The Daily COVID-19 Literature Surveillance Summary

July 7, 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

CLIMATE:

- Authors from Washington University outline the challenges that U.S. colleges face in reopening for fall 2020 which include lack of a central authority to implement policies, financial issues, and adherence to safety measures by the academic community. They propose symptom-based screening, widespread testing, contact tracing, quarantine of cases and contacts, use of masks, and dedensification of campuses to mitigate the risk of reopening.
- Authors review the literature on healthcare worker (HCW) exposure to COVID-19 and describe how the University of Washington (UW) implemented an effective system for returning HCW to work after exposure. This system implemented rapid testing to identify cases, and then required symptom resolution and negative RT-PCR testing before returning. The researchers conclude that this model provided UW's healthcare team with institutional support and transparency and recommend other healthcare facilities implement a similar framework for their frontline employees.

EPIDEMIOLOGY:

- To estimate the burden of deaths from COVID-19 in the US, authors from the Yale School of Public Health compared data from the National Center for Health Statistics (NCHS) to Centers for Disease Control and Prevention (CDC) reports from the same time frame in years prior. Out of an estimated 122,300 excess all-cause deaths, 78% were attributed to COVID-19. The authors postulate that the total COVID-19 related death toll is underestimated, though some of the additional excess deaths likely result from reduced access to care for chronic conditions.
- A case report of a 16-year-old girl with COVID-19 associated dactylitis that was successfully treated with naproxen (500mg every 12 hours for 5 days) suggests that similar cutaneous manifestations of COVID-19 may result from a Kawasaki-like vasculitis or inflammatory disease process that is responsive to NSAIDs.

UNDERSTANDING THE PATHOLOGY:

- A review of the minimal data on the association of COVID-19 severity and Vitamin D deficiency proposes decreased UV light and lower temperatures in the Northern hemisphere may partially explain the estimated 4.4% increase in mortality for each 1-degree latitude north of 28 degrees found in one study. Additionally, evidence from laboratory and clinical studies suggest that vitamin D may inhibit viral replication and downregulate inflammatory cytokines (IL-6 and TFN-alpha), leading authors to recommend replacing Vitamin D in deficient individuals with COVID-19, however more research is needed.

TRANSMISSION AND PREVENTION:

- Researchers at Johns Hopkins University analyzed anonymous mobile phone data of people in the top 25 U.S. counties most affected by COVID-19. They found a positive correlation between reduced mobility patterns and decreased COVID-19 cases ($r > 0.7$) in 20 of 25 counties, with mobility decreases ranging from 35%-63%. These findings highlight how social distancing is a key factor in effectively decreasing the number of new COVID-19 cases.
- An investigation launched by the Public Health Department in Pasadena, California found that in nine long-term care facilities, the proportion of asymptomatic COVID-19-positive residents and staff was over 40%, suggesting symptom screening alone is not enough to prevent spread in these facilities; residents and staff must also get tested routinely in the absence of symptoms.

MANAGEMENT:

- An analysis of 321 hospitalized COVID-19 patients in Chicago found co-infection in 3.7% of patients overall and 41% of patients admitted to the ICU while antibiotics were used in 69% of all patients. The authors concluded that antibiotics may not be indicated in most patients as co-infection was infrequent and often viral, but ICU patients may require antibiotic therapy due to higher incidence of co-infection.
- A multi-center study from Wuhan, China of 482 confirmed COVID-19 patients found that a mild elevation in liver biochemistries is common in COVID-19 patients, possibly from chronic hypoxia and excessive inflammation, and that elevations in these values are associated with chest distress or pain, dyspnea elevated C-reactive protein level, increased hemoglobin, and elevated white blood count.

ADJUSTING PRACTICE DURNIG COVID-19:

- Guidelines and recommendations for practice during the pandemic include:
    - Assessing and treating bipolar disorder
    - Resumption of respiratory outpatient services

- In light of data showing that elderly individuals were visiting the hospital pharmacy for refills at significantly lower rates during the pandemic, a group of investigators in Taiwan created an outdoor dispensary for multi-month drug refills which effectively returned pharmacy refills among the elderly to pre-pandemic numbers. These results suggest that the creation of alternative medication delivery mechanisms for citizens most at risk of COVID-19 disease may help prevent nonadherence to medical regimens for chronic disease.

R&D DIAGNOSIS AND TREATMENT:

- A prospective cohort study conducted at Tongji Hospital found improved accuracy of SARS-CoV-2 nucleic acid testing via oropharyngeal secretions (OS) as opposed to nasopharyngeal sampling (NPS), with false negative rates of 14% and 59%, respectively. This suggests the potential use of OS sampling as a key screening and diagnostic tool for detection of SARS-CoV-2 in the future.
    - However, a separate study of 95 patient-matched samples found no significant difference in the rates of viral detection between the two sampling methods suggesting that further study is needed in this area.

MENTAL HEALTH AND RESILIENCE:

- Investigators administered the General Anxiety Disorder and Patient Heath Questionnaire surveys to health care workers at a tertiary hospital in Dublin and found that 20.3% of respondents exhibited moderate to severe depression and 21% exhibited moderate to severe anxiety contributing to mounting evidence that the COVID-19 pandemic has had a significant negative psychological effect on healthcare workers as they continue to serve patients.

TABLE OF CONTENTS

CLIMATE

REOPENING COLLEGES AND UNIVERSITIES DURING THE COVID-19 PANDEMIC

Wrighton MS, Lawrence SJ.. Ann Intern Med. 2020 Jul 2. doi: 10.7326/M20-4752. Online ahead of print.
Level of Evidence: Other - Opinion

BLUF

Authors from Washington University outline the challenges that U.S. colleges face in reopening for fall 2020 which include lack of a central authority to implement policies, financial issues, and adherence to safety measures by the academic community. They propose symptom screening, diagnostic testing, contact tracing, quarantine of cases and contacts, use of masks, and dedensification of campuses to mitigate the risk of reopening.

GLOBAL

MAIN ROUTES OF ENTRY AND GENOMIC DIVERSITY OF SARS-COV-2, UGANDA

Bugembe DL, Kayiwa J, Phan MVT, Tushabe P, Balinandi S, Dhaala B, Lexow J, Mwebesa H, Aceng J, Kyobe H, Ssemwanga D, Lutwama J, Kaleebu P, Cotten M.. Emerg Infect Dis. 2020 Jul 2;26(10). doi: 10.3201/eid2610.202575. Online ahead of print.
Level of Evidence: Other - Mechanism-based reasoning

BLUF

This report from an international group of researchers assesses the first 20 viral genomes of SARS-CoV-2 sequenced in Uganda on samples taken from patients who were either international air travelers or truck drivers from entering from adjacent countries. Their analysis indicates that these genomes belong to 6 lineages, with links to America, Europe, Asia, and Africa (Figure 2, Table). The authors contend that their work can be used as a baseline to monitor further virus transmission, particularly between truck drivers and the general population within Uganda.

ABSTRACT

We established rapid local viral sequencing to document the genomic diversity of severe acute respiratory syndrome coronavirus 2 entering Uganda. Virus lineages closely followed the travel origins of infected persons. Our sequence data provide an important baseline for tracking any further transmission of the virus throughout the country and region.

FIGURES

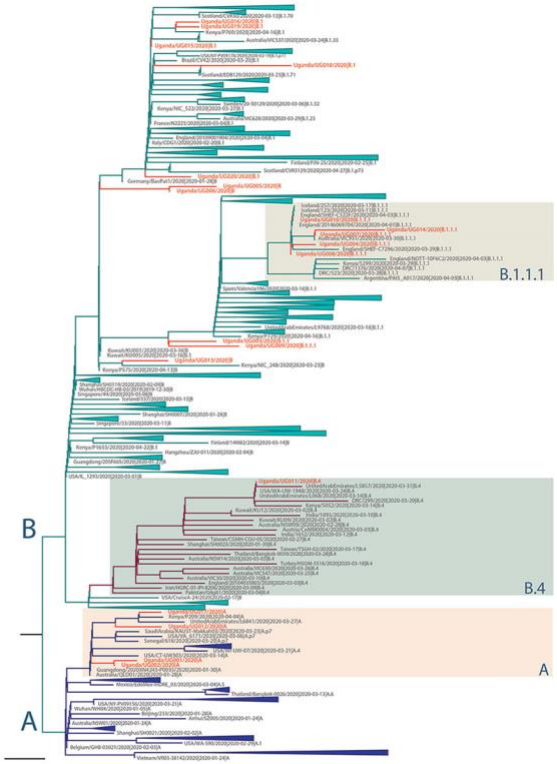

Figure 2. Maximum-likelihood phylogenetic tree of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) genomes in Uganda. The full SARS-CoV-2 genomes used for phylogenetic lineage nomenclature (A. Rambaut et al., unpub. data, https://doi.org/10.1101/2020.04.17.046086) as defined on May 19, 2020, were retrieved from GISAID (http://www.gisaid.org) (8). Identical sequences were removed, and a total of 395 global representative sequences from each phylogenetic lineage type were selected for further phylogenetic analyses. The reported Uganda sequences, combined with the global SARS-CoV-2 sequences, were aligned by using MAFFT (9) and untranslated regions at 5′ and 3′ were trimmed. Maximum-likelihood phylogenetic tree was constructed in RAxML (10), under the general time-reversible plus gamma distribution model as best-fitted substitution model determined by IQ-TREE (11) and run for 100 pseudo-replicates. The resulting tree was visualized in Figtree (12) and rooted at the point of splitting lineage A and B. Scale bar indicates 6 × 10–5 nucleotide substitutions per site. The branch length is drawn to the scale of nucleotide substitutions per site. The Uganda genomes are indicated in red. The 2 major lineages of SARS-CoV-2 (A and B) are indicated to the left of the tree; the main groups of the Uganda genomes (A, B1.1.1, B4) are indicated by colored boxes to the right of the tree.

