The Daily COVID-19 Literature Surveillance Summary

September 08, 2020

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COVID-19 Daily Literature Surveillance

COVID19LST

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

LEVEL OF EVIDENCE

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

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

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

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

How to cite the Levels of Evidence Table

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

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

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

EXECUTIVE SUMMARY

Epidemiology

- Experienced scientists from the Center for Tobacco Control Research and Education at the University of California San Francisco conducted a meta-analysis of 19 peer-reviewed papers (i^2 = 38%, p=0.048) involving 11,590 COVID-19 patients. They found a positive association between smoking and severe progression of COVD-19 (29.8% of smokers vs 17.6% of nonsmokers; OR 1.91, 95% CI 1.42–2.59, p = .001). Authors suggest that while this data clearly shows smoking puts COVID-19 patients at increased risk for disease progression, the actual risk may be even higher due to limitations in the reviewed papers.

Transmission & Prevention

- Infection control experts from West China Hospital of Sichuan University in Chengdu discuss prevention measures implemented to protect healthcare workers (HCW) across China, including mask-wearing for workers, securing and providing personal protective equipment, using fluid resistant protective clothing and respirators, allocating specific hospitals for COVID-19 patients, and enacting strict community lockdown procedures. Because none of the 42,600 HCWs dispatched to Hubei Province contracted SARS-CoV-2 after implementation of these measures (compared to 3387 prior), the authors suggest early adoption of these measures allowed for decreased transmission of COVID-19 to HCWs.

Adjusting Practice During COVID-19

- Spanish dermatologists discuss a scabies outbreak in their region during the nationwide lockdown in March-May, 2020, with a three-fold increase in reported cases at a single hospital compared to the same period in the previous five years. Authors suggest that time spent in confinement increased fomite transmission and that individuals were less likely to seek treatment until the scabies lesions became more serious leading to more cases in family clusters, longer infection time due to reinfection, and the need for more aggressive treatment regimens to treat resistant infections.

R&D: Diagnosis & Treatments

- Lab scientists from the Tamil Nadu Veterinary and Animal Sciences University in Chennai, India reviewed the limited existing literature related to antibody-dependent enhancement (ADE) and its potential impact on the effectiveness of immunotherapy and vaccine development for SARS-CoV-2. Citing evidence from research on MERS-CoV and SARS-CoV, authors suggest ADE, which occurs when non-neutralizing or poorly neutralizing antibodies increase viral entry into cells, may intensify coronavirus infection. However, they propose targeting receptor binding motifs as a possible mitigation strategy.

- Entomologists from Kyushu University in Japan describe their method for producing antigenic SARS-CoV-2 spike protein (S protein) using the baculovirus expression vector system (BEVS) to induce S protein secretion in silkworm serum in ten days. Citing the speed, low-cost, and success of antigen production with this method, authors suggest BEVS could allow larger scale SARS-CoV-2 S protein production for imumunodetection kits and vaccine development.

- Health policy experts from the University of Michigan and Boston University discuss the Orphan Drug Act, which incentivizes drug development for rare diseases, and its inconsistent application to diseases eventually shown to be common, citing remdesivir's designation during the early COVID-19 crisis as an example. The authors suggest pharmaceutical companies take advantage of policy loopholes and propose amending the Orphan Drug Act so that it better serves its intended purpose.

Mental Health & Resilience Needs

- A representative panel survey of adults (n=5,470) conducted across the United States by Australian and American researchers found the mental health impact of COVID-19 disproportionately affected young adults, certain racial/ethnic minorities, essential workers, unpaid adult caregivers, and individuals with pre-existing psychiatric conditions. Authors recommend COVID-19-specific mental health interventions and prevention efforts be implemented to improve care for the at-risk populations identified by this study (see summary).

Silver Linings

- Utilizing data from the Epidemiological Surveillance Network from Madrid Autonomous Community, epidemiologists from Madrid, Spain compared the number of cases of reportable communicable diseases in the first quarter of 2020 compared to 2019. They found a decrease in both food borne illnesses (Campylobacter [1308 vs 391], Salmonella [462 vs 111]) and sexually transmitted diseases (Neisseria gonorrhea [1056 vs 196], Chlamydia infection

[1212 vs 292], syphilis [425 vs 114]), though they do not provide levels of significance. The authors suggest that COVID-19 control measures (social distancing, shut down of restaurants and clubs, and decreased tourism) also drove this decrease in other communicable disease. However, they acknowledge underreporting and reluctance to seek treatment during a pandemic may also have affected data collection.

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EPIDEMIOLOGY

SYMPTOMS AND CLINICAL PRESENTATION

PULMONARY LIMITED ANCA-ASSOCIATED VASCULITIS MIMICKING COVID-19

Moezinia CJ, Ji-Xu A, Singh A, Stratton R.. J Clin Rheumatol. 2020 Sep;26(6):238-239. doi: 10.1097/RHU.0000000000001482.
Level of Evidence: Other - Case Report

BLUF

Rheumatologists from the UK describe a case report of a 69 year old woman with recent travel to Malaga, Spain who presented with severe myalgias, dyspnea, non-productive cough, and O2 saturation of 80% and was admitted with presumed COVID-19. Labs (leukocytosis) and CT findings (dense bilateral perihilar consolidation suggestive of pulmonary hemorrhage) (Figure 1) were atypical for a COVID-19 patient and she was SARS-CoV-2 negative twice. She was found to have proteinase 3 antibody and c-ANCA positivity and was diagnosed with ANCA-associated vasculitis. Authors suggest this case underscores the importance of considering other etiologies even in patients presenting with initially high clinical suspicion for COVID-19.

FIGURES

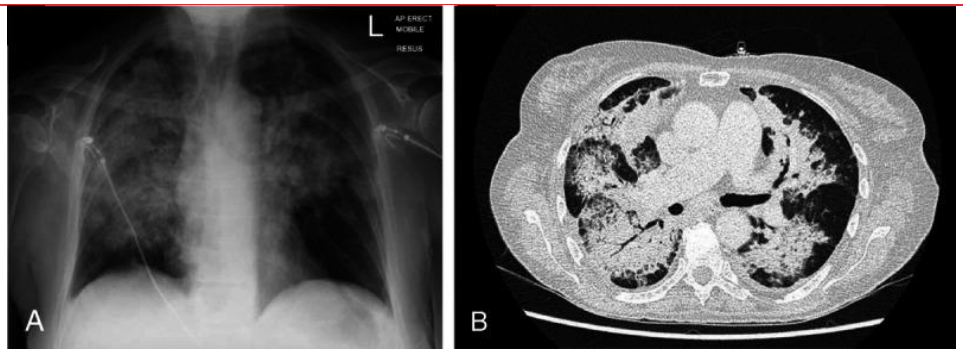


Figure 1. A, Chest radiograph showing perihilar consolidation with sparing of the peripheral fields, more prominent and diffuse in the right lung field, with blunting of the costophrenic angles, consistent with small bilateral pleural effusions. B, CT chest showed extensive bilateral consolidation with relative sparing of the peripheries and small bilateral pleural effusions.

ADULTS

SMOKING IS ASSOCIATED WITH COVID-19 PROGRESSION: A META-ANALYSIS

Patanavanich R, Glantz SA.. Nicotine Tob Res. 2020 Aug 24;22(9):1653-1656. doi: 10.1093/ntr/ntaa082.
Level of Evidence: 2 - Systematic review of surveys that allow matching to local circumstances

BLUF

Experienced scientists from the Center for Tobacco Control Research and Education at the University of California San Francisco conducted a meta-analysis of 19 peer-reviewed papers published between January 1 and April 28, 2020 (i^2 = 38%, p=0.048) involving 11,590 COVID-19 patients. They found a positive association between smoking and severe progression of COVD-19 (29.8% of smokers vs 17.6% of nonsmokers; OR 1.91, 95% CI 1.42–2.59, p = .001)(Figure 1). Authors suggest that while this data clearly shows smoking puts COVID-19 patients at increased risk for disease progression, the actual risk may be even higher due to limitations in the reviewed papers (Summary).

SUMMARY

As motivation for this study, the authors discuss a previous meta analysis which postulated that smoking might have a protective effect against COVID-19 disease progression and highlight the fact that the previous meta analysis only included 5 studies and used a nonstandard method of computation. (Previous meta-analysis: Lippi G, Henry BM. Active smoking is not associated with severity of coronavirus disease 2019 (COVID-19). Eur J Intern Med. 2020;75(May):107–108. doi:10.1016/j.ejim.2020.03.014).

