapeutic approaches are urgently needed to reduce the spread of the virus and its death toll. Here, we assess the possibility of using interferon lambda (IFNλ), a third type of interferon sharing low homology with type I IFNs and IL-10, for treating COVID-19 patients. We discuss the **unique role of IFNλ in fine-tuning antiviral immunity in the respiratory tract to achieve optimal protection and minimal host damage** and review early evidence that SARS-CoV-2 may impair IFNλ induction, leading to a **delayed type I IFN-dominated response that triggers hyperinflammation and severe disease**. We also consider the potential windows of opportunity for therapeutic intervention with IFNλ and potential safety considerations. We conclude that **IFNλ constitutes a promising therapeutic agent for reducing viral presence and hyperinflammation** in a single shot to prevent the devastating consequences of COVID-19 such as pneumonia and acute respiratory distress syndrome (ARDS). *(sic)*

The friendly use of chloroquine in the COVID-19 disease: a warning for the G6PD-deficient males and for the unaware carriers of pathogenic alterations of the G6PD gene.

Capoluongo, Ettore D; Amata, Felice; Gastaldo, Giuseppe
Clinical Chemistry and Laboratory Medicine
2020 Apr 24; PMID: 32333649
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter to the Editor

BLUF: Within the COVID-19-infected population, there is a need for all patients who will undergo hydroxychloroquine treatment to be tested for G6PD activity in the blood prior to initiation of treatment.

Summary: It is difficult to establish the true number of subjects who are deficient in G6PD due to a number of factors including the asymptomatic nature of some patients and the difficulty of detecting the disease prior to any exogenous haemolytic triggers. Given that chloroquine treatment's efficacy as an anti-viral treatment is debated and it is known to be a contraindication in G6PD patients, the population should have filtered access to chloroquine as it could lead to a severe unintended side effect in such patients. Additionally, **all patients who will undergo hydroxychloroquine treatment should be tested for G6PD activity in the blood prior to starting treatment.**

Adipose-Derived Stromal Stem Cells (ASCs) as a new regenerative immediate therapy combating Coronavirus (COVID-19)-Induced Pneumonia.

Gentile P, Sterodimas A.
Expert Opin Biol Ther.
2020 Apr 24; PMID: 32329380
Level of Evidence: 5 - Expert Opinion
Type of Article: Commentary

Summary: Mesenchymal stem cells (MSCs), from either adipose or bone marrow tissue, have been used in small sample studies to **reverse the lung damage done by COVID-19-induced pneumonia**. More clinical trials using stem cells against COVID-19 pathologies have arisen. **Adipose tissue is preferred for extraction** due to higher yield. Suggested protocols for fast and efficient infusion of adipose-derived stromal stem cells (ASCs) include labs approved through: Food and Drug Administration (FDA), European Medicines Agency (EMA), or Good Manufacturing Practice (GMP).

COVID-19's Impact on Healthcare Workforce

A Multinational, Multicentre Study on the Psychological Outcomes and Associated Physical Symptoms Amongst Healthcare Workers During COVID-19 Outbreak.

Chew NWS, Lee GKH, Tan BYQ, Jing M, Goh Y, Ngiam NJH, Yeo LLL, Ahmad A, Ahmed Khan F, Napolean Shanmugam G, Sharma AK, Komalkumar RN, Meenakshi PV, Shah K, Patel B, Chan BPL, Sunny S, Chandra B, Ong JJY, Paliwal PR, Wong LYH, Sagayanathan R, Chen JT, Ying Ng AY, Teoh HL, Tsivgoulis G, Ho CS, Ho RC, Sharma VK
2020 Apr 21; Brain Behav Immun.
PMID: 32330593
Level of Evidence: 4 - Cross-sectional study
Type of Article: Research

Summary: A cross-sectional study of 906 nurses, doctors, and allied healthcare professionals from India and Singapore that examined the association between psychological stress and physical symptoms. A questionnaire was administered to participants that collected data on the presence of physical symptoms over the past month and assessed psychological symptoms with validated scales of depression, anxiety, and distress. Experiencing physical symptoms in the past month was significantly correlated with depression (OR 2.79, 95% CI 1.54–5.07), anxiety (OR 2.18, 95% CI 1.36–3.48), stress (OR 3.06, 95% CI 1.27–7.41), and PTSD (OR 2.20, 95% CI 1.12–4.35). The authors suggest the relationship between psychological and physical symptoms is bi-directional, with each having the potential to exacerbate the other. They call for timely consideration of psychological support for healthcare workers presenting with physical symptoms once infection is ruled out.