Genome	GISAID ID†	Sample date	C_t	Patient age, y	Patient travel history	Lineage‡
hCoV-19/Uganda/UG001/2020	EPI_ISL_451183	2020 Mar 23	19	48	Miami to Istanbul	A
hCoV-19/Uganda/UG002/2020	EPI_ISL_451184	2020 Mar 26	19	43	Dubai	A
hCoV-19/Uganda/UG003/2020	EPI_ISL_451185	2020 Mar 27	22	10	UK	B.1.1
hCoV-19/Uganda/UG004/2020	EPI_ISL_451186	2020 Mar 27	18	25	UK to NL to Rwanda	B.1.1.1
hCoV-19/Uganda/UG005/2020	EPI_ISL_451187	2020 Mar 27	18	26	UK to NL to Rwanda	B
hCoV-19/Uganda/UG006/2020	EPI_ISL_451188	2020 Mar 30	23	27	UK to NL to Rwanda	B
hCoV-19/Uganda/UG007/2020	EPI_ISL_451189	2020 Mar 30	21	8	UK to NL to Rwanda	B.1.1.1
hCoV-19/Uganda/UG008/2020	EPI_ISL_451190	2020 Mar 30	22	7	UK to NL to Rwanda	B.1.1.1
hCoV-19/Uganda/UG009/2020	EPI_ISL_451191	2020 Mar 30	20	9	UK to NL to Rwanda	B.1.1.1
hCoV-19/Uganda/UG010/2020	EPI_ISL_451192	2020 Mar 30	22	27	UK to NL to Rwanda	B.1.1.1
hCoV-19/Uganda/UG011/2020	EPI_ISL_451193	2020 Mar 30	21	29	Contact	B.4
hCoV-19/Uganda/UG012/2020	EPI_ISL_451194	2020 Mar 22	24	37	Dubai	A
hCoV-19/Uganda/UG013/2020	EPI_ISL_451195	2020 Mar 22	23	35	Dubai	B
hCoV-19/Uganda/UG014/2020	EPI_ISL_451196	2020 Mar 25	27	31	Dubai	B.1.1.1
hCoV-19/Uganda/UG015/2020	EPI_ISL_451197	2020 Apr 27	16	27	Kenya, by truck	B.1
hCoV-19/Uganda/UG016/2020	EPI_ISL_451198	2020 Apr 27	19	52	Kenya, by truck	B.1
hCoV-19/Uganda/UG017/2020	EPI_ISL_451199	2020 Apr 20	22	42	Tanzania, by truck	A
hCoV-19/Uganda/UG018/2020	EPI_ISL_451200	2020 May 1	28	22	Tanzania, by truck	B.1
hCoV-19/Uganda/UG019/2020	EPI_ISL_451201	2020 Apr 30	29	39	Kenya, by truck	B.1
hCoV-19/Uganda/UG020/2020	EPI_ISL_451202	2020 May 1	25	47	Kenya, by truck	B.1

Table. Summary characteristics of SARS-CoV-2 genomes obtained from 20 persons entering Uganda* *Ct, cycle threshold (based on diagnostic real-time reverse transcription PCR; NL, the Netherlands; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; UK, United Kingdom. †Virus genomes sequences available from GISAID (https://www.gisaid.org). ‡SARS-CoV-2 lineages determined by using CoV-GLUE (13).

COMMENTARY: RAPID TESTING OF HEALTHCARE EMPLOYEES FOR COVID-19: WHAT CAN WE LEARN FROM THE SEATTLE EXPERIENCE?

Bryant KA, Isaacs P.. Clin Infect Dis. 2020 Jul 4:ciaa909. doi: 10.1093/cid/ciaa909. Online ahead of print.
Level of Evidence: Other - Opinion

BLUF

This report from Louisville, Kentucky reviews literature on healthcare worker (HCW) exposure to COVID-19 and describes the University of Washington's (UW) system for returning healthcare workers after exposure. Symptom resolution and negative rapid SARS-CoV-2 testing are required for return and UW instituted rapid testing to help achieve this. The researchers conclude that this model provided UW's healthcare team with institutional support which might reduce anxiety about virus spread and recommend other healthcare facilities implement a similar framework for their frontline employees.

SUMMARY

As of June 19th, 2020, 446 health care providers have died in the United States due to COVID-19. After the first case of COVID-19 was reported in the US in January, the University of Washington (UW) launched two testing centers for their healthcare employees. Over the course of six weeks, more than 3,000 employees were tested with results available 6-10 hours after the test. The authors believe it is imperative HCWs not work when they are sick and access to rapid and reliable COVID-19 testing is necessary to achieve this. Additionally, US healthcare providers have expressed worry about spreading the virus to their families, making testing even more necessary. By providing reliable and quick testing, UW was able to minimize these concerns and put an effective policy in place for protecting and supporting their workers. Overall, other healthcare facilities should look to implement a model of testing similar to UW's model.

EPIDEMIOLOGY

ESTIMATION OF EXCESS DEATHS ASSOCIATED WITH THE COVID-19 PANDEMIC IN THE UNITED STATES, MARCH TO MAY 2020

Weinberger DM, Chen J, Cohen T, Crawford FW, Mostashari F, Olson D, Pitzer VE, Reich NG, Russi M, Simonsen L, Watkins A, Viboud C.. JAMA Intern Med. 2020 Jul 1. doi: 10.1001/jamainternmed.2020.3391. Online ahead of print.
Level of Evidence: 4 - Local and current random sample surveys (or censuses)

BLUF

This study conducted in affiliation with Yale School of Public Health analyzed the number of excess deaths due to COVID-19 across the United States using public data from the National Center for Health Statistics (NCHS) from March 1st, 2020 through May 30th, 2020 and compared this data to Centers for Disease Control and Prevention (CDC) reports from the same time frame in years prior. Out of an estimated 122,300 excess all-cause deaths, 78% were attributed to COVID-19 (Table, Figure 1). The authors postulate that the total COVID-19 related death toll is underestimated, though some of the additional excess deaths likely can be attributed to reduced access to care for chronic conditions during the pandemic. They also note that there was significant variability in criteria for attributing deaths to COVID-19 between different states.

ABSTRACT

Importance: Efforts to track the severity and public health impact of coronavirus disease 2019 (COVID-19) in the United States have been hampered by state-level differences in diagnostic test availability, differing strategies for prioritization of individuals for testing, and delays between testing and reporting. Evaluating unexplained increases in deaths due to all causes or attributed to nonspecific outcomes, such as pneumonia and influenza, can provide a more complete picture of the burden of COVID-19. Objective: To estimate the burden of all deaths related to COVID-19 in the United States from March to May 2020. Design, Setting, and Population: This observational study evaluated the numbers of US deaths from any cause and deaths from pneumonia, influenza, and/or COVID-19 from March 1 through May 30, 2020, using public data of the entire US population from the National Center for Health Statistics (NCHS). These numbers were compared with those from the same period of previous years. All data analyzed were accessed on June 12, 2020. Main Outcomes and Measures: Increases in weekly deaths due to any cause or deaths due to pneumonia/influenza/COVID-19 above a baseline, which was adjusted for time of year, influenza activity, and reporting delays. These estimates were compared with reported deaths attributed to COVID-19 and with testing data. Results: There were approximately 781 000 total deaths in the United States from March 1 to May 30, 2020, representing 122 300 (95% prediction interval, 116 800-127 000) more deaths than would typically be expected at that time of year. There were 95 235 reported deaths officially attributed to COVID-19 from March 1 to May 30, 2020. The number of excess all-cause deaths was 28% higher than the official tally of COVID-19-reported deaths during that period. In several states, these deaths occurred before increases in the availability of COVID-19 diagnostic tests and were not counted in official COVID-19 death records. There was substantial variability between states in the difference between official COVID-19 deaths and the estimated burden of excess deaths. Conclusions and Relevance: Excess deaths provide an estimate of the full COVID-19 burden and indicate that official tallies likely undercount deaths due to the virus. The mortality burden and the completeness of the tallies vary markedly between states.