The authors conducted a systematic search for peer-reviewed papers published between January 1 and April 28, 2020 (search terms “smoking”, “smoker*”, “characteristics”, “risk factors”, “outcomes”, and “COVID-19”, “COVID”, “coronavirus”, “sar cov-2”, “sar cov 2”). They found 19 which included data on smoking and COVID-19 disease progression, including 11,590 patients in their analysis (i^2 = 38%, p=0.048). They found a positive association between smoking and severe progression of COVD-19 (29.8% of smokers vs 17.6% of nonsmokers; OR 1.91, 95% CI 1.42–2.59, p=0.001).

The authors acknowledge certain limitations in these findings, notably that they were unable to discern between history of smoking and active smokers due to inconsistency of data collection among studies. Additionally many smokers may have been classified as nonsmokers and none of the studies include e-cigarette use. Because data was collected from patients already diagnosed with COVID-19 who later admitted to smoking, the authors reiterate these data cannot speak to the effect of smoking on contraction of COVID-19. However, authors suggest that all of these limitations only serve to underestimate the negative effect that smoking has on disease progression of COVID-19, and its true negative effect is likely much higher.

FIGURES

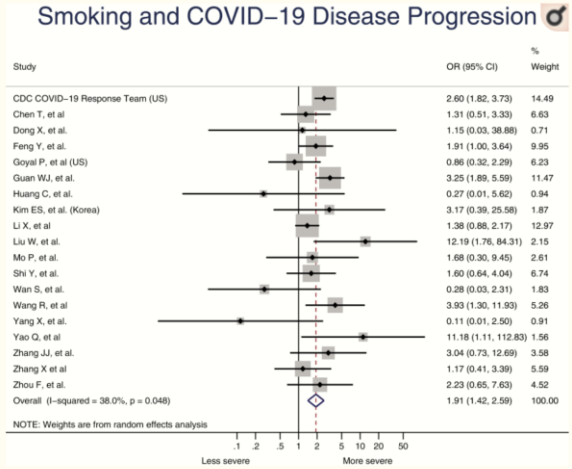


Figure 1.

Smoking is associated with COVID-19 progression. All papers from China unless otherwise indicated. CI = confidence interval; OR = odds ratio.

NEUROLOGICAL INJURIES IN COVID-19 PATIENTS: DIRECT VIRAL INVASION OR A BYSTANDER INJURY AFTER INFECTION OF EPITHELIAL/ENDOTHELIAL CELLS

Azizi SA, Azizi SA.. J Neurovirol. 2020 Sep 2. doi: 10.1007/s13365-020-00903-7. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

A review by a Global Neuroscience Institute neurologist discussed how the pathophysiology of SARS-CoV-2 can result in neurological injury such as stroke (Table 1), anosmia, and ageusia through endothelial cell damage and increased antibody response resulting in coagulopathy (Figure 3). This study suggests that COVID-19 indirectly causes neurological injury in patients and that the cause of more complicated neurological pathologies such as encephalopathy results from multiple factors including hypoxia, inflammation, and electrolyte imbalance (Figure 4).

ABSTRACT

A subset of patients with coronavirus 2 disease (COVID-19) experience neurological complications. These complications include loss of sense of taste and smell, stroke, delirium, and neuromuscular signs and symptoms. The etiological agent of COVID-19 is SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), an RNA virus with a glycoprotein-studded viral envelope that uses ACE2 (angiotensin-converting enzyme 2) as a functional receptor for infecting the host cells. Thus, the interaction of the envelope spike proteins with ACE2 on host cells determines the tropism and virulence of SARS-CoV-2. Loss of sense of taste and smell is an initial symptom of COVID-19 because the virus enters the nasal and oral cavities first and the epithelial cells are the receptors for these senses. Stroke in COVID-19 patients is likely a consequence of coagulopathy and injury to cerebral vascular endothelial cells that cause thrombo-embolism and stroke. Delirium and encephalopathy in acute and post COVID-19 patients are likely multifactorial and secondary to hypoxia, metabolic abnormalities, and immunological abnormalities. Thus far, there is no clear evidence that coronaviruses cause inflammatory neuromuscular diseases via direct invasion of peripheral nerves or muscles or via molecular mimicry. It appears that most of neurologic complications in COVID-19 patients are indirect and as a result of a bystander injury to neurons.

FIGURES

Table 1 A listing of studies on stroke in COVID-19 patients. In general, reports demonstrate coagulopathy and the ensuing complications including stroke. Case reports are not included

Studies	No. of COVID-19 patients	No. of strokes	Age
*Oxlely et al.	–	5	33–49
Helms et al.	150	7 (4.7%)	63
Klok et al.	184	5 (2.7%)	64
Mao et al.	214	6 (2.8%)	52.7
*Qin et al.	1875	50 (2.7%)	63
Yaghi et al.	3556	32 (0.9%)	40s–70s
Lodigiani et al.	362	9 (2.5%)	66
Merkler et al.	1916	31 (1.6%)	69

*These reports explore effects of stroke on COVID-19 and vice versa

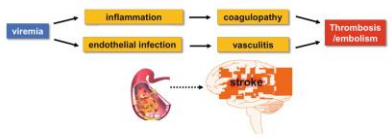


Fig. 3 A box-and-arrow diagram depicting the pathogenesis of stroke in COVID-19 patients. The two proximate causes of stroke are cerebral vascular endothelialitis and coagulopathy; these can result in embolic and thrombotic strokes

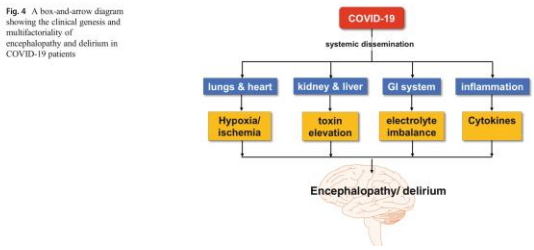


Fig. 4 A box-and-arrow diagram showing the clinical genesis and multifactoriality of encephalopathy and delirium in COVID-19 patients

ON HAPPY HYPOXIA AND ON SADLY IGNORED "ACUTE VASCULAR DISTRESS SYNDROME" IN COVID-19 PATIENTS

Jounieaux V, Rodenstein DO, Mahjoub Y.. Am J Respir Crit Care Med. 2020 Aug 19. doi: 10.1164/rccm.202006-2521LE. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

Pulmonologists from University Hospital Centre in Amiens, France discuss their disagreement with the conclusions of the publication “Why COVID-19 Silent Hypoxemia is Baffling to Physicians” by Tobin, et al. Based on the authors' own unpublished observation of a right-to-left pulmonary shunt in a single COVID-19 patient without radiologic lung lesions they propose that silent hypoxemia in COVID-19 patients may be the result of hypocapnia stemming from the described shunt physiology.

IN VITRO

GROWTH, DETECTION, QUANTIFICATION, AND INACTIVATION OF SARS-COV-2

Case JB, Bailey AL, Kim AS, Chen RE, Diamond MS.. Virology. 2020 Sep;548:39-48. doi: 10.1016/j.virol.2020.05.015. Epub 2020 Jun 13.
Level of Evidence: Other - Mechanism-based reasoning

BLUF

Physicians affiliated with Washington University School of Medicine in St. Louis, Missouri used adaptations of Vero cells and SARS-CoV-2 viral samples to assess multiple in vitro methods for SARS-CoV-2 analysis including viral stock generation, RT-qPCR quantification of viral RNA, plaque assays (Figure 2), focus-forming assay through immunostaining of the S protein (Figure 3), detection of viral antigen by flow cytometry (Figure 4), and validated protocols for virus inactivation. Authors propose protocols for each of these methods, suggesting they can be applied experimentally to study SARS-CoV-2 with the goal of advancing understanding of COVID-19.

ABSTRACT

Severe acute respiratory syndrome coronavirus (SARS-CoV)-2 is the agent responsible for the coronavirus disease 2019 (COVID-19) global pandemic. SARS-CoV-2 is closely related to SARS-CoV, which caused the 2003 SARS outbreak. Although numerous reagents were developed to study SARS-CoV infections, few have been applicable to evaluating SARS-CoV-2 infection and immunity. Current limitations in studying SARS-CoV-2 include few validated assays with fully replication-competent wild-type virus. We have developed protocols to propagate, quantify, and work with infectious SARS-CoV-2. Here, we describe: (1) virus stock generation, (2) RT-qPCR quantification of SARS-CoV-2 RNA; (3) detection of SARS-CoV-2 antigen by flow cytometry, (4) quantification of infectious SARS-CoV-2 by focus-forming and plaque assays; and (5) validated protocols for virus inactivation. Collectively, these methods can be adapted to a variety of experimental designs, which should accelerate our understanding of SARS-CoV-2 biology and the development of effective countermeasures against COVID-19.