Abstract:
Objective: Since the declaration of the coronavirus 2019 (COVID-19) outbreak as pandemic, there are reports on the increased prevalence of physical symptoms observed in the general population. We investigated the association between psychological outcomes and physical symptoms among healthcare workers.
Methods: Healthcare workers from 5 major hospitals, involved in the care for COVID-19 patients, in Singapore and India were invited to participate in a study by performing a self-administered questionnaire within the period of February 19 to April 17, 2020. Healthcare workers included doctors, nurses, allied healthcare workers, administrators, clerical staff and maintenance workers. This questionnaire collected information on demographics, medical history, symptom prevalence in the past month, Depression Anxiety Stress Scales (DASS-21) and the Impact of Events Scale-Revised (IES-R) instrument. The prevalence of physical symptoms displayed by healthcare workers and the associations between physical symptoms and psychological outcomes of depression, anxiety, stress, and post-traumatic stress disorder (PTSD) were evaluated.
Results: **Out of the 906 healthcare workers who participated in the survey, 48 (5.3%) screened positive for moderate to very-severe depression, 79 (8.7%) for moderate to extremely-severe anxiety, 20 (2.2%) for moderate to extremely-severe stress, and 34 (3.8%) for moderate to severe levels of psychological distress.** The commonest reported symptom was headache (32.3%), with a large number of participants (33.4%) reporting more than four symptoms. Participants who had experienced symptoms in the preceding month were more likely to be older, have pre-existing comorbidities and a positive screen for depression, anxiety, stress, and PTSD. **After adjusting for age, gender and comorbidities, it was found that**

depression (OR 2.79, 95% CI 1.54–5.07, p = 0.001), anxiety (OR 2.18, 95% CI 1.36–3.48, p = 0.001), stress (OR 3.06, 95% CI 1.27–7.41, p = 0.13), and PTSD (OR 2.20, 95% CI 1.12–4.35, p = 0.023) remained significantly associated with the presence of physical symptoms experienced in the preceding month. Linear regression revealed that the presence of physical symptoms was associated with higher mean scores in the IES-R, DASS Anxiety, Stress and Depression subscales.
Conclusions: **Our study demonstrates a significant association between the prevalence of physical symptoms and psychological outcomes among healthcare workers during the COVID-19 outbreak.** We postulate that **this association may be bi-directional**, and that timely psychological interventions for healthcare workers with physical symptoms should be considered once an infection has been excluded.

Impact on Public Mental Health

The Impact of Online Information on Self-isolation Intention during the COVID-19 Pandemic: A cross-sectional study.

Farooq A, Laato S, Islam AKMN.
J Med Internet Res.
2020 Apr 21. PMID: 32330115
Level of Evidence: 3 - Cross-sectional study
Type of Article: Research
BLUF: A cross-sectional study, surveyed n=225 participants from a Finnish University and found cyberchondria as a positive (b=0.07, t= 2.929, p=0.003), and information overload as a negative (b=-0.10, t=3.006, 0.003) indirect impact on self-isolation. Where **Cyberchondria** significantly impacts *perceived severity*, and **information overload** impacts on *self-efficacy* ("refers to the individual's beliefs of their capabilities to influence a situation. It also refers to the behavioural skills of a person") and *response cost* ("is the individual's evaluation of the negative impact of specific responses").

Abstract:
Background: During the COVID-19 pandemic, governments issued movement restrictions and placed areas into quarantine to combat the spread of the disease. In addition, individuals were encouraged to adopt personal health measures, such as social isolation. Information regarding the disease and measures were distributed through a variety of channels including social media, news websites and emails. **Previous research suggests that the vast amount of available information can be confusing, potentially resulting in over-concern and information overload.**
Objective: We investigate the impact of online information on individual-level intention to voluntarily self-isolate during the pandemic. Using the protection-motivation theory as a framework, **we propose a model outlining the effect of cyberchondria ["defined as obsessive online searching for health-related information, typically about specific symptoms [3]"] and information overload on individuals' perceptions and motivation**.
Methods: To test the proposed model, we **collected data with an online survey (N=225) [from Finnish participants] and analysed it using partial least square-structural equation modelling (PLS-SEM)**. The effects of social media and living situation were tested through multi-group analysis (PLS-MGA).
Results: Cyberchondria and information overload had a **significant impact on individuals' threat and coping perceptions, and through them on self-isolation intention**. Among the appraisal constructs, perceived severity (P=0.002) and self-efficacy (P=0.003) positively impacted self-isolation intention while response cost (P<0.001) affected the intention negatively. Cyberchondria (P=0.003) and information overload (P=0.003) indirectly affected self-isolation