FIGURES

Table. Reported Deaths Coded as COVID-19 Compared With Excess Deaths Coded as Pneumonia/Influenza/COVID-19 or All Causes From March 1, 2020, Through May 30, 2020*

Area	Observed deaths, No.	Expected deaths, No.	Estimated excess all-cause deaths, median (95% prediction interval)	COVID-19 deaths (U07.1), No.	Estimated excess pneumonia/influenza/ COVID-19 deaths, median (95% prediction interval)	Estimated excess all-cause deaths per 100 000, median (95% prediction interval)
United States	780 975	658 700	122 300 (116 800 to 127 000)	95 235	94 130 (92 350 to 95 690)	37.3 (35.6 to 38.7)
New York City	38 170	13 000	25 100 (24 800 to 25 400)	18 603	17 500 (17 280 to 17 670)	299.1 (295.3 to 302.7)
New Jersey	34 013	17 800	16 200 (15 800 to 16 500)	11 952	12 060 (11 910 to 12 180)	182.3 (178.1 to 186.2)
New York (excluding New York City)	36 871	24 600	12 300 (11 900 to 12 700)	9773	9220 (9040 to 9380)	111.4 (107.4 to 114.9)
Massachusetts	22 146	14 700	7400 (7100 to 7700)	6627	6400 (6280 to 6510)	107.6 (103 to 112.2)
District of Columbia	1950	1400	500 (400 to 600)	400	390 (350 to 420)	73.5 (58.9 to 86.6)
Louisiana	13 756	10 200	3080 (2700 to 3300)	2310	2140 (2270 to 2400)	64.7 (59.1 to 70.3)
Maryland	16 052	12 300	3700 (3500 to 4000)	2651	2650 (2560 to 2740)	62 (57.2 to 66.8)
Michigan	30 044	23 900	6100 (5700 to 6600)	4839	4740 (4620 to 4870)	61.4 (56.7 to 65.6)
Illinois	31 296	25 800	7500 (7100 to 7900)	4911	4920 (4800 to 5050)	59.2 (55.7 to 62.3)
Rhode Island	2881	2300	500 (400 to 700)	586	550 (510 to 580)	51.7 (39.3 to 62.9)
Delaware	2537	2100	400 (300 to 600)	365	370 (330 to 400)	45.3 (32.6 to 57.5)
Pennsylvania	37 258	31 800	5400 (4900 to 5900)	5840	5610 (5480 to 5730)	42.4 (38.5 to 45.9)
Mississippi	8787	7600	1100 (900 to 1400)	677	710 (640 to 780)	38.3 (30.6 to 45.9)
Colorado	11 804	9900	1900 (1600 to 2100)	1354	1330 (1260 to 1410)	32.4 (27.6 to 37)
Indiana	18 336	16 200	2100 (1800 to 2500)	2012	1990 (1900 to 2080)	31.9 (26.7 to 36.7)
Vermont	1580	1400	200 (100 to 300)	48	10 (−20 to 40)	29.8 (13.6 to 44.9)
South Carolina	13 601	12 200	1400 (1100 to 1700)	528	480 (400 to 550)	27.9 (21.8 to 33.6)
Virginia	19 219	16 900	2300 (1900 to 2600)	1471	1400 (1310 to 1480)	26.7 (22.8 to 30.6)
Arizona	16 929	15 200	1800 (1400 to 2100)	846	930 (840 to 1010)	24 (19.6 to 28.5)
Georgia	22 105	19 900	2200 (1800 to 2600)	1686	1800 (1710 to 1880)	21 (17.2 to 24.4)
New Hampshire	3383	3100	300 (100 to 400)	244	240 (200 to 280)	19.9 (7.9 to 30)
Alabama	13 436	12 500	900 (600 to 1200)	672	790 (720 to 860)	18 (12 to 24.1)
Washington	15 367	14 000	1300 (1000 to 1700)	1021	1010 (930 to 1090)	17.5 (13.4 to 21.7)
California	72 407	65 600	6800 (6100 to 7500)	4046	4130 (3940 to 4330)	17.2 (15.5 to 19)
Florida	56 462	52 900	3500 (2900 to 4100)	2457	2940 (2780 to 3080)	16.4 (13.4 to 19.3)
Minnesota	12 112	11 200	900 (600 to 1200)	1020	980 (910 to 1060)	15.4 (10.6 to 20.6)
Ohio	30 429	28 800	1600 (1200 to 2000)	1843	1890 (1780 to 1980)	13.8 (9.9 to 17.5)
Texas	51 994	48 400	3600 (3000 to 4200)	1622	2100 (1960 to 2260)	12.4 (10.4 to 14.5)
Missouri	16 043	15 300	700 (400 to 1000)	718	800 (720 to 880)	12.1 (6.6 to 17.1)
Tennessee	19 080	18 300	800 (400 to 1100)	348	380 (280 to 480)	11.5 (5.6 to 16.8)
Wisconsin	14 191	13 500	600 (300 to 900)	607	580 (510 to 660)	11 (5.6 to 16.2)
Oklahoma	9493	9100	400 (100 to 600)	328	320 (250 to 400)	9.1 (2.8 to 15.3)
Nevada	6735	6500	200 (0 to 400)	389	400 (350 to 460)	6.8 (−0.5 to 13.8)
Nebraska	4241	4100	100 (0 to 300)	153	130 (80 to 180)	6.4 (−2.1 to 15)
Oregon	9030	8800	300 (0 to 500)	183	150 (90 to 200)	6.1 (0.1 to 11.5)
New Mexico	4715	4600	100 (−100 to 300)	303	290 (240 to 340)	5.5 (−3.2 to 14.4)
Iowa	7801	7700	100 (−100 to 400)	529	470 (400 to 530)	4.4 (−2.4 to 11.5)
Utah	5044	4900	100 (−100 to 300)	109	100 (50 to 140)	4.2 (−2 to 9.8)
Arkansas	7905	7800	100 (−200 to 300)	123	170 (110 to 220)	2.9 (−5 to 10.4)
Montana	2465	2400	0 (−100 to 100)	21	0 (−30 to 30)	2.2 (−10.1 to 13.5)
Idaho	3656	3600	0 (−100 to 200)	77	70 (40 to 110)	1.7 (−7 to 10.9)
Kansas	6640	6600	0 (−200 to 200)	222	190 (140 to 240)	1.5 (−5.5 to 8.2)
Kentucky	11 382	11 300	100 (−200 to 300)	413	410 (320 to 480)	1.5 (−4.9 to 7.6)
Maine	3749	3800	0 (−200 to 100)	86	0 (−60 to 50)	−1.6 (−12.9 to 10.5)
Hawaii	2821	2900	−100 (−200 to 100)	15	0 (−30 to 40)	−5.2 (−15.5 to 4.4)
South Dakota	1961	2000	−100 (−200 to 0)	52	60 (20 to 90)	−7.7 (−21.3 to 4.7)
Alaska	932	1000	−100 (−200 to 0)	9	−10 (−30 to 0)	−10.8 (−23 to −0.4)
West Virginia	4446	5100	−600 (−800 to −500)	94	70 (20 to 120)	−36.2 (−46.7 to −26)
Wyoming	830	1200	−300 (−400 to −300)	16	20 (0 to 40)	−58.4 (−76.2 to −43.5)
North Dakota	1350	1900	−500 (−700 to −400)	36	70 (50 to 100)	−71.9 (−87.4 to −55.9)

* As reported by the National Center for Health Statistics. States are ordered by highest to lowest estimated excess all-cause deaths per 100 000. Data from Connecticut and North Carolina are not included because of missing mortality data from recent months.

Table. Reported deaths coded as COVID-19 compared with excess deaths coded as pneumonia/influenza/COVID-19 or all causes from March 1, 2020 through May 30, 2020.

SYMPTOMS AND CLINICAL PRESENTATION

ADULTS

INCREASED CSF LEVELS OF IL-1B, IL-6, AND ACE IN SARS-COV-2-ASSOCIATED ENCEPHALITIS

Bodro M, Compta Y, Llansó L, Esteller D, Doncel-Moriano A, Mesa A, Rodríguez A, Sarto J, Martínez-Hernandez E, Vlagea A, Egri N, Filella X, Morales-Ruiz M, Yagüe J, Soriano Á, Graus F, García F; "Hospital Clínic Infecto-COVID-19" and "Hospital Clínic Neuro-COVID-19" groups.. Neurol Neuroimmunol Neuroinflamm. 2020 Jul 1;7(5):e821. doi: 10.1212/NXI.0000000000000821. Print 2020 Sep.
Level of Evidence: 4 - Case-series

BLUF

Authors from Spain present case reports of two patients presenting with neurological symptoms. Investigations on both patients showed normal findings on brain CT/MRI, while CSF analysis (Table 1) showed lymphocytic pleocytosis, increased proteins, and increased inflammatory markers. SARS-CoV-2 PCR testing was positive on nasopharyngeal swab but negative on CSF. The authors suggest COVID-19 patients may present with encephalitis due to "cytokine-mediated systemic inflammation" leading to increased levels of CSF IL-1 beta, IL-6 and ACE levels.

SUMMARY

Case reports of two patients presenting with neurological symptoms are discussed in this article:
-Patient 1: 25-year-old man with one day of headache, left-sided paraesthesia, ipsilateral paresis, progressing to agitation and confusion in 12 hours, and temperature of 38.2 degrees Celcius.
-Patient 2: 49-year-old man with fever, myalgia, and headache for one week developing confusion, agitation, and temporospatial disorientation only a few hours following admission.
- Investigations: Both patients had normal findings on brain CT/MRI. CSF analysis showed lymphocytic pleocytosis and increased proteins, IL-6, and ACE (Table 1). Patient 1 also had increased CSF IL-1 beta. SARS-CoV-2 PCR testing was negative in CSF but positive in nasopharyngeal swab in both cases.
- Treatment: Both patients were started on IV acyclovir, ampicillin, and ceftriaxone but discontinued once the CSF cultures and PCR ruled out bacterial and other viral organisms.
Both patients recovered in two and three days, respectively, except for amnesia of the symptomatic days.
-The pathogenic mechanisms of CSF involvement in COVID-19, as described by the authors, are direct invasion, systemic

infection leading to recrudescence of symptoms from prior lesions, and inflammatory mechanisms. Cytokine storm syndrome in COVID-19 is associated with increased levels of IL-1 and IL-6 which suggests this may be the possible mechanism (systemic inflammation) for CNS involvement in these patients as both presented with increased cytokines in CSF.