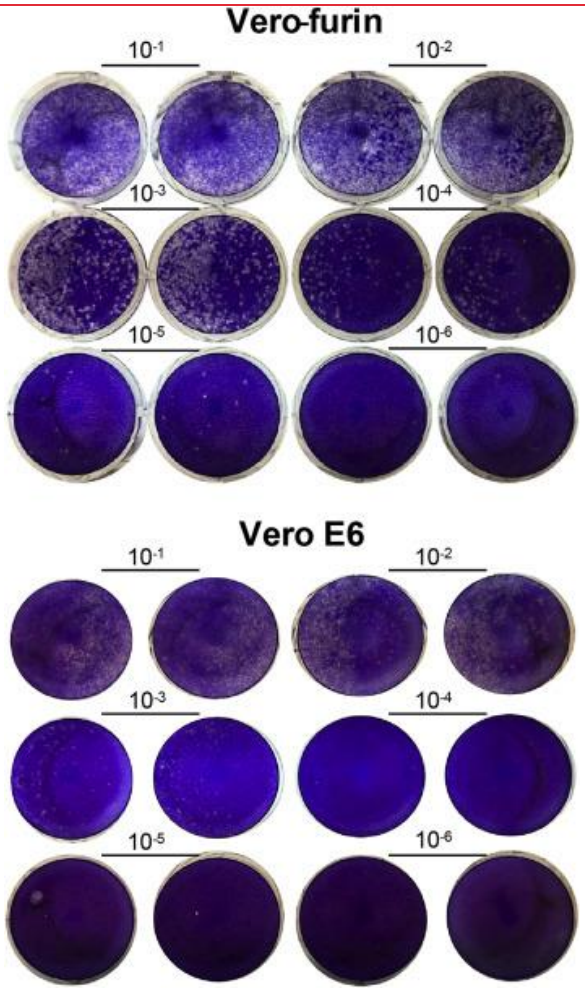


Figure 2. Crystal violet stained plaque assay plates. Vero-furin or Vero E6 cells were inoculated with 10-fold serial dilutions of a SARS-CoV-2 stock. Plates were fixed three days post-infection and stained with crystal violet. Wells with individual plaques were used to determine the virus titer (Vero-furin 10−4, Vero E6 10−3).

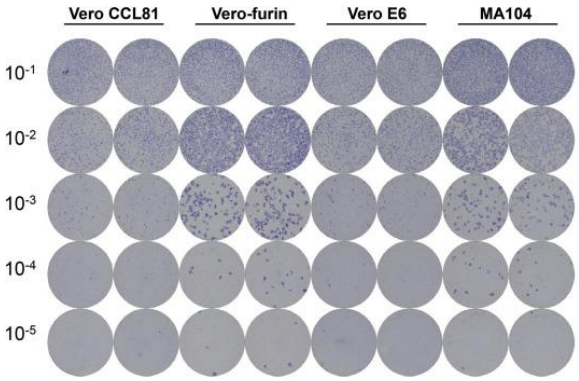


Figure 3. SARS-CoV-2 focus-forming assay. CCL81, Vero-furin, Vero E6, and MA104 cells were inoculated with 10-fold serial dilutions of a SARS-CoV-2 stock. Plates were fixed 30 h post-infection and stained with CR3022 anti-SARS-CoV-2 antibody (1 µg/mL) overnight followed by anti-human IgG-HRP (1:500) for 2 h. Foci were visualized using TrueBlue substrate and wells with discrete foci were used to determine virus titer (10−3 - 10−4).

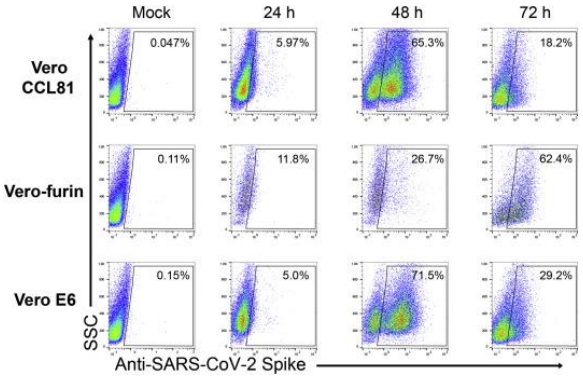


Figure 4. SARS-CoV-2 infected cell flow cytometry plots. Indicated cell types were inoculated with SARS-CoV-2 at an MOI of 0.01 PFU/cell. At each indicated timepoint post-infection, cells were collected and prepared for flow cytometry using CR3022 anti-S as the primary antibody followed by goat-anti-human IgG Alexa 647 as the secondary antibody.

TRANSMISSION & PREVENTION

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

. Am J Health Syst Pharm. 2020 Sep 1:zxaa311. doi: 10.1093/ajhp/zxaa311. Online ahead of print.
Level of Evidence: Other - Guidelines and Recommendations

BLUF

The American Society of Health-System Pharmacists (ASHP) Board of Directors proposed ten principles for mass distribution, allocation, administration, monitoring and surveillance of an approved COVID-19 vaccine (see summary), suggesting that administration of a vaccine globally could be the largest single vaccination effort in history so adhering to these principles may be crucial to provide access to the vaccine in an ethical, equitable and efficient manner.

SUMMARY

The ten ASHP principles are as follows:
"1. Enforce a transparent and rigorous process for vaccine development, approval, and post marketing surveillance.
2. Collaborate and coordinate with domestic and international public health partners to establish and implement a framework for the ethical and equitable global distribution of COVID-19 vaccines.
3. Engage, prepare, and protect the immunizer workforce.
4. Expand patient access to COVID-19 vaccines by leveraging a highly qualified and empowered clinical pharmacy workforce in all settings of care.
5. Adhere to established best practices for proper storage and handling of COVID-19 vaccines throughout the supply chain, from distribution to patient administration.
6. Ensure equitable allocation of COVID-19 vaccines across populations and communities, prioritized for greatest public health impact.
7. Achieve high acceptance and uptake of COVID-19 vaccines by minimizing vaccine hesitancy and misinformation.
8. Seek innovative solutions for adverse drug event monitoring and documentation to improve the thoroughness, accuracy, and usefulness of data collection for improved vaccine safety.
9. Ensure patient access to COVID-19 vaccines by preventing and removing financial barriers.
10. Remain vigilant with continued research and comprehensive surveillance procedures for COVID-19 vaccine use, safety, and effectiveness."

ABSTRACT

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

PREVENTION IN THE COMMUNITY

THE BURDEN OF ALCOHOL ON HEALTH CARE DURING COVID-19

Stockwell T, Andreasson S, Cherpitel C, Chikritzhs T, Dangardt F, Holder H, Naimi T, Sherk A.. Drug Alcohol Rev. 2020 Aug 24. doi: 10.1111/dar.13143. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

An international team of substance use researchers comment on alcohol's impact on healthcare utilization (e.g. increased risk for lung infections, violence, and psychiatric problems). They invoke the 105,065 alcohol-related hospitalizations in Canada in 2017 (Table 1) as evidence of the burden alcohol use places on the healthcare system and criticize governments' lax regulation of a dangerous substance, arguing easy access to alcohol contradicts attempts to protect health systems during the COVID-19 pandemic. They recommend higher taxes on alcohol, mandated health warnings on containers, and reduced opening hours in bars to alleviate healthcare attention and resources used in alcohol-related utilization of healthcare.

ABSTRACT

Alcohol's impact on global health is substantial and of a similar order of magnitude to that from COVID-19. Alcohol now also poses specific concerns, such as increased risk of severe lung infections, domestic violence, child abuse, depression and suicide. Its use is unlikely to aid physical distancing or other preventative behavioural measures. Globally, alcohol contributes to 20% of injury and 11.5% of non-injury emergency room presentations. We provide some broad comparisons between alcohol-attributable and COVID-19-related hospitalisations and deaths in North America using most recent data. For example, for Canada in 2017 it was recently estimated there were 105 065 alcohol-attributable hospitalisations which represent a substantially higher rate over time than the 10 521 COVID-19 hospitalisations reported during the first 5 months of the pandemic. Despite the current importance of protecting health-care services, most governments have deemed alcohol sales to be as essential as food, fuel and pharmaceuticals. In many countries, alcohol is now more readily available and affordable than ever before, a situation global alcohol producers benefit from and have helped engineer. We argue that to protect frontline health-care services and public health more generally, it is essential that modest, evidence-based restrictions on alcohol prices, availability and marketing are introduced. In particular, we recommend increases in excise taxation coupled with minimum unit pricing to both reduce impacts on health-care services and provide much-needed revenues for governments at this critical time.

