The Daily COVID-19 Literature Surveillance Summary

October 12, 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".
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EXECUTIVE SUMMARY

Understanding the Pathology

- Findings from models of the change in energy (ΔΔG) of the binding of the SARS-CoV-2 spike (S) protein to the angiotensin converting enzyme-2 (ACE2) receptors from primates, rodents, birds, reptiles, and fish (n=215 vertebrates) suggest that a broad range of mammals are susceptible to SARS-CoV-2, indicating the need for surveillance of animals that are potential reservoirs.

Adjusting Practice During COVID-19

- A review of the major impacts of COVID-19 on specialty fields that treat non-communicable disease including cardiology (e.g alteration to STEMI), nephrology (e.g. dialysis centers complying with CDC recommendations and social distancing guidelines), obstetrics and gynecology (e.g. ACOG recommendations to separate neonates from COVID-19 positive mothers), hematology oncology (e.g. dramatic decreases in blood donations in some areas), as well as other specialties, found that the pandemic will likely result in negative impacts on many patients with non-communicable diseases, and may even lead to the development of de novo sequelae due to impaired healthcare practices.

Mental Health & Resilience Needs

- A opinion piece by a psychiatrist at Massachusetts General Hospital highlights that the rapidly changing nature of COVID-19 research and management has caused "Bayesian fatigue" by making the sum total knowledge a physician has gathered over their career less important than the most recent research, which has caused a negative psychological toll on physicians who long to see mastery and makes it difficult for physicians to counsel friends, family and patients as our knowledge on the COVID-19 pandemic is rapidly evolving.

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SARS-COV-2 SPIKE PROTEIN PREDICTED TO FORM COMPLEXES WITH HOST RECEPTOR PROTEIN ORTHOLOGUES FROM A BROAD RANGE OF MAMMALS

Lam SD, Bordin N, Waman VP, Scholes HM, Ashford P, Sen N, van Dorp L, Rauer C, Dawson NL, Pang CSM, Abbasian M, Sillitoe I, Edwards SJL, Fraternali F, Lees JG, Santini JM, Orengo CA.. Sci Rep. 2020 Oct 5;10(1):16471. doi: 10.1038/s41598-020-71936-5.

Level of Evidence: Other - Modeling

BLUF

Structural biologists from Malaysia, United Kingdom, and India modeled the change in energy (ΔΔG) of the binding of the SARS-CoV-2 spike (S) protein to the angiotensin converting enzyme-2 (ACE2) receptors from primates, rodents, birds, reptiles, and fish (n=215 vertebrates) to analyze COVID-19 infection risk. Authors suggest that a broad range of mammals, though few fish, birds, or reptiles are susceptible to SARS-CoV-2 and call for surveillance of animals that are potential reservoirs.

SUMMARY

Additional study findings below:

- With the exception of non-placental mammals, most mammals were found to be at high risk for SARS-CoV-2 infection (Table 1, Figure 6).
- Mutations of vertebrate orthologues of transmembrane serine protease 2 (TMPRSS2; required by SARS-CoV-2 for cell entry) represented more conservative changes (Figure 4), therefore authors predicted ACE2 mutations are more likely to impact chances of viral binding compared to mutations in TMPRSS2.

ABSTRACT

SARS-CoV-2 has a zoonotic origin and was transmitted to humans via an undetermined intermediate host, leading to infections in humans and other mammals. To enter host cells, the viral spike protein (S-protein) binds to its receptor, ACE2, and is then processed by TMPRSS2. Whilst receptor binding contributes to the viral host range, S-protein:ACE2 complexes from other animals have not been investigated widely. To predict infection risks, we modelled S-protein:ACE2 complexes from 215 vertebrate species, calculated changes in the energy of the complex caused by mutations in each species, relative to human ACE2, and correlated these changes with COVID-19 infection data. We also analysed structural interactions to better understand the key residues contributing to affinity. We predict that mutations are more detrimental in ACE2 than TMPRSS2. Finally, we demonstrate phylogenetically that human SARS-CoV-2 strains have been isolated in animals. Our results suggest that SARS-CoV-2 can infect a broad range of mammals, but few fish, birds or reptiles. Susceptible animals could serve as reservoirs of the virus, necessitating careful ongoing animal management and surveillance.