FIGURES

	Case 1	Case 2
Age	25	49
Sex	Male	Male
Comorbidities[a]	No	No
Respiratory symptoms	No	Yes
Rash	Yes	No
Anosmia and ageusia	No	No
Headache	Yes	No
Neck stiffness	No	No
C-reactive protein (CRP) [<1 mg/dL]	<0.40	1.70
Ferritin (20–400 ng/mL)	151	428
Procalcitonin (<0.50 ng/mL)	—	<0,03
LDH (<234 U/L)	190	254
Dimer D (<500 ng/mL)	600	600
Leukocyte count (4–11 × 109/dL)	9	5.74
Lymphocyte count (0.9–4.5 × 109/dL) (17–55%)	1.9 (21%)	0.8 (13.1%)
Platelets (130–400 × 109/dL)	147	113
CSF proteins (150–450 mg/L)	1,055	1,155
CSF glucose (40–80 mg/dL) (2.8–4.2 mmol/L)	80 (3.6)	54 (2.99)
CSF nucleated cells/mm3	95 neutrophils 0% Lymphocytes 98% Macrophages 2%	90 neutrophils 0% Lymphocytes 99% Monocytes 1%
CSF erythrocytes/mm3	0	260
CSF IL-1β (pg/mL)	14.8	<2.56
CSF IL-6 (pg/mL)	190	25
CSF IFNα (pg/mL)	<0.58	<0.58
CSF IFNβ (pg/mL)	<8.78	<8.78
CSF ACE (U/L)	15.5	10.9

Abbreviations: ACE = angiotensin-converting enzyme; IL = interleukin.
[a] Hypertension, respiratory chronic disease, cardiovascular disease, diabetes, cancer, chronic hepatopathy, or immunosuppression. CSF IL-1β and IL-6 were considered increased when greater than 2.56 pg/mL and 7 pg/mL, respectively. As for ACE, the normal range was 0–2.5 U/L.

Table 1: Basic demographic and clinical data of both cases.

IDIOPATHIC NONHISTAMINERGIC ACQUIRED ANGIOEDEMA IN A PATIENT WITH COVID-19

Azmy V, Benson J, Love K, Steele R.. Ann Allergy Asthma Immunol. 2020 Jul 1:S1081-1206(20)30447-6. doi: 10.1016/j.anai.2020.06.039. Online ahead of print.
Level of Evidence: Other - Case Report

BLUF

This case study describes a 29-year-old African American female with obesity, hyperlipidemia, and poorly controlled type 2 diabetes who developed idiopathic nonhistaminergic acquired angioedema (InH-AAE, Figure 1) of the tongue 7 days post-intubation for SARS-CoV-2 acute respiratory distress syndrome. Due to a lack of family history of angioedema and poor response to steroids and antihistamines, the authors suggest that an InH-AAE presentation may be another hyperinflammatory response to SARS-CoV-2.

SUMMARY

In this case study, a 29-year-old African American female with a history of class 3 obesity, poorly controlled type 2 diabetes mellitus, hyperlipidemia, and no known drug allergies or previous angioedema was admitted in New Haven, CT with SARS-CoV-2-associated hypoxemia. This later progressed to acute respiratory distress requiring intubation. She was treated with hydroxychloroquine, midazolam, antibiotics for enterococcal bacteremia (piperacillin/tazobactam and vancomycin), and lovenox. She also received four doses of remdesivir as part of a clinical trial. On day 7 of intubation, she developed severe tongue angioedema (Figure 1) without urticaria in the setting of normal C4, C1 esterase inhibitor protein and function, and C1q that was nonresponsive to diphenhydramine and methylprednisone. Her tongue angioedema subsided with administration of C1 esterase inhibitor, and she was later extubated and discharged home. The authors indicate that the progression and duration of her tongue angioedema mirrors nonhistaminergic angioedema and hypothesize that the patient's development of idiopathic nonhistaminergic acquired angioedema may be a presentation of a hyperimmune response to SARS-CoV-2 infection.

FIGURES

Figure 1: Tongue angioedema in an intubated patient with COVID-19. Photo was taken one day after onset of tongue swelling. Dry, cracked blistering lesions on tongue noted. A bedside exam did not reveal laryngeal swelling, evidence of traumatic intubation, or self-inflicted trauma such as bite marks. No lip or periorbital swelling were present.

PEDIATRICS

COVID-19 RELATED DACTYITIS

Salvatierra J, Martínez-Peñalver D, Salvatierra-Velasco L.. Joint Bone Spine. 2020 Jul 1:S1297-319X(20)30121-4. doi: 10.1016/j.jbspin.2020.06.009. Online ahead of print.
Level of Evidence: 4 - Case Report

BLUF

Authors affiliated with the Clinico San Cecilio University Hospital in Spain present the case of a 16-year-old girl with 10 days of swelling in the 2nd, 4th, and 5th metatarsophalangeal joints consistent with dactylitis. Her dactylitis was assumed to be associated with COVID-19 based on patient's history (anosmia, aguesia, odynophagia, fever 3 weeks prior to presentation) and positive COVID-19 serology. Based on the symptom resolution with naproxen (500mg every 12 hours for 5 days) authors suggest that similar presentations of dactylitis may be successfully treated with this therapy alone.

PERSPECTIVE: VITAMIN D DEFICIENCY AND COVID-19 SEVERITY - PLAUSIBLY LINKED BY LATITUDE, ETHNICITY, IMPACTS ON CYTOKINES, ACE2, AND THROMBOSIS (R1)

Rhodes JM, Subramanian S, Laird E, Griffin G, Kenny RA.. J Intern Med. 2020 Jul 2. doi: 10.1111/joim.13149. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

This review reports that Vitamin D deficiency secondary to low UV light exposure might be a determining factor for COVID-19 severity (Table 4). Considering the biological evidence outlined below and the relative safety of vitamin D supplementation, the authors urge providers to consider Vitamin D supplementation, particularly for individuals at risk of vitamin D deficiency and severe COVID-19.

SUMMARY

• The authors report a significant association between COVID-19 mortality and patients residing in countries in the Northern Hemisphere. One study found that there was an estimated 4.4% increase in COVID-19 mortality for each 1-degree latitude north of 28 degrees after adjusting for the age of the population (P=0.031) (Table 1, Figure 1). Pollution and population density per country did not significantly affect the associations.
• The mechanism underlying the association between latitude and COVID-19 mortality is not particularly clear and may involve multiple factors. One factor identified was ultraviolet light, particularly UVB, was shown to have immunosuppressive effects on the skin.
• There is contradictory evidence suggesting UV light reduces free virus viability with one study reporting that UVB and higher temperature were associated with lower SARS-CoV-2 infection rates. However, a study in China did not find an association between either UVB or temperature and COVID-19 infection rates.
• Evidence from laboratory and clinical studies suggests that vitamin D deficiency may have an impact on the inflammatory response, and therefore the severity of the infection in respiratory diseases. One study found that infants with bronchiolitis and lower levels of vitamin D were more likely to need intensive care (22% of vitamin D <20ng/ml (50 nmol/l), compared with 12% if vitamin D >30 ng/ml (75 nmol/l); P=0.003).
• Experimental lab evidence demonstrated that while vitamin D may have inconsistent effects on viral replication in human respiratory epithelial cell culture, vitamin D markedly down-regulate the production of pro-inflammatory cytokines (i.e., TNFalpha and IL-6) by various mechanisms including inhibition of viral-induced NF-kappaB activation.
• Evidence suggests the immunosuppressive effects of Vitamin D may differ among men and women. The observed gender difference is speculated to be related to estrogen-dependent effects on the synthesis of the vitamin D binding protein.
• It was suggested that vitamin D may play a protective role against acute respiratory distress syndrome (ARDS) in COVID-19. However, exact mechanism was not discussed

ABSTRACT

BACKGROUND: SARS-CoV-2 coronavirus infection ranges from asymptomatic through to fatal COVID-19 characterised by a "cytokine storm" and lung failure. Vitamin D deficiency has been postulated as a determinant of severity. OBJECTIVES: To review the evidence relevant to vitamin D and COVID-19 METHODS: Narrative review RESULTS: Regression modelling shows that more northerly countries in the Northern Hemisphere are currently (May 2020) showing relatively high COVID-19 mortality, with an estimated 4.4% increase in mortality for each 1 degree latitude north of 28 degrees North (P=0.031) after adjustment for age of population. This supports a role for ultraviolet B acting via vitamin D synthesis. Factors associated with worse COVID-19 prognosis include old age, ethnicity, male sex, obesity, diabetes and hypertension and these also associate with deficiency of vitamin D or its response. Vitamin D deficiency is also linked to severity of childhood respiratory illness. Experimentally, vitamin D increases the ratio of angiotensin converting enzyme 2 (ACE2) to ACE, thus increasing angiotensin II hydrolysis and reducing subsequent inflammatory cytokine response to pathogens and lung injury. CONCLUSIONS: Substantial evidence supports a link between vitamin D deficiency and COVID-19 severity but it is all indirect. Community-based placebo-controlled trials of vitamin D supplementation may be difficult. Further evidence could come from study of COVID-19 outcomes in large cohorts with information on prescribing data for vitamin D supplementation or assay of serum unbound 25(OH) vitamin D levels. Meanwhile vitamin D supplementation should be strongly advised for people likely to be deficient.

Table 1:

Associations between COVID-19 mortality by country, latitude, and % of population ≥65 years (from [3], data accessed 18th May 2020).