FIGURES

Table 1. *A comparison of alcohol-attributable hospital stays and deaths with COVID-19 outcomes for Canada*

Condition type	Time period	Hospital stays	Deaths
COVID-19 [19]	1 February to 8 July 2020	10 521	8737
Alcohol-attributable [10]	All 2017	105 065	18 320

PREVENTION IN THE HOSPITAL

ENVIRONMENTAL DISINFECTION AGAINST COVID-19 IN DIFFERENT AREAS OF HEALTH CARE FACILITIES: A REVIEW

Sharafi SM, Ebrahimpour K, Nafez A.. Rev Environ Health. 2020 Aug 26:/j/reveh.ahead-of-print/reveh-2020-0075/reveh-2020-0075.xml. doi: 10.1515/reveh-2020-0075. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

Engineering and environmental health researchers at Isfahan University of Medical Sciences in Iran conducted a review of literature published in a single database through April 15, 2020 related to use of environmental disinfecting agents against SARS-CoV-2 in healthcare settings (Table 1). They reviewed 34 articles and found that the most used methods were UV radiation, ethanol (62-71% concentration), hydrogen peroxide (0.5% concentration), and bleach (0.1% concentration) suggesting that commonly used surface cleaners, when used properly, may adequately inactivate the SARS-CoV-2 virus. Of note, some of the articles cited looked at viruses and bacteria other than SARS-CoV-2 and this review did not include an in-depth comparison of efficacy.

ABSTRACT

The coronavirus disease 2019 (COVID-19) originated in bats and human-to-human transmission through respiratory droplets and contact with surfaces of infected aerosol are the main ways of transmitting this virus. Until now, there is no effective pharmaceutical treatment; conclusively it is important to evaluate the types of applied disinfectants in different areas against Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2), the virus that causes COVID-19. The aim of this review was to summarize the information about environmental disinfection for preventing of COVID-19. We performed a review of the science direct database to find articles providing information on disinfection used for SARS-CoV-2. The extracted results were given the original data on inactivation coronaviruses by disinfectants in different places of health care facilities. The final search recognized that five groups of disinfectants include: chlorine containing disinfectants, alcohol, UV irradiation, Hydrogen peroxide, and other disinfectant were used against SARS-CoV-2 in different environments. Among these groups, bleach (chlorine containing disinfectants) has the most applicability. Also, in many studies by using disinfectants with 62-71% ethanol can reduce coronavirus in contaminated areas. Furthermore, after the using of operating room for COVID-19 patients, hydrogen peroxide and UV irradiation should be used for 24 h before it can be used again. The povidone-iodine or the chlorhexidine, could be recommended when there is a risk of SARS-CoV-2 contamination especially for open wounds.

According to the different studies on SARS-CoV-2 disinfection, because of the SARS-CoV-2 can remain in the air and on surfaces, as well as observing individual disinfection guidelines in different hospital areas, disinfection of surfaces is necessary to decrease SARS-CoV-2 spreading. Moreover, the most suggested disinfectants have been limited to bleach and alcohol, it's better to be considered the potential of other disinfectants in different areas.

FIGURES

Table 1: Types of disinfectants in various places.

		Types of disinfectants					Ref
		Bleach	Alcohol	UV irradiation	Hydrogen peroxide	Other disinfectant	
Various places	Burn ward	✓		✓	✓		[10]
	Histopathology and cytology laboratories	✓	✓	✓		✓	[13, 14]
	Endoscopy	✓			✓	✓	[15, 16]
	Radiology	✓	✓		✓		[17–19]
	Radiotherapy	✓	✓	✓	✓	✓	[20]
	Hemodialysis patients	✓					[21]
	Eye care practitioners	✓					[22]
	Oxygen therapy and respiratory care	✓	✓				[23]
	Dermatology and wound care	✓					[24]
	Doctors fighting the COVID-19	✓					[25]
	Long-term care facilities	✓					[26]
	Trauma patients	✓	✓		✓	✓	[27]
	Pathology-urology interaction		✓				[28]
	Indoor air sampling in patient rooms		✓			✓	[29]
	Disinfection of respirator			✓	✓		[30, 31]
	Cardiac point of care ultrasound and ultrasound examination services			✓	✓		[5, 32]
	Noncontact ultraviolet surface disinfection			✓			[33]
	Center of diagnosis and treatment			✓			[34]
	Tracheal intubation			✓			[35]
	Anesthesia management				✓	✓	[36, 37]

WHY DID SO FEW HEALTHCARE WORKERS IN CHINA GET COVID-19 INFECTION

Zhu S, Zong Z.. QJM. 2020 Aug 18:hcaa254. doi: 10.1093/qjmed/hcaa254. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

Infection control experts from West China Hospital of Sichuan University in Chengdu discuss prevention measures implemented to protect healthcare workers (HCW) across China, including mask-wearing for workers, securing and providing personal protective equipment, using fluid resistant protective clothing and respirators, allocating specific hospitals for COVID-19 patients, and enacting strict community lockdown procedures. Because none of the 42,600 HCWs dispatched to Hubei Province contracted SARS-CoV-2 after implementation of these measures (compared to 3387 prior), the authors suggest early adoption of these measures allowed for decreased transmission of COVID-19 to HCWs.

MANAGEMENT

ACUTE CARE

DIAGNOSTIC RADIOLOGY

CONTRAST-ENHANCED ULTRASOUND IN COVID-19 PNEUMONIA: THE PULMONARY CIRCULATION IS A HIGHLY SPECIALIZED VASCULAR SYSTEM

Quarato CMI, Lacedonia D, Venuti M, Simeone A, Sperandeo M.. J Ultrasound Med. 2020 Aug 31. doi: 10.1002/jum.15452. Online ahead of print.
Level of Evidence: 5 - Expert Opinion

BLUF

A letter to the editor by Italian researchers with expertise in radiology and respiratory medicine discuss their concerns about use of contrast-enhanced ultrasound (US) to diagnose pulmonary embolism (PE) in COVID-19 patients as described in a paper by Soldati et al, 2020. They suggest the pattern used for PE diagnosis was non-specific, variations in US machine settings can cause diagnostic error, US only enables visualization of 70% the lungs (Figure 1), and US contrast is contraindicated in cases of adult acute respiratory distress syndrome (ARDS). Authors recommend using chest CT for accurate diagnosis of PE.

FIGURES

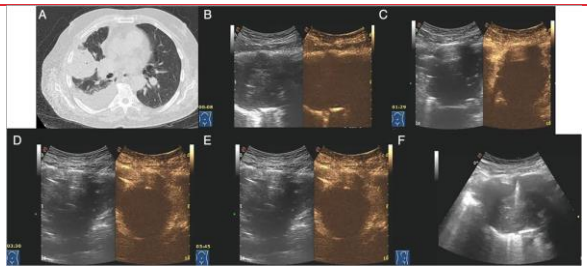


Figure 1. A, Axial CT (lung windows) shows a lung adenocarcinoma in the periphery of the anterior segment of the right lower lobe. B–E, Consecutive CEUS scans show no contrast enhancement over several times after the injection of the contrast medium. F, Ultrasound-guided transthoracic needle biopsy shows the needle during lesion biopsy.

MEDICAL SUBSPECIALTIES

CARDIOLOGY

CARDIAC MANIFESTATIONS IN COVID-19 PATIENTS-A SYSTEMATIC REVIEW

Shafi AMA, Shaikh SA, Shirke MM, Iddawela S, Harky A.. J Card Surg. 2020 Jul 11. doi: 10.1111/jocs.14808. Online ahead of print.
Level of Evidence: 1 - Systematic review of inception cohort studies

BLUF

A group of researchers in the UK performed a systematic review of 61 articles to identify cardiac manifestations in COVID-19 patients with pre-existing cardiovascular comorbidities. They found that cardiac biomarkers such as elevated troponin (17%; 278/1659), CK (18%; 84/466), CK-MB (12%; 133/1148), and BNP (28%; 106/380) are useful as prognostic indicators for patients at high risk of cardiovascular mortality. They believe these markers will help healthcare workers identify patients with cardiovascular comorbidities who might be prone to more severe complications, allowing for timely escalation of treatment.

ABSTRACT

OBJECTIVES: The coronavirus disease-2019 (COVID-19) pandemic has resulted in the worst global pandemic of our generation, affecting 215 countries with nearly 5.5 million cases. The association between COVID-19 and the cardiovascular system has been well described. We sought to systematically review the current published literature on the different cardiac manifestations and the use of cardiac-specific biomarkers in terms of their prognostic value in determining clinical outcomes and correlation to disease severity. METHODS: A systematic literature review across PubMed, Cochrane database, Embase, Google Scholar, and Ovid was performed according to PRISMA guidelines to identify relevant articles that discussed risk factors for cardiovascular manifestations, cardiac manifestations in COVID-19 patients, and cardiac-specific biomarkers with their clinical implications on COVID-19. RESULTS: Sixty-one relevant articles were identified which described risk factors for cardiovascular manifestations, cardiac manifestations (including heart failure, cardiogenic shock, arrhythmia, and myocarditis among others) and cardiac-specific biomarkers (including CK-MB, CK, myoglobin, troponin, and NT-proBNP). Cardiovascular risk factors can play a crucial role in identifying patients vulnerable to developing cardiovascular manifestations of COVID-19 and thus help to save lives. A wide array of cardiac manifestations is associated with the interaction between COVID-19 and the cardiovascular system. Cardiac-specific biomarkers provide a useful prognostic tool in helping identify patients with the severe disease early and allowing for escalation of treatment in a timely fashion. CONCLUSION: COVID-19 is an evolving pandemic with predominate respiratory manifestations, however, due to the interaction with the cardiovascular system; cardiac manifestations/complications feature heavily in this disease, with cardiac biomarkers providing important prognostic information.