Animal	Evidence of infection	In vivo infection	In vitro infection	Real world infection	ΔΔG	Grantham score
Baboon	1		1[48]		-0.115	5
Bat (horseshoe)	1		1[21 22 48]		3.723	981
Bear	1		1[48]		0.044	493
Buffalo	1		1[48]			
Camel	1		1[21]		0.940	634
Capuchin	0		0[48]		3.404	280
Cat	1	1[49]	1[21 22 48]	1[14]	1.472	433
Chicken	0	0[49]	0[21]		5.001	1350
Chimp	1		1[48]		0.000	0
Civet	1		1[21 22]			
Colobus	1		1[48]		0.000	0
Cow	1		1[21 48]		0.560	470
Dog	1	1[49]	1[22 48]	1[16 17]	0.446	516
Dolphin	1		1[48]		1.399	548
Donkey	0		0[21]		1.293	627
Duck	0	0[49]			5.889	1394
Ferret	1	1[49 50]			1.049	827
Fox	1		1[48]		1.770	610
Gelada	1		1[48]		-0.055	5
Gibbon	1		1[48]		0.089	26
Goat	1		1[21 48]		1.165	467
Golden snub-nosed monkey	1		1[48]		0.140	48
Gorilla	1		1[48]		0.000	0
Guinea pig	0		0[21]		1.299	621
Hamster	1		1[48]		0.420	526
Horse	1		1[21 48]		1.293	627
Jerboa	1		1[48]			
Koala	0		0[48]		2.503	848
Leopard	1		1[48]		1.154	433
Lynx	1		1[48]		0.734	433
Macaques	1	1[19 51]	1[48]		0.166	5
Marmoset	1	1[19]	0[48]		3.438	280
Mink	1			1[16 17]	0.632	800
Mouse	0		1[21 22 48]		5.552	837
White footed mouse	1		1[48]			
Orangutan	1		1[48]		0.000	0
Panda	1		1[48]		0.882	493
Pangolin	1		1[21 22 48]			
Pig	1	0[49]	1[21 48]		1.770	514
Puma	1		1[48]			
Rabbit	1		1[21 22 48]		0.909	412
Rat	0		0[21 22]		5.947	818
Rhinoceros	1		1[48]			
Roussete	1		1[48]			
Hawaiian monk seal	0		0[48]			
Sealion	1		1[48]			
Sheep	1		1[21 48]		-0.055	470
Stoat	0		0[48]			
Squirrel	1		1[48]		0.919	501
Squirrel monkey	0		0[48]		2.479	280
Tiger	1			1[15]		
Whales	1		1[48]		0.784	563
Yak	1		1[48]		0.560	470

Table 1. Collated evidence of in vivo, in vitro and real world animal infections to date14–17,19,21,22,55,56,58,87. ΔΔG values calculated by protocol 2 (mCSM-PPI2) and Grantham scores are also shown. Cell colours denote animals that have been infected (red), not infected (blue) or no experimental evidence (grey). Animals are categorised according to risk of infection by SARS-CoV-2, with $\Delta\Delta G \leq 3.72$ being at risk (red), and $\Delta\Delta G > 3.72$ not at risk (blue). These thresholds were chosen as they agree well with the available experimental data (Fig. 3).

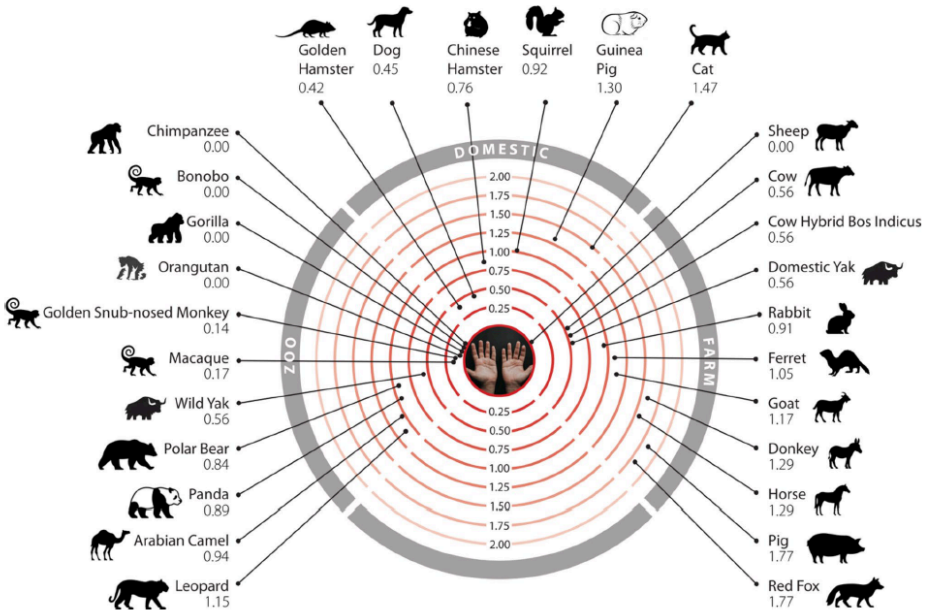

Figure 6. Mammals that humans come into contact with that are at risk of infection by SARS-CoV-2. Twenty-six mammals are categorized into domestic, agricultural or zoological settings. Numbers represent the change in binding energy (ΔΔG) of the S-protein:ACE2.