intention through the aforementioned perceptions. **Using social media as an information source increased both cyberchondria and information overload**. **No difference in perceptions was found between people living alone and those living with their families**. (P>0.05).
Conclusions: During COVID-19, frequent use of social media contributed to information overload and over concern among individuals. In addition, to boost individuals' motivation to adopt preventive measures such as self-isolation, actions should focus on lowering individuals' perceived response costs in addition to informing them about the severity of the situation.

Physical Distancing in COVID-19 May Exacerbate Experiences of Social Isolation among People Living with HIV.

Marziali ME, Card KG, McLinden T, Wang L, Trigg J, Hogg RS.Marziali ME, et al.
AIDS Behav.
2020 Apr 23; PMID: 32328849
Level of Evidence: 5 - Expert Opinion
Type of Article: Editorial
Summary: People living with HIV (PLHIV) have been shown in previous studies to be at greater risk of social isolation, and they are more susceptible to loneliness due to the social distancing needed during the COVID-19 crisis. It is recommended to **contribute funds towards online projects to prevent social isolation for PLHIV, since loneliness is correlated with poorer health outcomes.**

From Helpless to Hero: Promoting Values-Based Behavior and Positive Family Interaction in the Midst of COVID-19.

Szabo TG, Richling S, Embry DD, Biglan A, Wilson KG
Behav Anal Pract.
2020 Apr 23; PMID: 32328219
Level of Evidence: 5- Expert opinion
Type of Article: Technical and Tutorials
BLUF: This article is a summary of tools for behavior analysts serving families with small children during this COVID-19 pandemic on the various behavior-change strategies that are deemed evidence-based “kernels,” (practices).

Abstract: Parents managing their home environments during government-ordered stay-at-home periods are likely to need new skills for occupying their children's time with activities that promote health and emotional well-being. Moreover, parents and children know they need help managing these circumstances. Perhaps for the first time, behavior analysts hold the reinforcers for increasing parental involvement in effective child-rearing practices. In fact, behavior analysts can help parents enlist their children in managing the household by framing their behavior in terms of hidden superpowers. In the current article, we argue that **behavior analysts have a range of tools to offer that are grounded in evidence-based principles, strategies, and kernels-or essential units of behavioral influence. When combined into scheduled daily practices and invoked by children taught to see their use of the tools as nothing short of heroic, these practices function as "vaccinations" that inoculate families against toxic and unsafe behaviors**.

Effect of COVID-19 on the Mental Health Care of Older People in Canada.

Flint AJ, Bingham KS, Iaboni A.Flint AJ, et al.
Int Psychogeriatr.

2020 Apr 24; PMID: 32326993
Level of Evidence: 5 - Expert Opinion
Type of Article: Commentary
Summarizing Excerpt: " [Social distancing] has made it challenging to provide mental health care to residents of [long term care homes; nursing homes] LTCH, where psychogeriatric staff would previously visit the homes to provide care. Among the challenges are the limited availability of portable telemedicine technology in some LTCH and the difficulty of providing virtual care to residents who are in isolation because of infection…The current model of widespread provision of virtual care will remain in place until social distancing rules are significantly relaxed, which will likely depend on the development of a vaccine, and possibly efficacious therapeutics, to manage the COVID-19 pandemic (Powell, 2020). However, the current crisis will hopefully lead to more sustained integration of virtual care into geriatric psychiatry practice in the future, leading to more person-centred care and improved access to care."

Drawing on Kinship Care Support for Older People during a Pandemic (COVID-19): Practice Considerations for Social Workers in Ghana.