DERMATOLOGY

SCABIES OUTBREAK DURING HOME CONFINEMENT DUE TO THE SARS-COV-2 PANDEMIC

Martínez-Pallás I, Aldea-Manrique B, Ramírez-Lluch M, Vinuesa-Hernando JM, Ara-Martín M.. J Eur Acad Dermatol Venereol. 2020 Aug 18. doi: 10.1111/jdv.16879. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

Spanish dermatologists discuss a scabies outbreak in their region during the nationwide lockdown in March-May, 2020, with a three-fold increase in reported cases at a single hospital compared to the same period in the previous five years. Authors suggest that time spent in confinement increased fomite transmission and that individuals were less likely to seek treatment until the scabies lesions became more serious (see Figure 1) leading to more cases in family clusters, longer infection time due to reinfection, and the need for more aggressive treatment regimens to treat resistant infections (Table 1).

ABSTRACT

In response to the rapid spread of COVID-19 at the start of the pandemic, governments introduced severe measures of home confinement and isolation of the population in an effort to prevent their health systems from collapsing. On March 14, with more than 4000 confirmed cases1 , Spain began its nationwide lockdown which has extended for almost three months.

FIGURES

TABLE 1

		Confinement[a]	No confinement[b]	Statistical comparison
N		64	93	
Gender	*Male*	32	48	$\chi^2(1)= 0.01$, $p>0.05$
	Female	32	45	
Age (mean+SD)		30.87±21.28	32.16±25.11	$t(155)= -0.336$, $p>0.05$
Cohabitants +		52 (81.25%)	61 (65.59%)	$\chi^2(1) = 3.865$, $p<0.05$
Family Cluster		35 (54.68%)	18 (19.35%)	$\chi^2(1) = 19.61$, $p<0.05$
Symptoms duration		9.75±5.85	5.77±5.172	(t (154)= 4.47, p<0.05)
Previous treatment		48 (75%)	14 (15.05%)	$\chi^2(1) = 54.53$, $p<0.05$

Treatment with permethrin	64 (100%)	93 (100%)	
Previous applications of permethrin (mean+SD)	4.10±2.94	1.64±0.84	*t(59.9)= -5.123, p<0.05*
Treatment with ivermectin	36 (60.93%)	4 (4.3%)	$\chi^2(1) = 58.33$, $p<0.05$

a) Period between March and May 2020.

b) Period between March and May from 2015 to 2019.

Table 1: Comparison of demographic, clinical and therapeutic data between scabies cases diagnosed during the months of confinement and non-confinement

FIGURES

FIGURE 1

FIGURE LEGENDS

Figure 1: Home-confinement effect on scabies infestation

ROLE OF ANTIBODY-DEPENDENT ENHANCEMENT (ADE) IN THE VIRULENCE OF SARS-COV-2 AND ITS MITIGATION STRATEGIES FOR THE DEVELOPMENT OF VACCINES AND IMMUNOTHERAPIES TO COUNTER COVID-19

Karthik K, Senthilkumar TMA, Udhayavel S, Raj GD.. Hum Vaccin Immunother. 2020 Aug 26:1-6. doi: 10.1080/21645515.2020.1796425. Online ahead of print.
Level of Evidence: 5 - Mechanism-based reasoning

BLUF

Lab scientists from the Tamil Nadu Veterinary and Animal Sciences University in Chennai, India review the limited existing literature related to antibody-dependent enhancement (ADE) and its potential impact on the effectiveness of immunotherapy and vaccine development for SARS-CoV-2. Citing evidence from research on MERS-CoV and SARS-CoV, authors suggest ADE, which occurs when non-neutralizing or poorly neutralizing antibodies increase viral entry into cells (Figure 1), may intensify coronavirus infection. However, they propose targeting receptor binding motifs as a possible mitigation strategy (Figure 2).

ABSTRACT

Coronavirus disease-2019 (COVID-19) pandemic has become a global threat and death tolls are increasing worldwide. The SARS-CoV-2 though shares similarities with SARS-CoV and MERS-CoV, immunopathology of the novel virus is not understood properly. Previous reports from SARS and MERS-CoV documents that preexisting, non-neutralizing or poorly neutralizing antibodies developed as a result of vaccine or infection enhance subsequent infection, a phenomenon called as antibody-dependent enhancement (ADE). Since immunotherapy has been implicated for COVID-19 treatment and vaccine is under development, due consideration has to be provided on ADE to prevent untoward reactions. ADE mitigation strategies like the development of vaccine or immunotherapeutics targeting receptor binding motif can be designed to minimize ADE of SARS-CoV-2 since full-length protein-based approach can lead to ADE as reported in MERS-CoV. The present mini-review aims to address the phenomenon of ADE of SARS-CoV-2 through the lessons learned from SARS-CoV and MERS-CoV and ways to mitigate them so as to develop better vaccines and immunotherapeutics against SARS-CoV-2.

FIGURES

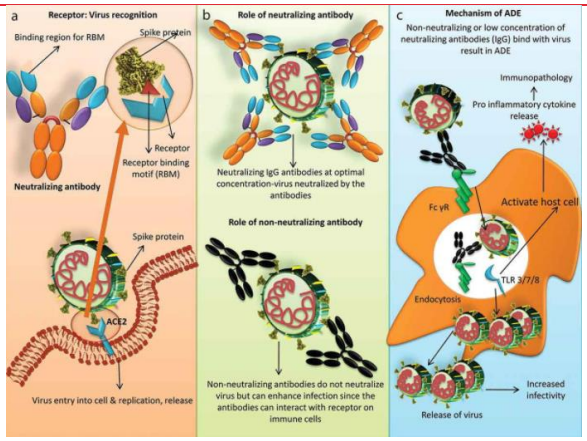


Figure 1. Role of neutralizing and non-neutralizing antibodies in viral infection and mechanism of ADE in SARS-CoV-2. (a) Spike protein of SARS-CoV-2 binds with Angiotensin-Converting Enzyme 2 (ACE2) receptor and undergoes replication. ACE2 recognizes receptor binding motif on the spike protein and the same receptor-binding motif (RBM) is recognized by antibodies. (b) Neutralizing antibodies at optimal concentration neutralizes virus while non-neutralizing antibodies can enhance infection. (c) Mechanism of ADE in SARS-CoV-2. Virus-antibody (neutralizing or non-neutralizing) complex bind to Fcγ receptor on the surface immune cells like monocytes or macrophages leading to virus entry without the use of ACE2 receptor. This leads to increased virus replication and release. Virus-antibody binding to FcγR can also induce proinflammatory response. Viral RNA in the endosomes signal through Toll-like receptor 3 (TLR3), TLR7 or TLR8 activating the host cell to release proinflammatory cytokines which leads to immunopathology.

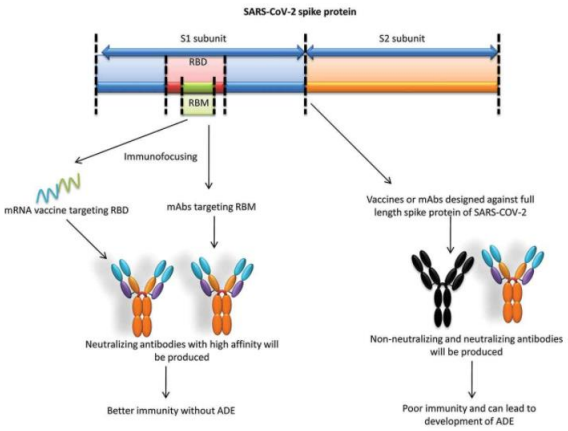


Figure 2. Mitigation strategies of ADE in SARS-CoV-2. Targeting full length spike protein can produce antibody-dependent enhancement (ADE) while immunofocusing or targeting the receptor-binding motif (RBM) can elicit high affinity neutralizing antibodies that can prevent ADE.