	Variable	Regression coefficient	Standard error	p-value	% of variation explained	Effect size (95% CI) **
Univariate models						
	Latitude	0.1074	0.0142	<0.0005	33.1	11.3% (8.3%-14.5%)
	% ≥ 65	0.1766	0.0199	<0.0005	40.4	19.3% (14.8%-24.1%)
Multivariate model						
	Latitude	0.0428	0.0196	0.031	43.0	4.4% (0.4%-8.5%)
	% ≥ 65	0.1281	0.0291	<0.0005		13.7% (7.4%-20.3%)

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Table 4. Summary

Vitamin D deficiency as a possible factor determining COVID-19 severity
• Lower population mortality in countries South of 28 degrees N latitude where there will have been sufficient sunlight to maintain vitamin D levels during the past months

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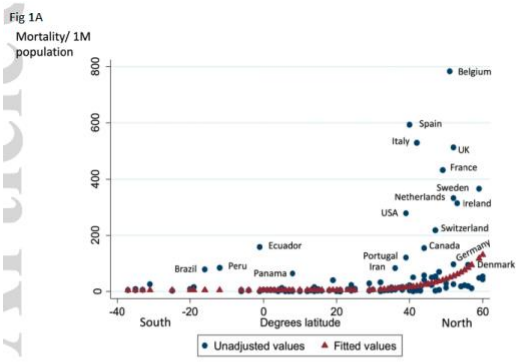
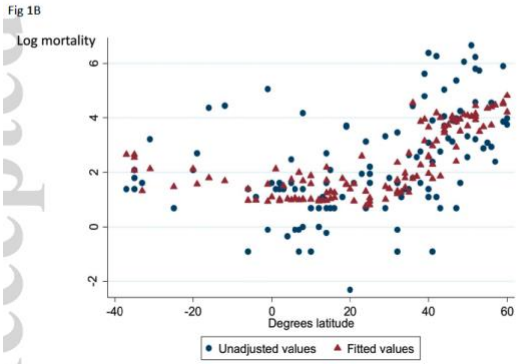
- Vitamin D deficiency correlates with hypertension, diabetes, obesity, ethnicity, institutionalisation all of which are features associated with increased risk of severe COVID-19
- Vitamin D moderates inflammatory cytokine response by macrophages and respiratory epithelial cells to pathogens including respiratory viruses
- Vitamin D's effect on cytokines and reduced risk for experimental lung injury is likely mediated by its increase in ACE2:ACE ratio and consequential reduction of angiotensin II – highly relevant to COVID-19 since ACE2 is the SARS-CoV-2 receptor
- Vitamin D deficiency and vitamin D receptor polymorphisms are associated with increased risk of severe viral bronchiolitis in infants
- Vitamin D deficiency is easily prevented by supplementation which is very safe





COVID-19: FROM PATHOGENESIS MODELS TO THE FIRST DRUG TRIALS

Brüssow H.. Microb Biotechnol. 2020 Jun 23. doi: 10.1111/1751-7915.13611. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

A biosystems researcher in Belgium provides a brief review summarizing the following topics related to COVID-19 disease: pathogenesis, molecular biology, tissue tropism, clinical trials and antivirals. The author proposes that trials for novel therapies should be designed with our latest understanding of COVID-19 pathology in mind.

SUMMARY

Notable points include:
- Autopsies of COVID-19 patients have shown diffuse alveolar damage, hyaline membranes and pulmonary edema.
- Hypotheses regarding pathogenesis of COVID-19 are related to infection induced cytokine storm and coagulopathy. Certain mechanisms in these inflammatory cascades may serve as targets for therapeutic intervention.
- SARS-CoV-2 may induce viral septic shock.
- Immune dysregulation of cytokines, such as interleukin-6 was shown to inhibit HLA-DR on CD14 monocytes leading to impaired immune response.
- A study demonstrated SARS-CoV-2 may dampen antiviral response through inhibiting cellular transcription of interferon (INF I & III) and upregulating chemokine transcription.
- Cellular expression of ACE-2 and a viral fusion protease may be linked to genetic variability among individuals which may explain the different clinical symptomatology and geographic differences in disease prevalence.
- SARS-CoV-2 has shown tissue tropism for pulmonary, intestinal and neural tissues.
- Animal models using ferrets, cats, dogs, hamsters, primates, pangolins and mice have been used to study SARS-CoV-2 in other mammals.
- Hydroxychloroquine has not been definitively shown to be beneficial or harmful.
- Numerous clinical trials have explored remdesivir, lopinavir, arbidol, and a triple therapy: lopinavir, ribavirin, interferon beta-1b, to see if these combinations confer a therapeutic benefit. Results should be interpreted with caution as many studies lack statistical significance or power.
- More research is needed to elucidate the impact anti-hypertensive medications such as Angiotensin II receptor blockers (ARB) and ACE inhibitors (ACEI), have on patient outcomes
- Reports from clinical trials should be carefully scrutinized and data interpreted with caution as some studies lack a true

control group and administer concomitant treatments, which makes it difficult to assess for correlations between therapies and outcomes.

ABSTRACT

The number of people infected with SARS-CoV-2, and sadly dying from COVID-19, has exploded, and so the amount of literature on the novel coronavirus and the disease it causes has increased proportionately. The case numbers in some countries are beyond the epidemic peak, but the uncertainty about a second wave keeps politicians and societies under pressure. Appropriate decision-making and winning support from the population depends on precise scientific information rather than leaving the field to scaremongers of all proveniences. This mini-review is an update of earlier reports (Brussow, Microb Biotechnol 2020a;13:607; Brussow, Microb Biotechnol 2020b; https://doi.org/10.1111/1751-7915.13592).

ASSOCIATION BETWEEN MOBILITY PATTERNS AND COVID-19 TRANSMISSION IN THE USA: A MATHEMATICAL MODELLING STUDY

Badr HS, Du H, Marshall M, Dong E, Squire MM, Gardner LM.. Lancet Infect Dis. 2020 Jul 1:S1473-3099(20)30553-3. doi: 10.1016/S1473-3099(20)30553-3. Online ahead of print.
Level of Evidence: 2 - Modeling

BLUF

A mathematical analysis conducted at Johns Hopkins University collected anonymous mobile cell phone data from January 1st to April 20, 2020 to measure relative changes in mobility of people in the top 25 U.S. counties most affected by COVID-19 (Figures 1-2). They found positive correlation between reduced mobility patterns and decreased COVID-19 cases (Table 1; r > 0.7 in 20 of top 25 counties), with mobility decreases ranging from 35%-63%. These findings suggest social distancing is a key factor in effectively decreasing the number of new COVID-19 cases.

ABSTRACT

BACKGROUND: Within 4 months of COVID-19 first being reported in the USA, it spread to every state and to more than 90% of all counties. During this period, the US COVID-19 response was highly decentralised, with stay-at-home directives issued by state and local officials, subject to varying levels of enforcement. The absence of a centralised policy and timeline combined with the complex dynamics of human mobility and the variable intensity of local outbreaks makes assessing the effect of large-scale social distancing on COVID-19 transmission in the USA a challenge. METHODS: We used daily mobility data derived from aggregated and anonymised cell (mobile) phone data, provided by Teralytics (Zurich, Switzerland) from Jan 1 to April 20, 2020, to capture real-time trends in movement patterns for each US county, and used these data to generate a social distancing metric. We used epidemiological data to compute the COVID-19 growth rate ratio for a given county on a given day. Using these metrics, we evaluated how social distancing, measured by the relative change in mobility, affected the rate of new infections in the 25 counties in the USA with the highest number of confirmed cases on April 16, 2020, by fitting a statistical model for each county. FINDINGS: Our analysis revealed that mobility patterns are strongly correlated with decreased COVID-19 case growth rates for the most affected counties in the USA, with Pearson correlation coefficients above 0 7 for 20 of the 25 counties evaluated. Additionally, the effect of changes in mobility patterns, which dropped by 35-63% relative to the normal conditions, on COVID-19 transmission are not likely to be perceptible for 9-12 days, and potentially up to 3 weeks, which is consistent with the incubation time of severe acute respiratory syndrome coronavirus 2 plus additional time for reporting. We also show evidence that behavioural changes were already underway in many US counties days to weeks before state-level or local-level stay-at-home policies were implemented, implying that individuals anticipated public health directives where social distancing was adopted, despite a mixed political message. INTERPRETATION: This study strongly supports a role of social distancing as an effective way to mitigate COVID-19 transmission in the USA. Until a COVID-19 vaccine is widely available, social distancing will remain one of the primary measures to combat disease spread, and these findings should serve to support more timely policy making around social distancing in the USA in the future. FUNDING: None.

FIGURES

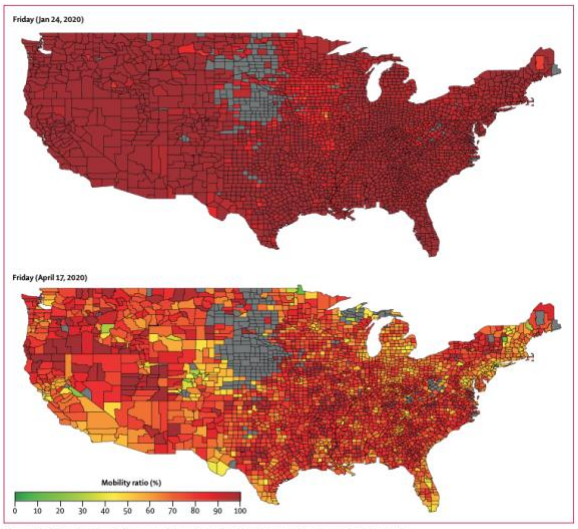


Figure 1: **Mobility ratio for each US county on Friday, Jan 24, 2020 (top), and on Friday, April 17, 2020 (bottom)**
The greyed-out areas in the Midwest are filtered because of low coverage in the Teralytics dataset.* This includes all counties with total trip counts less than two SDs below the mean.

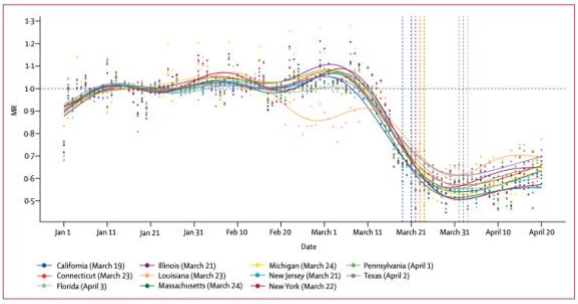


Figure 2: **Timeseries of MR for US states and the corresponding dates of stay-at-home orders**
The dots represent the raw MR data while the plotted lines are smoothed using a generalised additive model. Vertical dashed lines are stay-at-home orders (dates listed in the appendix pp 12–13). Some orders occurred on the same day; thus, only eight of 11 orders are visible. MR=mobility ratio.