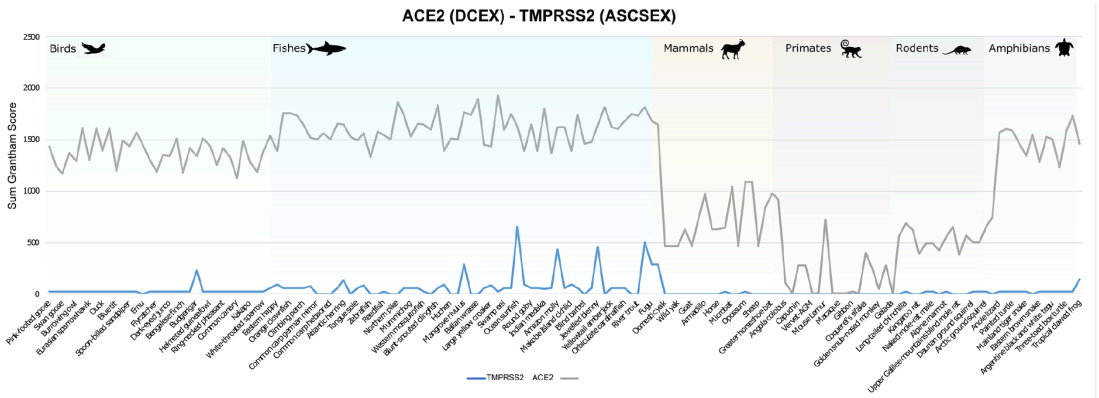

Figure 4. Comparison of Grantham score sums for ASCSEX residues in ACE2 and TMPRSS2.

TRANSMISSION & PREVENTION

ATYPICAL CLINICAL PRESENTATION OF COVID-19 INFECTION IN RESIDENTS OF A LONG-TERM CARE FACILITY

Blain H, Rolland Y, Benetos A, Giacosa N, Albrand M, Miot S, Bousquet J.. Eur Geriatr Med. 2020 Oct 6. doi: 10.1007/s41999-020-00352-9. Online ahead of print.
Level of Evidence: 4 - Local non-random sample

BLUF

Geriatricians performed a single center observational study to investigate prevalence of COVID-19 and outcomes in residents and staff at a long-term-care facility (LTCF) in France after the first resident was diagnosed with COVID-19 in March, 2020 (see summary). Authors report an atypical presentation led to delayed diagnosis of the first case and may have resulted in rapid dissemination of COVID-19 within the LTCF, emphasizing the importance of early COVID-19 detection for prompt implementation of infection control.

SUMMARY

Additional study findings include:
- Between March 18 and March 20, 2020 (seven days after the first COVID-19 diagnosis), 48.1% (n=38) of LTCF residents and 27.5% of staff members (n=11) tested positive for SARS-CoV-2 via real-time reverse transcriptase polymerase chain reaction (RT-PCR).
- There were 12 deaths among residents diagnosed with COVID-19.
- Early COVID-19 symptoms among LTCF residents included diarrhea, fall, delirium, hypothermia (Table 1).

ABSTRACT

PURPOSE: To assess the magnitude of the infection in residents from-and staff working in-a long-term-care facility (LTCF) 7 days after the identification of one resident with confirmed COVID-19 infection and to assess the clinical presentation of the infected residents. METHODS: All residents and staff members of a LTCF were tested for SARS-CoV-2 by real-time reverse-transcriptase polymerase chain reaction on nasopharyngeal swab. Residents were studied clinically 4 weeks after the first COVID diagnosis. RESULTS: Thirty-eight of the 79 residents (48.1%) tested positive for SARS-CoV-2. Respiratory symptoms were preceded by diarrhea (26.3%), a fall (18.4%), fluctuating temperature with hypothermia (34.2%) and delirium in one resident. Respiratory symptoms, including cough and oxygen desaturation, appeared after those initial symptoms or as the first sign in 36.8% and 52.2%, respectively. At any time of the disease, fever was observed in 65.8%. Twelve deaths occurred among the COVID-19 residents. Among the 41 residents negative for SARS-CoV-2, symptoms included cough (21.9%), diarrhea (7.3%), fever (21.9%), hypothermia (9.7%), and transient hypoxemia (9.8%). No deaths were observed in this group. 27.5% of the workers were also COVID-19 positive. CONCLUSION: The rapid dissemination of the COVID-19 infection may be explained by the delay in the diagnosis of the first cases due to atypical presentation. Early recognition of symptoms compatible with COVID-19 may help to diagnose COVID-19 residents earlier and test for SARS-CoV-2 symptomatic and asymptomatic staff and residents earlier to implement appropriate infection control practices.