EFFICIENT PRODUCTION OF RECOMBINANT SARS-COV-2 SPIKE PROTEIN USING THE BACULOVIRUS-SILKWORM SYSTEM

Fujita R, Hino M, Ebihara T, Nagasato T, Masuda A, Lee JM, Fujii T, Mon H, Kakino K, Nagai R, Tanaka M, Tonooka Y, Moriyama T, Kusakabe T.. Biochem Biophys Res Commun. 2020 Aug 20;529(2):257-262. doi: 10.1016/j.bbrc.2020.06.020. Epub 2020 Jun 9.
Level of Evidence: Other - Mechanism-based reasoning

BLUF

Entomologists from Kyushu University in Japan describe their method for producing antigenic SARS-CoV-2 spike protein (S protein) using the baculovirus expression vector system (BEVS) to induce S protein secretion in silkworm serum in ten days (Figure 1). Citing the speed, low-cost, and success of antigen production with this method (Figure 2), authors suggest BEVS could allow larger scale SARS-CoV-2 S protein production for imumunodetection kits and vaccine development.

ABSTRACT

In the case of a new viral disease outbreak, an immediate development of virus detection kits and vaccines is required. For COVID-19, we established a rapid production procedure for SARS-CoV-2 spike protein (S protein) by using the baculovirus-silkworm expression system. The baculovirus vector-derived S proteins were successfully secreted to silkworm serum, whereas those formed insoluble structure in the larval fat body and the pupal cells. The ectodomain of S protein with the native sequence was cleaved by the host furin-protease, resulting in less recombinant protein production. The S protein modified in furin protease-target site was efficiently secreted to silkworm serum and was purified as oligomers, which showed immunoreactivity for anti-SARS-CoV-2 S2 antibody. By using the direct transfection of recombinant bacmid to silkworms, we achieved the efficient production of SARS-CoV-2 S protein as fetal bovine serum (FBS)-free system. The resultant purified S protein would be useful tools for the development of immunodetection kits, antigen for immunization for immunoglobulin production, and vaccines.

FIGURES

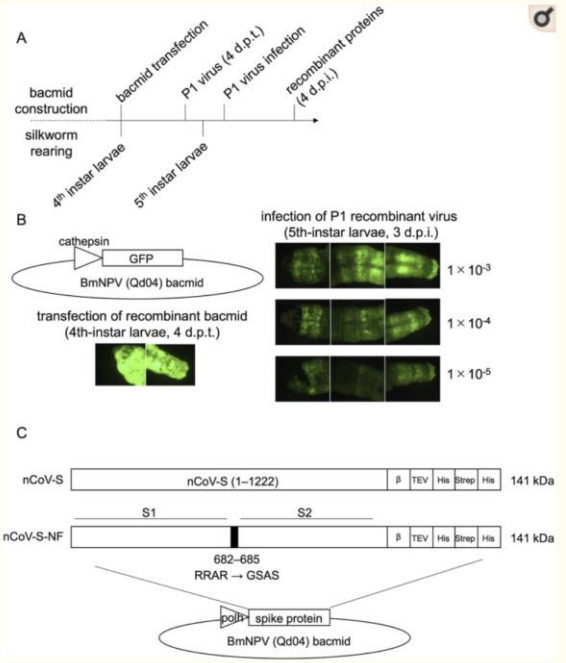
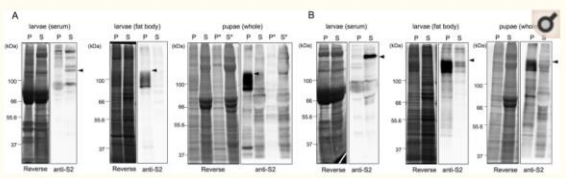


Fig. 1

Construction of recombinant baculovirus and the procedure for protein production. **A:** Schedule for the production of the recombinant viruses and the proteins. Extracted bacmid DNA was transfected to early stages of 4th-instar larvae, and recombinant viruses were recovered four days post-transfection. The viruses were infected to the same rearing series of 5th-instar larvae, and the recombinant proteins were extracted at four days post-infection. **B:** BmNPV bacmid harboring GFP gene under the control of cathepsin promoter was used to monitor the recombinant virus infection. Ten micro litter of the recovered viruses were infected to 5th-instar larvae with the dilution concentration indicated. **C:** Construction of the recombinant BmNPV. The ectodomain of the SARS CoV-2 S gene was fused with the β-sheet domain of CELO knob (β), Tobacco Etch virus protease targeting site (TEV), His-tags (His), and Strep-tag (Strep). The amino acid sequence of 682–685 was replaced with GSAS not to be target by furin protease (nCoV-S-NF).



Open in a separate window

Fig. 2

Expression of recombinant SARS-CoV-2 S proteins in silkworms. **A:** The expression of nCoV-S was analyzed in silkworm larvae and pupae at four days post-infection. The extracted serum and homogenate of fat body and pupal body was separated in pellets (P) and supernatants (S). The left side of each image shows the reverse staining image of SDS-PAGE, and the right sides indicate the Western blot using the anti-SARS-CoV-2 S2 antibody. Black arrowheads indicate the expected size of the expressed proteins. Asterisks indicate the sample from mock-infected pupae. The positions of the molecular marker are also indicated. **B:** The expression analysis of nCoV-S-NF protein.

POLICY IMPLICATIONS OF THE ORPHAN DRUG DESIGNATION FOR REMDESIVIR TO TREAT COVID-19

Chua KP, Conti RM.. JAMA Intern Med. 2020 Aug 17. doi: 10.1001/jamainternmed.2020.2759. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

Health policy experts from the University of Michigan and Boston University discuss the Orphan Drug Act, which incentivizes drug development for rare diseases, and its inconsistent application to diseases eventually shown to be common, citing remdesivir's designation during the early COVID-19 crisis as an example. The authors suggest pharmaceutical companies take

advantage of policy loopholes and propose amending the Orphan Drug Act so that it better serves its intended purpose (Summary).

SUMMARY

Health policy experts from the University of Michigan and Boston University discuss the Orphan Drug Act, which incentivizes drug development for rare diseases. Typically, the act allocated a 25% federal tax credits to sponsors of drugs treating diseases that affect fewer than 200,000 people in an attempt to financially support drugs that would otherwise be unprofitable. The authors suggest drug sponsors take advantage of policy loopholes to acquire orphan drug benefits for diseases that aren't rare, discussing the cases of remdesivir and COVID-19. Earlier in 2020, remdesivir was designated as an orphan drug to treat COVID-19 when it was less common, but the authors argue it no longer deserves orphan drug status since COVID-19 is now common. To close this loophole, authors recommend amending the act so that the Food and Drug Administration could deny this designation for diseases likely to become widespread or revoke the status if the number affected exceeds 200,000. The authors suggest these changes would better allow the act to serve its intended purpose and ensure funding remains in place for developing treatments for truly rare diseases.

MENTAL HEALTH, SUBSTANCE USE, AND SUICIDAL IDEATION DURING THE COVID-19 PANDEMIC - UNITED STATES, JUNE 24-30, 2020

Czeisler MÉ, Lane RI, Petrosky E, Wiley JF, Christensen A, Njai R, Weaver MD, Robbins R, Facer-Childs ER, Barger LK, Czeisler CA, Howard ME, Rajaratnam SMW.. MMWR Morb Mortal Wkly Rep. 2020 Aug 14;69(32):1049-1057. doi: 10.15585/mmwr.mm6932a1.

Level of Evidence: 1 - Local and current random sample surveys (or censuses)

BLUF

A representative panel survey of adults (n=5,470) conducted across the United States from June 24th to June 30th, 2020 by Australian and American researchers found the mental health impact of COVID-19 disproportionately affected young adults, certain racial/ethnic minorities, essential workers, unpaid adult caregivers, and individuals with pre-existing psychiatric conditions (Tables 2,3). Authors recommend COVID-19-specific mental health interventions and prevention efforts be implemented to improve care for the at-risk populations identified by this study (see summary).

SUMMARY

Authors' mental health recommendations as follows:

- Further studies investigating drivers of adverse mental and behavioral health, focused on stressors such as social isolation, financial worries, violence, and absence of school structure.
- Community-level evaluation of mental health, substance use, and suicidal ideation to better determine the impact of the pandemic on psychological distress over time, followed by efforts to reduce stressors.
- Improved communication strategies including culturally and linguistically tailored prevention messaging to promote health services and emotional well-being.
- COVID-19-specific mental health screening instruments for early identification and prevention of COVID-19-related trauma or stressor-related disorders regarding the pandemic.
- Involvement of public health institutions to identify and address mental health disparities as the pandemic evolves.