	Correlation coefficient	Intercept	Slope
Essex, NJ (34013)	0·90	0·86	0·26
New York City, NY* (36061)	0·86	0·94	0·14
Middlesex, NJ (34023)	0·85	0·89	0·24
Cook, IL (17031)	0·85	0·89	0·22
Hudson, NJ (34017)	0·84	0·90	0·23
Nassau, NY (36059)	0·84	0·89	0·22
Union, NJ (34039)	0·84	0·85	0·28
Middlesex, MA (25017)	0·83	0·90	0·24
Suffolk, NY (36103)	0·83	0·85	0·26
Miami-Dade, FL (12086)	0·83	0·86	0·28
Bergen, NJ (34003)	0·82	0·87	0·24
Passaic, NJ (34031)	0·81	0·87	0·26
Suffolk, MA (25025)	0·81	0·90	0·27
Philadelphia, PA (42101)	0·80	0·84	0·33
Wayne, MI (26163)	0·80	0·82	0·32
Westchester, NY (36119)	0·80	0·88	0·22
Monmouth, NJ (34025)	0·76	0·83	0·28
Rockland, NY (36087)	0·74	0·81	0·36
Jefferson, LA (22051)	0·71	0·77	0·38
Oakland, MI (26125)	0·71	0·86	0·27
Orange, NY (36071)	0·66	0·80	0·34
Los Angeles, CA (06037)	0·62	0·89	0·22
Fairfield, CT (09001)	0·61	0·85	0·27
Orleans, LA (22071)	0·61	0·84	0·26
Harris, TX (48201)	0·53	0·78	0·38
All counties	0·71	0·88	0·24

The list is presented by the correlation coefficient in descending order. The last row represents the results of a single model for all 25 US counties. All coefficients are statistically significant at 95% CI. Federal Information Processing Standards code for each county is given. *To be consistent with the Johns Hopkins University Center for Systems Science and Engineering COVID-19 dashboard reporting,[5] New York City is used to represent New York County, Queens County, Bronx County, Kings County, and Richmond County in one location.

Table: **The selected 25 US counties and the associated Pearson correlation coefficient and generalised linear model coefficients (intercept and slope) between 11-day lagged mobility ratio and growth rate ratio**

HIGH PROPORTION OF ASYMPTOMATIC SARS-COV-2 INFECTIONS IN 9 LONG-TERM CARE FACILITIES, PASADENA, CALIFORNIA, USA, APRIL 2020

Feaster M, Goh YY.. Emerg Infect Dis. 2020 Jul 2;26(10). doi: 10.3201/eid2610.202694. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

An investigation launched by the City of Pasadena Public Health Department in California found that in nine long-term care facilities, the proportion of asymptomatic COVID-19-positive residents and staff is over 40%, suggesting symptom screening alone is not enough to prevent spread in these facilities; residents and staff must also get tested routinely in the absence of symptoms.

ABSTRACT

Our analysis of coronavirus disease prevalence in 9 long-term care facilities demonstrated a high proportion (40.7%) of asymptomatic infections among residents and staff members. Infection control measures in congregate settings should include mass testing-based strategies in concert with symptom screening for greater effectiveness in preventing the spread of severe acute respiratory syndrome coronavirus 2.

CURRENT SITUATION OF COVID-19 IN NORTHERN CYPRUS

Sultanoglu N, Baddal B, Suer K, Sanlidag T.. East Mediterr Health J. 2020 Jun 24;26(6):641-645. doi: 10.26719/emhj.20.070.
Level of Evidence: 4 - Expert Opinion

BLUF

A group of researchers from Near East University in Cyprus tracked COVID-19 cases in northern Cyprus and examined the efficacy of prevention measures. They found that the first confirmed COVID-19 positive case was a German tourist on March 9, 2020, and in response, those who had close contact with the tourist were quarantined in hotels. The Council of Ministers enacted strict precautions to prevent the spread of the virus (detailed in summary below). Between March 9 and May 4, 2020, northern Cyprus saw 108 COVID-19 cases (linked to tourists from Germany and the United Kingdom) and four COVID-19 deaths in total, with no new confirmed cases since April 17 (Figure 1). These findings suggest that northern Cyprus may set a good example for other countries in minimizing the COVID-19 outbreak.

SUMMARY

The precautionary measures taken in Cyprus following the first positive COVID-19 case on March 9, 2020 were as follows:
- Placement of non-essential civil workers on administrative leave.
- Closing non-essential businesses.
- Restricting travel and stopping the entrance of non-citizens.
- Placing citizens who recently returned to the country on 14-day quarantine.
- Enacting a curfew from 9:00 PM to 6:00 AM.
- Mandating the use of face masks in public areas (since April 24).
- Quarantining the villages that had the initial cases.
- Establishment of a pandemic hospital and hotlines.

ABSTRACT

Background: The public health burden of the novel coronavirus disease 2019 (COVID-19) is expected to increase and urgent strict measures by decision-makers is critical for the containment of the novel coronavirus (SARS-CoV-2) outbreak worldwide. Aims: This study aimed to give a real-time analysis of COVID-19 presence in northern Cyprus. Methods: All official SARS-CoV-2 positive cases were tracked and reported in terms of the origin, nationality, and transmission routes. Preventive measures taken after the first reported case were analyzed for their effectiveness as control strategies. Results: The index case of SARS-CoV-2 in northern Cyprus was identified as a female German tourist. First local case had travel history from the United Kingdom after which local transmission occurred. Rapid and strict containment measures have currently delayed a peak in observed cases. Conclusions: Rapid implementation of social-distancing measures, good hygiene measures and travel/gathering bans in northern Cyprus has been effective in controlling the outbreak.

FIGURES

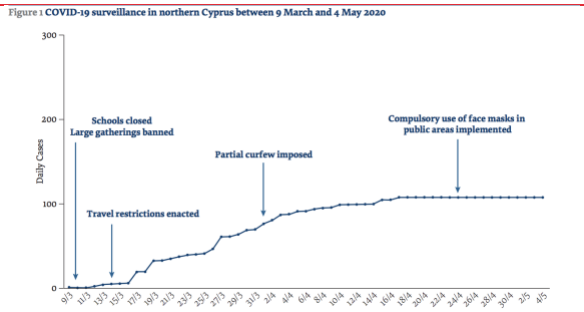


Figure 1. This graph displays the number of confirmed total cases (mislabeled in figure) of COVID-19 in northern Cyprus with respect to the date (Sultanoglu, Baddal, Suer, & Sanlidag, 2020).

HOMELESS PERSONS WITH MENTAL ILLNESS AND COVID PANDEMIC: COLLECTIVE EFFORTS FROM INDIA

Gowda GS, Chithra NK, Moirangthem S, Kumar CN, Math SB.. Asian J Psychiatr. 2020 Jun 24;54:102268. doi: 10.1016/j.ajp.2020.102268. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

This expert opinion piece from the National Institute of Mental Health and Neuro Sciences (NIMHANS) in India considers the challenges of the COVID-19 lockdown and the government's response to Homeless Persons with Mental Illness (HPMI) in the country. They note that in response to the pandemic and in accordance with research recommendations, the government has converted a myriad of buildings into centers in which HPMI are housed, fed, screened, and given primary care, psychiatric, and substance abuse treatment, including provisions to prevent the spread of SARS-CoV-2. The authors suggest that these measures are a worthwhile investment and should be maintained post-lockdown.

ABSTRACT

COVID-19 pandemic had made an unprecedented impact worldwide. India has entered into a total lockdown by invoking the special provision of Epidemic Diseases Act of 1897 and Disaster Management Act, 2015. The complete lockdown policy has a direct and indirect impact on Homeless Persons with Mental Illness (HPMI) concerning shelter, basic needs and access to health care, besides the transmission of COVID infection. In this manuscript, we highlight the collective efforts undertaken by both the Government and Civil Society in providing care and protection to HPMI against COVID during the lockdown in India.

PREVENTION IN THE HOSPITAL

LESSONS FROM A LUMBAR BURST FRACTURE PATIENT INFECTED WITH SARS-COV-2

Yu S, Zhang H, Chen W, Wan S, Zhang Y, Xiong X, Ding F.. Aging (Albany NY). 2020 Jun 22;12. doi: 10.18632/aging.103414. Epub 2020 Jun 22.

Level of Evidence: Other - Case Report

BLUF

Orthopedic surgeons in Wuhan discuss the case of a 52-year-old man who presented for emergency surgery with a lumbar burst fracture and who on postoperative day three developed chills, high fever (39.5°C) and chest CT findings consistent with COVID-19 (Figures 2 and 4). The patient was transferred to Infectious Disease after testing positive for SARS-CoV-2 via nucleic acid test. No one involved in the patient's care became infected, however, the authors emphasize the importance of transmission precautions when providing emergency surgery for patients with unknown SARS-CoV-2 status.