Cudjoe E, Abdullah A.
J Gerontol Soc Work
2020 Apr 24; PMID: 32326853
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter to Editor
Summarizing excerpt: "In a low-income country like Ghana with few resources to meet the needs of older people at risk of the COVID-19, we write this to propose alternative approaches [kinship care practices] for social workers working to promote the wellbeing of older people during a period of physical distancing."

Abstract: Undoubtedly, the ongoing COVID-19 pandemic has brought both systemic, practice changes and limitations to social workers' commitment to the welfare of vulnerable populations such as older people. A golden preventive rule of the COVID-19 pandemic; maintaining physical and social distancing, has limited social workers' direct practice support for older people who are considered as an at-risk population. **Within jurisdictions such as Ghana where kinship care practices are culturally engrained, social workers should promote kinship care support as substitute mechanisms and pathways to safeguard or meet the welfare needs of older people**.

Suicide Risk and Prevention during the COVID-19 Pandemic.

Gunnell D, Appleby L, Arensman E, Hawton K, John A, Kapur N, Khan M, O'Connor RC, Pirkis J.
Lancet Psychiatry.
2020 Apr 21. PMID: 32330430
Level of Evidence: 5- Expert Opinion
Type of Article: Comment
Summary [excerpt]: "These are unprecedented times. The pandemic will cause distress and leave many people vulnerable to mental health problems and suicidal behaviour. Mental health consequences are likely to be present for longer and peak later than the actual pandemic. However, research evidence and the experience of national strategies provide a strong basis for suicide prevention…The views and recommendations in this Comment are endorsed by the International Association of Suicide Prevention, the American Foundation for Suicide Prevention, and the International Academy of Suicide Research."

Resources

COVID-19 Research in Brief: 18 April to 24 April, 2020

DCarvalho, Thiago
Nat Med
2020 Apr 26; PMID: 32332875
Level of Evidence: 5 – Expert Opinion
Type of Article: Commentary

Summary:
A summary of some of the research that has taken place this week:

- Human trials of Oxford University's COVID-19 vaccine have begun.
- Hypertension has consistently been reported as a frequent comorbidity in COVID-19 patients.
- A study found that 64.4% of those surveyed reported an altered sense of smell or taste.
- Reliable data on the levels and kinetics of antibodies to SARS-CoV-2 in subclinical patients remains severely lacking.

Keeping up with studies on covid-19: systematic search strategies and resources.

Shokraneh F
BMJ
2020 Apr 23; PMID: 32327431
Level of Evidence: 6 - No data cited
Type of Article: Letter

Summary: The author of this letter provides a recommended list of various resources for accessing the evolving literature on COVID-19:

- PubMed for Recent Published Literature on COVID-19
- Live Strategy and Results in Current PubMed: https://tinyurl.com/waj7hmj
- Live Strategy and Results in Future PubMed: https://tinyurl.com/uwbsvo2
- medRxiv and bioRxiv for Unpublished Studies on COVID-19: https://connect.medrxiv.org/relate/content/181
- ClinicalTrials.Gov for Clinical Trials on COVID-19
- Live Strategy and Results: https://tinyurl.com/t9vwzfo
- Google Scholar for Published and Unpublished Literature on COVID-19
- Live Strategy and Results: https://tinyurl.com/spj6oox
- zCOVID-19: Living Map of the Evidence: https://tinyurl.com/rw5ym7x
- Cochrane Resources on Coronavirus (COVID-19): https://www.cochranelibrary.com/covid-19
- Oxford COVID-19 Evidence Service: https://www.cebm.net/covid-19/
- NICE Rapid Guideline and Summaries on COVID-19: https://www.nice.org.uk/covid-19
- WHO Coronavirus disease (COVID-19) Pandemic: https://www.who.int/emergencies/diseases/novel-coronavirus-2019

SARS-CoV-2 causing pneumonia-associated respiratory disorder (COVID-19): diagnostic and proposed therapeutic options.

Chakraborty C, Sharma AR, Sharma G, Bhattacharya M, Lee SS.Chakraborty C, et al.
Eur Rev Med Pharmacol Sci.
2020 Apr 24; PMID: 32329877
Level of Evidence: 5 - Expert Opinion

Type of Article: Review

BLUF: This review attempts to briefly summarize much of what is currently known about COVID-19 - epidemiology, common and severe clinical features, disease in patients with comorbid conditions, diagnostic approaches, imaging, the current array of proposed therapies, and possible vaccine candidates.