ABSTRACT

The coronavirus disease 2019 (COVID-19) pandemic has been associated with mental health challenges related to the morbidity and mortality caused by the disease and to mitigation activities, including the impact of physical distancing and stay-at-home orders.* Symptoms of anxiety disorder and depressive disorder increased considerably in the United States during April-June of 2020, compared with the same period in 2019 (1,2). To assess mental health, substance use, and suicidal ideation during the pandemic, representative panel surveys were conducted among adults aged >=18 years across the United States during June 24-30, 2020. Overall, 40.9% of respondents reported at least one adverse mental or behavioral health condition, including symptoms of anxiety disorder or depressive disorder (30.9%), symptoms of a trauma- and stressor-related disorder (TSRD) related to the pandemic (26.3%), and having started or increased substance use to cope with stress or emotions related to COVID-19 (13.3%). The percentage of respondents who reported having seriously considered suicide in the 30 days before completing the survey (10.7%) was significantly higher among respondents aged 18-24 years (25.5%), minority racial/ethnic groups (Hispanic respondents [18.6%], non-Hispanic black [black] respondents [15.1%]), self-reported unpaid caregivers for adults (30.7%), and essential workers (21.7%). Community-level intervention and prevention efforts, including health communication strategies, designed to reach these groups could help address various mental health conditions associated with the COVID-19 pandemic.

Characteristic	Prevalence ratio[¶] (95% CI[¶])			
	Symptoms of anxiety disorder or depressive disorder[†]	Symptoms of a TSRD related to COVID-19[§]	Started or increased substance use to cope with stress or emotions related to COVID-19	Serious consideration of suicide in past 30 days
Gender				
Female vs. male	1.04 (0.96–1.12)	0.88 (0.81–0.97)	0.85 (0.75–0.98)	0.70 (0.60–0.82)**
Age group (yrs)				
18–24 vs. 25–44	1.56 (1.44–1.68)**	1.28 (1.16–1.41)**	1.31 (1.12–1.53)**	1.59 (1.35–1.87)**
18–24 vs. 45–64	3.10 (2.79–3.44)**	2.67 (2.35–3.03)**	3.35 (2.75–4.10)**	6.66 (5.15–8.61)**
18–24 vs. ≥65	7.73 (6.19–9.66)**	5.01 (4.04–6.22)**	8.77 (5.95–12.93)**	12.51 (7.88–19.86)**
25–44 vs. 45–64	1.99 (1.79–2.21)**	2.09 (1.86–2.35)**	2.56 (2.14–3.07)**	4.18 (3.26–5.36)**
25–44 vs. ≥65	4.96 (3.97–6.20)**	3.93 (3.18–4.85)**	6.70 (4.59–9.78)**	7.86 (4.98–12.41)**
45–64 vs. ≥65	2.49 (1.98–3.15)**	1.88 (1.50–2.35)**	2.62 (1.76–3.9)**	1.88 (1.14–3.10)
Race/Ethnicity[††]				
Hispanic vs. non-Hispanic black	1.35 (1.18–1.56)**	1.15 (1.00–1.33)	1.19 (0.97–1.46)	1.23 (0.98–1.55)
Hispanic vs. non-Hispanic Asian	2.27 (1.73–2.98)**	1.59 (1.24–2.04)**	3.29 (2.05–5.28)**	2.82 (1.74–4.57)**
Hispanic vs. non-Hispanic other race or multiple races	1.23 (0.98–1.55)	1.24 (0.96–1.61)	1.99 (1.27–3.13)**	1.89 (1.16–3.06)
Hispanic vs. non-Hispanic white	1.40 (1.27–1.54)**	1.50 (1.35–1.68)**	2.09 (1.79–2.45)**	2.35 (1.96–2.80)**
Non-Hispanic black vs. non-Hispanic Asian	1.68 (1.26–2.23)**	1.38 (1.07–1.78)	2.75 (1.70–4.47)**	2.29 (1.39–3.76)**
Non-Hispanic black vs. non-Hispanic other race or multiple races	0.91 (0.71–1.16)	1.08 (0.82–1.41)	1.67 (1.05–2.65)	1.53 (0.93–2.52)
Non-Hispanic black vs. non-Hispanic white	1.03 (0.91–1.17)	1.30 (1.14–1.48)**	1.75 (1.45–2.11)**	1.90 (1.54–2.36)**
Non-Hispanic Asian vs. non-Hispanic other race or multiple races	0.54 (0.39–0.76)**	0.78 (0.56–1.09)	0.61 (0.32–1.14)	0.67 (0.35–1.29)
Non-Hispanic Asian vs. non-Hispanic white	0.62 (0.47–0.80)**	0.95 (0.74–1.20)	0.64 (0.40–1.02)	0.83 (0.52–1.34)
Non-Hispanic other race or multiple races vs. non-Hispanic white	1.14 (0.91–1.42)	1.21 (0.94–1.56)	1.05 (0.67–1.64)	1.24 (0.77–2)

Table 2. Comparison of symptoms of adverse mental health outcomes among all respondents who completed surveys (N = 5,470), by respondent characteristic* — United States, June 24–30, 2020. See table footnotes on "TABLE 2. (Continued)"

Characteristic	Prevalence ratio[¶] (95% CI[¶])			
	Symptoms of anxiety disorder or depressive disorder[†]	Symptoms of a TSRD related to COVID-19[§]	Started or increased substance use to cope with stress or emotions related to COVID-19	Serious consideration of suicide in past 30 days
Employment status				
Employed vs. unemployed	0.96 (0.87–1.07)	1.28 (1.12–1.46)**	2.30 (1.78–2.98)**	3.21 (2.31–4.47)**
Employed vs. retired	3.01 (2.58–3.51)**	2.84 (2.42–3.34)**	4.30 (3.28–5.63)**	5.97 (4.20–8.47)**
Unemployed vs. retired	3.12 (2.63–3.71)**	2.21 (1.82–2.69)**	1.87 (1.30–2.67)**	1.86 (1.16–2.96)
Essential vs. nonessential worker[§§]	1.42 (1.30–1.56)**	1.52 (1.38–1.69)**	2.36 (2.00–2.77)**	2.76 (2.29–3.33)**
Unpaid caregiver for adults vs. not[¶¶]	2.55 (2.37–2.75)**	2.63 (2.42–2.86)**	5.28 (4.59–6.07)**	8.64 (7.23–10.33)**
Rural vs. urban residence[***]	0.94 (0.82–1.07)	0.96 (0.83–1.11)	0.84 (0.67–1.06)	0.95 (0.74–1.22)
Knows someone with positive SARS-CoV-2 test result vs. not	0.95 (0.86–1.05)	0.78 (0.69–0.88)**	0.96 (0.81–1.14)	0.65 (0.52–0.81)**
Knew someone who died from COVID-19 vs. not	0.99 (0.85–1.15)	1.08 (0.92–1.26)	0.84 (0.64–1.11)	0.69 (0.49–0.97)
Receiving treatment for anxiety vs. not	2.43 (2.26–2.63)**	2.21 (2.01–2.43)**	2.27 (1.94–2.66)**	2.54 (2.13–3.03)**
Receiving treatment for depression vs. not	2.20 (2.03–2.39)**	1.88 (1.70–2.09)**	2.13 (1.81–2.51)**	2.35 (1.96–2.82)**
Receiving treatment for PTSD vs. not	2.75 (2.55–2.97)**	2.87 (2.61–3.16)**	3.78 (3.23–4.42)**	4.95 (4.21–5.83)**

Table 2. (Continued) Comparison of symptoms of adverse mental health outcomes among all respondents who completed surveys (N = 5,470), by respondent characteristic* — United States, June 24–30, 2020

Abbreviations: CI = confidence interval; COVID-19 = coronavirus disease 2019; PTSD = posttraumatic stress disorder; TSRD= trauma- or stress-related disorder.

* Number of respondents for characteristics: gender (female = 2,784, male = 2,676), age group in years (18–24 = 731; 25–44 = 1,911; 45–64 = 1,895; ≥65 = 933), race/ethnicity (non-Hispanic white = 3453, non-Hispanic black = 663, non-Hispanic Asian = 256, non-Hispanic other race or multiple races = 164, Hispanic = 885).

† Symptoms of anxiety disorder and depressive disorder were assessed via the four-item Patient Health Questionnaire (PHQ-4). Those who scored ≥3 out of 6 on the Generalized Anxiety Disorder (GAD-2) and Patient Health Questionnaire (PHQ-2) subscales were considered to have symptoms of these disorders.

§ Disorders classified as TSRDs in the Diagnostic and Statistical Manual of Mental Disorders (DSM–5) include PTSD, acute stress disorder (ASD), and adjustment disorders (ADs), among others. Symptoms of a TSRD precipitated by the COVID-19 pandemic were assessed via the six-item Impact of Event Scale (IES-6) to screen for overlapping symptoms of PTSD, ASD, and ADs. For this survey, the COVID-19 pandemic was specified as the traumatic exposure to record peri- and posttraumatic symptoms associated with the range of stressors introduced by the COVID-19 pandemic. Persons who scored ≥1.75 out of 4 were considered to be symptomatic.