ABSTRACT

In December 2019, the 2019 novel coronavirus (SARS-CoV-2) began spreading in China. At present, there are no special protocols for treating lumbar burst fracture (LBF) patients infected with SARS-CoV-2. Here, we present our lessons and experiences with a patient presenting with a severe LBF complicated by an occult SARS-CoV-2 infection. The clinical data for a 52-year-old male LBF patient were collected during the incubation period of COVID-19. The patient exhibited no obvious COVID-19-related symptoms prior to his surgery, and his vital signs were stable on the first day after the operation. By postoperative day 3, however, the patient was exhibiting chills and high fever. A chest CT showed a patchy high-density shadow surrounded by ground-glass opacity in the lower portion of his right lung. A nucleic acid test for SARS-CoV-2 was positive, and the patient was then transferred to the Department of Infectious Disease for further special treatment. This case taught that when treating patients with severe trauma within an epicenter of this pandemic, it is crucial for healthcare workers to be vigilant so as to avoid potential widespread outbreaks of COVID-19 within hospitals.

FIGURES

Figure 2. Preoperative chest CT examination of the patient.

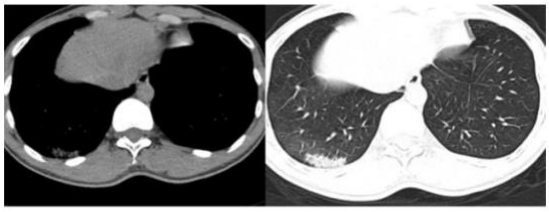


Figure 4. Chest CT examination of the patient on postoperative day 3.

MANAGEMENT

ACUTE CARE

COMMUNITY ACQUIRED CO-INFECTION IN COVID-19: A RETROSPECTIVE OBSERVATIONAL EXPERIENCE

Lehmann CJ, Pho MT, Pitrak D, Ridgway JP, Pettit NN.. Clin Infect Dis. 2020 Jul 1:ciaa902. doi: 10.1093/cid/ciaa902. Online ahead of print.
Level of Evidence: 3 - Non-randomized controlled cohort/follow-up study

BLUF

A retrospective observational analysis of 321 adult patients (≥ 18 years) hospitalized at the University of Chicago Medical Center between 1 March and 11 April 2020 examined rates of community acquired co-infection (Table 1) and antibiotic use in COVID-19 positive patients (confirmed via SARS-CoV-2 reverse transcription-polymerase chain reaction [RT-PCR]). Medical record review conducted by authors (date of admission, intensive care unit [ICU] admission, mortality, antibiotic administration, and microbiologic test results) found that 3.7% of patients (n=12) had a co-infection (clinical signs/symptoms of infection and detection of a pathogen by diagnostic test) and 41% of patients admitted to the ICU had co-infection (n=7, p<0.005), while antibiotics were used in 69% of patients (n=222). Authors concluded that antibiotics may not be indicated in most patients as co-infection was infrequent and often viral, but ICU patients may require antibiotic therapy due to higher incidence of co-infection.

ABSTRACT

Community acquired co-infection in COVID-19 is not well defined. Current literature describes co-infection in 0-40% of COVID-19 patients. In this retrospective report, co-infection was identified in 3.7% of patients and 41% of patients admitted to intensive care (p<0.005). Despite infrequent co-infection, antibiotics were used in 69% of patients.

FIGURES

Table 1. Coinfection rates by pathogen

Variable		N (%)
COVID-19 Patients		321 (100)
	Any Coinfection	12 (3.7)
	Bacterial [a]	7 (2.2)
	Viral	5 (1.6)
Culture [b, c]		
		66 (21)
	Staphylococcus aureus [a]	2 (0.6)
	Proteus mirabilis [a]	1 (0.3)
RBVP		291 (91)
	Influenza A	3 (0.9)
	Rhino/enterovirus	2 (0.6)
	Bordetella parapertussis	1 (0.3)
RSV/Flu PCR		15 (5)
		0 (0)
S. pneumoniae UrAg		236 (74)
		4 (1.2)
L. pneumophilia UrAg		240 (75)
		0 (0)

Table 1: N: number of patients who received the specified test and number of positive tests by pathogen aOne patient grew S. aureus and P. mirabilis from the same ET aspirate culture b Endotracheal Aspirate n=33, Expectorated Sputum n=33. c Candida and Aspergillus isolates not included Abbreviations: RVBP, Respiratory Viral Bacterial Pathogen Panel; RSV, Respiratory Syncytial Virus; Flu, Influenza; UrAg, Urine Antigen

EMERGENCY MEDICINE

CLINICAL FEATURES OF COVID-19-INFECTED PATIENTS WITH ELEVATED LIVER BIOCHEMISTRIES: A MULTICENTER, RETROSPECTIVE STUDY

Fu Y, Zhu R, Bai T, Han P, He Q, Jing M, Xiong X, Zhao X, Quan R, Chen C, Zhang Y, Tao M, Yi J, Tian D, Yan W.. Hepatology. 2020 Jun 30. doi: 10.1002/hep.31446. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

A retrospective multi-centered study from Wuhan, China analyzed clinical characteristics and factors (chest pain, dyspnea, and laboratory values) related to abnormal liver biochemistries from confirmed COVID-19 patients (n=482) between February 1-20, 2020 (see summary for results). The data suggests a mild elevation in liver biochemistries is common in COVID-19 patients, possibly from chronic hypoxia and excessive inflammation and researchers recommend close monitoring for cardiac injury in patients with elevated TBIL, AST, or ALT.

SUMMARY

The researchers found the following:
- 142 of the 482 patients had elevated liver biochemistries (ALT 67.6%, AST 69%, TBIL 16.2%).
- Independent predictors of abnormal liver biochemistries: chest pain (p=0.018), dyspnea (p=0.001), elevated CRP (p=0.008), WBC (p=0.013) and Hb (p=0.001).
- Compared to patients with normal levels, those patients with liver biochemistry elevations had poorer prognosis and higher mortality rates: with elevated ALT (29.6% vs. 6.5%, p<0.001), with elevated AST (33.7% vs. 8.1%, p<0.001) and with elevated TBIL (60.9% vs 10.9%, p<0.001).

ABSTRACT

In December 2019, an outbreak of coronavirus disease 2019 (COVID-19) emerged in Wuhan, China. Although it has been reported that some COVID-19 patients showed elevated liver biochemistries, there are few studies regarding clinical features and prognosis of these patients. In this multicenter, retrospective study, we collected data on laboratory-confirmed COVID-19 patients from three hospitals in Wuhan, China, who died or were discharged between February 1, 2020, and February 20, 2020. The data on demographics, comorbidities, clinical symptoms, laboratory examinations on admission, complications, treatment, and outcome were collected. A total of 482 patients were enrolled in this study. Of those, 142 (29.5%) patients showed abnormal liver biochemistries on admission, and patients with elevated alanine aminotransferase (ALT), aspartate aminotransferase (AST), and total bilirubin (TBIL) accounted for 67.6%, 69.0%, and 16.2%, respectively. Those with abnormal liver biochemistries showed higher percentages of severe cases and comorbidities and were more likely to have dyspnea, chest distress or pain, and increased hemoglobin (Hb) on admission. Higher rates of complications and mortality and worse recovery when discharged were observed in patients with abnormal AST or TBIL. The multivariable regression analysis showed that chest distress or pain (odds ratio [OR], 1.765; P = 0.018), dyspnea (OR, 2.495; P = 0.001), elevated C-reactive protein [CRP] level (OR, 1.007; P = 0.008), elevated white blood count (WBC) (OR, 1.139; P = 0.013), and elevated Hb concentration (OR, 1.024; P = 0.001) were independent factors associated with elevated liver biochemistries in COVID-19 patients. Conclusion: Elevated liver biochemistries were common in COVID-19 patients. Patients with hypoxia or severe inflammation are more likely to experience increased liver biochemistries on admission. Those with abnormal AST or TBIL on admission are more likely to suffer from severe complications and death.

MEDICAL SUBSPECIALTIES

OROPHARYNGEAL CANDIDIASIS IN HOSPITALIZED COVID-19 PATIENTS FROM IRAN: SPECIES IDENTIFICATION AND ANTIFUNGAL SUSCEPTIBILITY PATTERN

Salehi M, Ahmadikia K, Mahmoudi S, Kalantari S, Jamalimoghadam Siahkali S, Izadi A, Kord M, Dehghan Manshadi SA, Seifi A, Ghiasvand F, Khajavirad N, Ebrahimi S, Koohfar A, Boekhout T, Khodavaisy S.. Mycoses. 2020 Jul 1. doi: 10.1111/myc.13137. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

A cross-sectional study conducted in Iran from 1 March to 30 April 30 2020 studied 53 hospitalized COVID-19 patients with oropharyngeal candidiasis (OPC) to assess prevalence, causative agents (identification by 21-plex PCR), and in vitro antifungal susceptibility (azoles, polyenes, echinocandins). Authors found 80% of patients were ≥50 years of age (p=0.03), females were affected slightly more than males (56.6% vs 43.3%), 71% of participants exhibited lymphopenia (p<0.001), and the most frequent underlying conditions were cardiovascular disease (52.8%) and diabetes (37.7%) (Table 1). They also report generally high antifungal susceptibility to all three antifungals (Table 2), with C. albicans (70.7%) being the most common isolate. Researchers suggest that further studies may be useful for OPC prophylaxis and management in critically ill COVID-19 patients.