	COVID+ residents, $N=38$ n (%)	COVID− residents, $N=41$ N (%)	P value**
Age (years)*	89.2 (5.6)	87.3 (9.8)	0.44
Gender, male	8 (29.6)	13 (50.0)	0.13
Symptoms before respiratory symptoms			
Fluctuating temperature with hypothermia	13 (34.2)	2 (4.8)	**< 0.01**
Diarrhea	10 (26.3)	3 (7.3)	0.06
Fall	7 (18.4)	0 (0)	**< 0.01**
Respiratory symptoms			
Cough	14 (36.8)	9 (21.9)	0.29
Oxygen desaturation	21 (55.2)	4 (9.8)	**< 0.01**
Symptoms at any time of the 27-day follow-up			
Fever	25 (65.8)	9 (21.9)	**< 0.01**
Hypothermia	13 (34.2)	4 (0.7)	**0.03**
Diarrhea	15 (39.5)	10 (24.4)	0.29
Fall	9 (23.7)	2 (4.9)	0.07
Severe myalgia	10 (26.3)	1 (2.4)	**< 0.01**
Deaths	13 (31.6)	0 (0)	**< 0.01**

Table 1. Demographic and clinical characteristics. *Continuous variable age is expressed as mean (SD); **P for Chi-square test (or Fisher's exact test if Chi-square was not a valid test) for categorical variables and Student test for continuous variables.

CARDIOLOGY

HIGHLIGHTS FROM STUDIES IN CARDIOVASCULAR DISEASE PREVENTION PRESENTED AT THE DIGITAL 2020 EUROPEAN SOCIETY OF CARDIOLOGY CONGRESS: PREVENTION IS ALIVE AND WELL

Jia X, Al Rifai M, Hussain A, Martin S, Agarwala A, Virani SS.. Curr Atheroscler Rep. 2020 Oct 3;22(12):72. doi: 10.1007/s11883-020-00895-z.
Level of Evidence: Other - Review / Literature Review

BLUF

A literature review, conducted primarily by Baylor College of Medicine (U.S.) cardiologists, discussed promising studies about cardiovascular disease prevention (illustrated below) presented at the 2020 European Society of Cardiology Congress. The review highlights the improvement in cardiovascular disease prevention strategies, which are particularly important considering that cardiovascular disease is a significant contributing risk factor in COVID-19 severity. Further, the authors summarized an article demonstrating that there is no benefit to discontinuing use of angiotensin-converting enzyme inhibitors or angiotensin receptor blockers in mild and moderate COVID-19 patients.

SUMMARY

Studies reviewed in this article include, but are not limited to, the following:
-clinical trials on RNA interference-based lipid-lowering therapies [AKCEA-APOCIII-LRx and vupanorsen (AKCEA-ANGPTL3-LRx)]
-several potential drug candidates (icosapent ethyl, low-dose colchicine, and empagliflozin)
-a study analyzing the possible need to discontinue use of angiotensin-converting enzyme inhibitors (ACEis) and angiotensin receptor blockers (ARBs) in hospitalized, COVID-19 patients.

ABSTRACT

PURPOSE OF REVIEW: The review highlights selected studies related to cardiovascular disease (CVD) prevention that were presented at the 2020 European Society of Cardiology (ESC) Congress-The Digital Experience. RECENT FINDINGS: The studies reviewed include clinical trials on novel RNA interference-based lipid-lowering therapies AKCEA-APOCIII-LRx and vupanorsen (AKCEA-ANGPTL3-LRx); the EVAPORATE trial assessing the effects of icosapent ethyl on coronary plaque volume progression; the LoDoCo2 trial evaluating the efficacy of low-dose colchicine in cardiovascular disease risk reduction among patients with chronic coronary artery disease; as well as the EMPEROR-Reduced trial evaluating cardiovascular and renal outcomes with empagliflozin in patients with heart failure and reduced ejection fraction. In addition, we review the BPLTTC analysis on blood pressure treatment across blood pressure levels and CVD status and discuss findings from the BRACE CORONA study that examined continuing versus suspending angiotensin-converting enzyme inhibitor or angiotensin receptor blockers in patients on these antihypertensive medications who were hospitalized with COVID-19 infection. The studies presented at the 2020 digital ESC Congress highlight the continuing advancements in the field of CVD prevention.