¶ Comparisons within subgroups were evaluated on weighted responses via Poisson regressions used to calculate a prevalence ratio, 95% CI, and p-value (not shown). Statistical significance was evaluated at a threshold of a = 0.005 to account for multiple comparisons. In the calculation of prevalence ratios for started or increased substance use, respondents who selected "Prefer not to answer" (n = 104) were excluded.

** P-value is statistically significant (p<0.005).

†† Respondents identified as a single race unless otherwise specified. The non-Hispanic, other race or multiple races category includes respondents who identified as not Hispanic and as more than one race or as American Indian or Alaska Native, Native Hawaiian or Pacific Islander, or 'Other'.

§§ Essential worker status was self-reported. The comparison was between employed respondents (n = 3,431) who identified as essential vs. nonessential. For this analysis, students who were not separately employed as essential workers were considered nonessential workers.

¶¶ Unpaid adult caregiver status was self-reported. The definition of an unpaid caregiver for adults was having provided unpaid care to a relative or friend aged ≥18 years
to help them take care of themselves at any time in the last three months. Examples provided included helping with personal needs, household chores, health care
tasks, managing a person's finances, taking them to a doctor's appointment, arranging for outside services, and visiting regularly to see how they are doing.

*** Rural-urban classification was determined by using self-reported ZIP codes according to the Federal Office of Rural Health Policy definition of rurality. https://
www.hrsa.gov/rural-health/about-us/definition/datafiles.html.

	Essential worker† vs. all other employment statuses (nonessential worker, unemployed, retired)				Unpaid caregiver for adults§ vs. not unpaid caregiver			
	Unadjusted		Adjusted¶		Unadjusted		Adjusted**	
Symptom or behavior	OR (95% CI)††	p-value††	OR (95% CI)††	p-value††	OR (95% CI)††	p-value††	OR (95% CI)††	p-value††
Symptoms of anxiety disorder§§	1.92 (1.29–2.87)	0.001	1.63 (0.99–2.69)	0.056	1.97 (1.25–3.11)	0.004	1.81 (1.14–2.87)	0.012
Symptoms of depressive disorder§§	1.49 (1.00–2.22)	0.052	1.13 (0.70–1.82)	0.606	2.29 (1.50–3.50)	<0.001	2.22 (1.45–3.41)	<0.001
Symptoms of anxiety disorder or depressive disorder§§	1.67 (1.14–2.46)	0.008	1.26 (0.79–2.00)	0.326	1.84 (1.19–2.85)	0.006	1.73 (1.11–2.70)	0.015
Symptoms of a TSRD related to COVID–19¶¶	1.55 (0.86–2.81)	0.146	1.27 (0.63–2.56)	0.512	1.88 (0.99–3.56)	0.054	1.79 (0.94–3.42)	0.076
Started or increased substance use to cope with stress or emotions related to COVID–19	2.36 (1.26–4.42)	0.007	2.04 (0.92–4.48)	0.078	3.51 (1.86–6.61)	<0.001	3.33 (1.75–6.31)	<0.001
Serious consideration of suicide in previous 30 days	0.93 (0.31–2.78)	0.895	0.53 (0.16–1.70)	0.285	3.00 (1.20–7.52)	0.019	3.03 (1.20–7.63)	0.019

TABLE 3. Odds of incidence* of symptoms of adverse mental health, substance use to cope with stress or emotions related to COVID–19 pandemic, and suicidal ideation in the third survey wave, by essential worker status and unpaid adult caregiver status among respondents who completed monthly surveys from April through June (N = 1,497) — United States, April 2–8, May 5–12, and June 24–30, 2020.

Abbreviations: CI = confidence interval, COVID–19 = coronavirus disease 2019, OR = odds ratio, TSRD = trauma– and stressor–related disorder.

* For outcomes assessed via the four-item Patient Health Questionnaire (PHQ–4), odds of incidence were marked by the presence of symptoms during May 5–12 or June 24–30, 2020, after the absence of symptoms during April 2–8, 2020. Respondent pools for prospective analysis of odds of incidence (did not screen positive for symptoms during April 2–8): anxiety disorder (n = 1,236), depressive disorder (n = 1,301) and anxiety disorder or depressive disorder (n = 1,190). For symptoms of a TSRD precipitated by COVID–19, started or increased substance use to cope with stress or emotions related to COVID–19, and serious suicidal ideation in the previous 30 days, odds of incidence were marked by the presence of an outcome during June 24–30, 2020, after the absence of that outcome during May 5–12, 2020. Respondent pools for prospective analysis of odds of incidence (did not report symptoms or behavior during May 5–12): symptoms of a TSRD (n = 1,206),
started or increased substance use (n = 1,408), and suicidal ideation (n = 1,456).

† Essential worker status was self–reported. For Table 3, essential worker status was determined by identification as an essential worker during the June 24–30 survey.
Essential workers were compared with all other respondents, not just employed respondents (i.e., essential workers vs. all other employment statuses [nonessential
worker, unemployed, and retired], not essential vs. nonessential workers).

§ Unpaid adult caregiver status was self–reported. The definition of an unpaid caregiver for adults was having provided unpaid care to a relative or friend 18 years or
older to help them take care of themselves at any time in the last three months. Examples provided included helping with personal needs, household chores, health
care tasks, managing a person's finances, taking them to a doctor's appointment, arranging for outside services, and visiting regularly to see how they are doing. ¶ Adjusted for gender, employment status, and unpaid adult caregiver status.

** Adjusted for gender, employment status, and essential worker status.

†† Respondents who completed surveys from all three waves (April, May, June) were eligible to be included in an unweighted longitudinal analysis. Comparisons
within subgroups were evaluated via logit–linked Binomial regressions used to calculate unadjusted and adjusted odds ratios, 95% confidence intervals, and p–values. Statistical significance was evaluated at a threshold of $\alpha = 0.05$. In the calculation of odds ratios for started or increased substance use, respondents who selected "Prefer not to answer" (n = 11) were excluded.

§§ Symptoms of anxiety disorder and depressive disorder were assessed via the PHQ–4. Those who scored ≥3 out of 6 on the two–item Generalized Anxiety Disorder (GAD–2) and two–item Patient Health Questionnaire (PHQ–2) subscales were considered symptomatic for each disorder, respectively.

¶¶ Disorders classified as TSRDs in the Diagnostic and Statistical Manual of Mental Disorders (DSM–5) include posttraumatic stress disorder (PTSD), acute stress disorder (ASD), and adjustment disorders (ADs), among others. Symptoms of a TSRD precipitated by the COVID–19 pandemic were assessed via the six–item Impact of Event Scale (IES–6) to screen for overlapping symptoms of PTSD, ASD, and ADs. For this survey, the COVID–19 pandemic was specified as the traumatic exposure to record peri– and posttraumatic symptoms associated with the range of potential stressors introduced by the COVID–19 pandemic. Those who scored ≥1.75 out of 4 were considered symptomatic.

SOCIAL DISTANCING TO COMBAT COVID-19 LED TO A MARKED DECREASE IN FOOD-BORNE INFECTIONS AND SEXUALLY TRANSMITTED DISEASES IN SPAIN

de Miguel Buckley R, Trigo E, de la Calle-Prieto F, Arsuaga M, Díaz-Menéndez M.. J Travel Med. 2020 Aug 25:taaa134. doi: 10.1093/jtm/taaa134. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

Utilizing data from the Epidemiological Surveillance Network from Madrid Autonomous Community, epidemiologists from Madrid, Spain compared the number of cases of reportable communicable diseases in the first quarter of 2020 compared to 2019. They found a decrease in both food borne illnesses (Campylobacter [1308 vs 391], Salmonella [462 vs 111]) and sexually transmitted diseases (Neisseria gonorrhea [1056 vs 196], Chlamydia infection [1212 vs 292], syphilis [425 vs 114]), though they do not provide levels of significance (Figure 1). The authors suggest that COVID-19 control measures (social distancing, shut down of restaurants and clubs, and decreased tourism) also drove this decrease in other communicable disease. However, they acknowledge underreporting and reluctance to seek treatment during a pandemic may also have affected data collection.

ABSTRACT

Data from a recent epidemiological surveillance network showed a decrease in the reported number of sexually transmitted diseases and food-borne infections. We reflect on the possible drivers and consequences of a decrease in these transmittable infectious diseases linked to human contact in relation to social distancing due to the COVID-19 pandemic in Madrid (Spain).

FIGURES

Table 1. Number of accumulated cases of sexually transmitted diseases and food-borne infections declared in Madrid between weeks 1-26 of 2019 and 2020[2].

	Disease	2019	2020
Sexually transmitted diseases	Chlamydia infection (excluding *Lymphogranuloma venereum*)	1212	292
	Gonococcal infection	1056	196
	Syphilis	425	114
Food-borne infections	Campylobacteriosis	1308	391
	Salmonellosis (excluding typhoid and paratyphoid fever)	462	111

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