Abstract:

SARS-CoV-2 is responsible for the outbreak of severe respiratory illness (COVID-19) in Wuhan City, China and is now spreading rapidly throughout the world. The prompt outbreak of COVID-19 and its quick spread without any controllable measure defines the severity of the situation. In this crisis, a collective pool of knowledge about the advancement of clinical diagnostic and management for COVID-19 is a prerequisite. Here, we summarize all the available updates on the multidisciplinary approaches for the advancement of diagnosis and proposed therapeutic strategies for COVID-19. Moreover, the review discusses different aspects of the COVID-19, including its epidemiology; incubation period; the general clinical features of patients; the clinical features of intensive care unit (ICU) patients; SARS-CoV-2 infection in the presence of co-morbid diseases and the clinical features of pediatric patients infected with the SARS-CoV-2. Advances in various diagnostic approaches, such as the use of real-time polymerase chain reaction (RT-PCR), chest radiography, and computed tomography (CT) imaging; and other modern diagnostic methods, for this infection have been highlighted. However, due to the unavailability of adequate evidence, presently there are no officially approved drugs or vaccines available against SARS-CoV-2. Additionally, we have discussed various therapeutic strategies for COVID-19 under different categories, like the possible treatment plans with drug (antiviral drugs and anti-cytokines) therapy for disease prevention. Lastly, potentials *(sic)* candidates for the vaccines against SARS-CoV-2 infection have been described. Collectively, the review provides an overview of the SARS-CoV-2 infection outbreak along with the recent advancements and strategies for diagnosis and therapy of COVID-19.

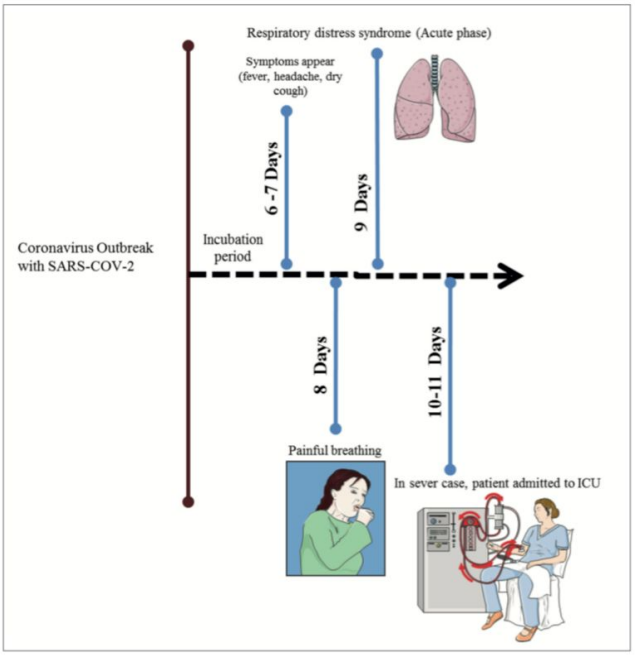


Figure 2. The appearance of symptoms of COVID-19 in respect of days.

Leveraging open hardware to alleviate the burden of COVID-19 on global health systems.

Maia Chagas A, Molloy JC, Prieto-Godino LL, Baden T.
PLoS Biology
2020 Apr 24; PMID: 32330124
Level of Evidence: 5 – Descriptive projects
Type of Article: Review
BLUF: This review provides a summary of current Free and Open Source scientific and medical Hardware (FOSH) related initiatives aiming to meet the global challenge of COVID-19.

Abstract:
With the current rapid spread of COVID-19, global health systems are increasingly overburdened by the sheer number of people that need diagnosis, isolation and treatment. Shortcomings are evident across the board, from staffing, facilities for rapid and reliable testing to availability of hospital beds and key medical-grade equipment. The scale and breadth of the problem calls for an equally substantive response not only from frontline workers such as medical staff and scientists, but from skilled members of the public who have the time, facilities and knowledge to meaningfully contribute to a consolidated global response. Here, we summarise community-driven approaches based on Free and Open Source scientific and medical Hardware (FOSH) as well as personal protective equipment (PPE) currently being developed and deployed to support the global response for COVID-19 prevention, patient treatment and diagnostics.

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