THE IMPACT OF NOVEL CORONAVIRUS COVID-19 ON NON-COMMUNICABLE DISEASE PATIENTS AND HEALTH SYSTEMS: A REVIEW

Chang AY, Cullen MR, Harrington RA, Barry M.. J Intern Med. 2020 Oct 5. doi: 10.1111/joim.13184. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

A review written by Stanford physicians outlines the major impacts of COVID-19 on specialty fields that treat non-communicable disease including cardiology (e.g alteration to STEMI protocols in COVID-19 unknown or COVID-19 positive patients), nephrology (e.g. dialysis centers complying with CDC recommendations and social distancing guidelines), obstetrics and gynecology (e.g. ACOG recommendations to separate neonates from COVID-19 positive mothers), hematology oncology (e.g. dramatic decreases in blood donations in some areas), as well as other specialties. The pandemic will likely result in negative impacts on many patients with non-communicable diseases, and may even lead to the development of de novo sequelae due to impaired healthcare practices (Figure 1).

ABSTRACT

Coronavirus Disease 2019 (COVID-19) is an ongoing global pandemic affecting all levels of health systems. This includes the care of patients with noncommunicable diseases (NCDs) who bear a disproportionate burden of both COVID-19 itself and the public health measures enacted to combat it. In this review, we summarize major COVID-19 related considerations for NCD patients and their care providers, focusing on cardiovascular, pulmonary, renal, hematologic, oncologic, traumatic, obstetric/gynecologic, operative, psychiatric, rheumatologic/immunologic, neurologic, gastrointestinal, ophthalmologic, and endocrine disorders. Additionally, we offer a general framework for categorizing the pandemic's disruptions by disease-specific factors, direct health system factors, and indirect health system factors. We also provide references to major NCD medical specialty professional society statements and guidelines on COVID-19. COVID-19 and its control policies have already resulted in major disruptions to the screening, treatment, and surveillance of NCD patients. In addition, it differentially impacts those with pre-existing NCDs and may lead to de novo NCD sequelae. Likely, there will be long-term effects from this pandemic that will continue to affect practitioners and patients in this field for years to come.

FIGURES

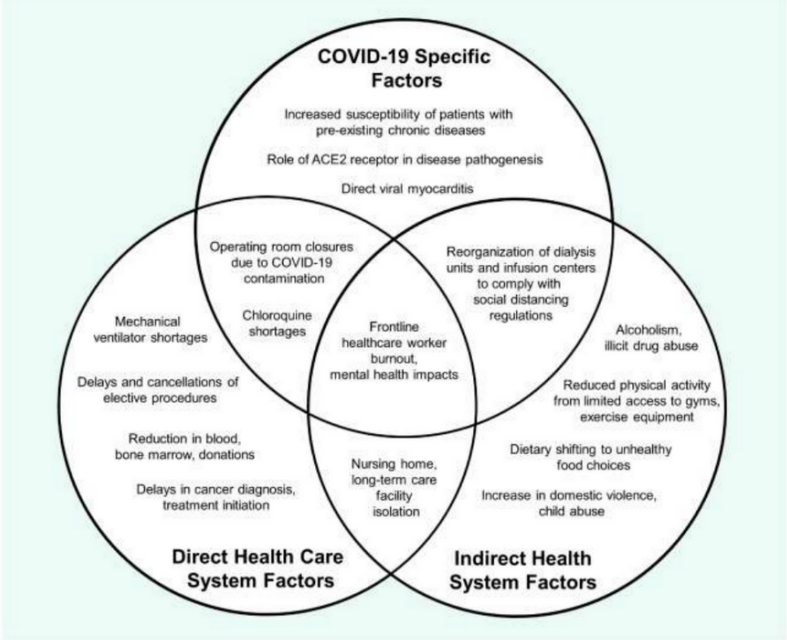

Figure 1. Example Impacts of COVID-19 on NCDs.

THE STRESS OF BAYESIAN MEDICINE - UNCOMFORTABLE UNCERTAINTY IN THE FACE OF COVID-19

Rosenquist JN.. N Engl J Med. 2020 Oct 7. doi: 10.1056/NEJMp2018857. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

This opinion article written by a psychiatrist at Massachusetts General Hospital highlights that the rapidly changing nature of COVID-19 research and management has caused "Bayesian fatigue" by making the sum total knowledge a physician has gathered over their career less important than the most recent research. He believes this has caused a negative psychological toll on physicians who long to see mastery, making it difficult for physicians to counsel friends, family and patients as our knowledge on the COVID-19 pandemic is rapidly evolving.

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