ABSTRACT

BACKGROUND: Emergence of coronavirus disease 2019 (COVID-19) is a major healthcare threat. Apparently, the novel coronavirus (SARS-CoV-2) is armed by special abilities to spread and dysregulate the immune mechanisms. The likelihood of oropharyngeal candidiasis (OPC) development in COVID-19 patients with a list of attributable risk factors for oral infections has not yet been investigated. OBJECTIVES: We here aim to investigate the prevalence, causative agents, and antifungal susceptibility pattern of OPC in Iranian COVID-19 patients. PATIENTS AND METHODS: A total of 53 hospitalized COVID-19 patients with OPC were studied. Relevant clinical data were mined. Strain identification was performed by 21-plex PCR and sequencing of the internal transcribed spacer region (ITS1-5.8S-ITS2). Antifungal susceptibility testing to fluconazole, itraconazole, voriconazole, amphotericin B, caspofungin, micafungin and anidulafungin was performed according to the CLSI broth dilution method. RESULTS: In 53 COVID-19 patients with OPC, cardiovascular diseases (52.83 %), and diabetes (37.7 %) were the principal underlying conditions. The most common risk factor was lymphopenia (71%). In total, 65 Candida isolates causing OPC were recovered. C. albicans (70.7%) was the most common, followed by C. glabrata (10.7%), C. dubliniensis (9.2%), C. parapsilosis sensu stricto (4.6%), C. tropicalis (3%), and Pichia kudriavzevii (=C. krusei, 1.5%). Majority of the Candida isolates were susceptible to all three classes of antifungal drugs. CONCLUSION: Our data clarified some concerns regarding the occurrence of OPC in Iranian COVID-19 patients. Further studies should be conducted to design an appropriate prophylaxis program and improve management of OPC in critically ill COVID-19 patients.

FIGURES

Table 1. Demographic and clinical characteristics of patients with Iranian COVID-19 infection and

Variables	Frequency	Percentage
Gender		
Male	23	43.4
Female	30	56.6
Age groups		
<50	11	20.7
≥50	42	79.3
Underlying conditions		
Cardiovascular diseases	28	52.8
Diabetes	20	37.7
Chronic kidney diseases	11	20.7
Hematological malignancies	5	9.4
Risk factors		
Recipient broad-spectrum antibiotics	49	92
Corticosteroid therapy	25	47
Admission to ICU	26	49
Mechanical ventilation	16	30
Respiratory support		
Non-invasive	49	92.4
Invasive	4	7.5
Clinical presentations		
Lymphopenia	38	71.7
Leukopenia	10	18.9
Leukocytosis	10	18.9
Prolonged fever	39	73.5
Respiratory distress	50	94.3

Table 1: Demographic and clinical characteristics of patients with Iranian COVID-19 infection and oropharyngeal candidiasis.

Table 2. *In vitro* antifungal susceptibility pattern of *Candida* isolates recovered from oropharyngeal lesions of Iranian COVID-19 patients

Candida species (n)	Antifungal drugs	Distribution of isolates based on MIC values (μg/mL)									MIC range (μg/mL)	MIC_{50} (μg/mL)	GM (μg/mL)	% of S/WT
		0.008	0.016	0.031	0.062	0.125	0.25	0.5	1	2	4				
C. albicans (46)	FLU					8	25*	10	2	1		0.125–2	0.25	0.286	100
	ITR		1	3	11	22	8	1				0.016–0.5	0.125	0.107	80.43
	VRC		6	19	16	3	2					0.016–0.25	0.031	0.043	95.65
	AmB		27	11	6	1		1				0.016–0.5	0.016	0.025	100
	CAS	2	5	16	14	6	1	2				0.008–0.5	0.031	0.048	95.65
	MCF	41	5									0.008–0.016	0.008	0.009	100
	AN1	21	15	7	3							0.008–0.062	0.016	0.014	100
C. glabrata (7)	FLU							4	1	2		0.5–2	0.5	0.82	100
	ITR				1	2	2	1	1			0.062–1	0.25	0.226	100
	VRC			3	3	1						0.031–0.125	0.062	0.051	100
	AmB		3	1	3							0.031–0.125	0.031	0.031	100
	CAS						7					0.25	0.25	0.25	0
	MCF	7										0.008	0.008	0.008	100
	AN1	3	2	2								0.008–0.031	0.016	0.014	100
C. dubliniensis † (6)	FLU					3	2			1		0.125–2	0.125	0.25	83.33
	ITR		1		1	4						0.016–0.125	0.125	0.079	100
	VRC		2		4							0.016–0.062	0.062	0.039	100
	AmB		2	3			1					0.016–0.25	0.031	0.035	100
	CAS		3	1	1				1			0.016–1	0.016	0.044	83.33
	MCF	5	1									0.008–0.016	0.008	0.009	100
	AN1	4	1	1								0.008–0.031	0.008	0.011	100
C. parapsilosis (3)	FLU							3				0.5	0.5	0.5	100
	ITR			3								0.031	0.031	0.031	100
	VRC			3								0.031	0.031	0.031	100
	AmB			3								0.031	0.031	0.031	100
	CAS						3					0.25	0.25	0.25	100
	MCF	3										0.008	0.008	0.008	100

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	AN1	3										0.008	0.008	0.008	100
C. tropicalis (2)	FLU							2				0.5	-	-	100
	ITR					2						0.125	-	-	100
	VRC			1		1						0.031–0.125	-	-	100
	AmB		1		1							0.016–0.062	-	-	100
	CAS					2						0.125	-	-	100
	MCF	1	1									0.008–0.016	-	-	100
	AN1		1	1								0.016–0.031	-	-	100
Pichia kudriavzevii (= *C. krusei*) (1)	FLU										1	-	-	-	0*
	ITR						1					-	-	-	100
	VRC					1						-	-	-	100
	AmB				1							-	-	-	100
	CAS									1		-	-	-	0
	MCF		1									-	-	-	100
	AN1				1							-	-	-	100

Table 2: In vitro antifungal susceptibility pattern of Candida isolates recovered from oropharyngeal lesions of Iranian COVID19 patients.

CARDIOLOGY

INCIDENCE OF ARRHYTHMIAS AND ELECTROCARDIOGRAPHIC ABNORMALITIES IN SYMPTOMATIC PEDIATRIC PATIENTS WITH PCR POSITIVE SARS-COV-2 INFECTION INCLUDING DRUG INDUCED CHANGES IN THE CORRECTED QT INTERVAL (QTC)

Samuel S, Friedman RA, Sharma C, Ganigara M, Mitchell E, Schleien C, Blaufox AD.. Heart Rhythm. 2020 Jul 1:S1547-5271(20)30632-9. doi: 10.1016/j.hrthm.2020.06.033. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

Pediatricians from Cohen Children's Medical Center in New York City conducted a single center retrospective chart review of 36 pediatric patients with PCR-confirmed SARS-CoV-2 hospitalized between March 1-April 30, 2020. 6/36 (17%) patients had significant arrhythmias (Table 2) and hydroxychloroquine use was associated with QTc prolongation (411+19 msec vs 426+15 msec, p<0.0001)(Figure 1). The authors suggest a distinction between adult and pediatric data due to the lack of common associations between arrhythmias and clinical findings normally seen in adults (Summary) and urge for more research on cardiac complications of COVID-19 in the pediatric population.

SUMMARY

Children were included for analysis if they were SARS-CoV-2 positive by PCR of nasopharyngeal sample and had been on continuous telemetry for their entire hospitalization. The authors excluded patients with IgG antibodies for SARS-CoV-2 or with known history of arrhythmias, long QT syndrome, other channelopathies, or hemodynamically significant congenital heart disease. Of the six children with arrhythmias (Table 2) five were monomorphic ventricular tachycardia and one sustained atrial tachycardia, all self-resolved. Four of these six (67%) had non-cardiac comorbidities, but this proportion was similar in those without arrhythmias (20/30, p=1). The proportion of patients with elevated troponin was the same in those with and without arrhythmias (2/6 vs 6/23, p = 0.87). There was no association between arrhythmias and:

- Demographic variables (age, weight, gender, race)
- Pre-hospitalization symptoms
- Laboratory values (pro-BNP, maximum CRP, electrolytes)

- Echocardiographic findings (ejection fraction, LV dysfunction)
- Other significant ECG findings (baseline abnormalities, maximum QTc)

16/36 (44%) of patients received hydroxychloroquine. Its use was associated with QTc prolongation (411+19 msec vs 426+15 msec, p<0.0001). However, there was no difference in QTc between patients with and without arrhythmias (425+15 msec vs 425+15 msec, p=1)(Figure 1).

ABSTRACT

BACKGROUND: There is limited data regarding the electrophysiological abnormalities and arrhythmias in children with COVID-19, including those associated with treatment using potentially pro-arrhythmic Hydroxychloroquine (HCQ) and Azithromycin (AZN). OBJECTIVES: To describe the electrophysiologic findings and arrhythmias associated with pediatric COVID-19 and its treatment. METHODS: A single center retrospective chart review was undertaken and included all patients with 1) symptoms of COVID-19, and 2) PCR (+) nasopharyngeal swabs for SARS-CoV-2 who were placed on continuous telemetry for the duration of their hospitalization during March through May, 2020. RESULTS: Thirty-six patients were included in the study. Significant arrhythmias were found in 6 (non-sustained (ns) ventricular tachycardia in 5 and sustained atrial tachycardia in 1). All were self-resolving and half prompted prophylactic anti-arrhythmic therapy. Patients with significant arrhythmias were likely to have non-cardiac co-morbidities (4/6), but these were not more common than in patients without arrhythmias (20/30, p=1). The use of HCQ with or without AZN was associated with statistically significant QTc prolongation (411+19 msec vs 426+15 msec, p<0.0001). QTc was not statistically different in patients with and without arrhythmias (425+15 msec vs 425+15 msec, p=1). CONCLUSIONS: In pediatric patients with PCR positive active COVID-19 infection, significant arrhythmias are infrequent, but more common than expected in a general pediatric population. Comorbidities are not more common in patients with arrhythmias than in patients without arrhythmias. COVID-19 treatment using HCQ is associated with QTc prolongation, but was not associated with arrhythmias in pediatric patients.

FIGURES

Table 2. Patient demographic and characteristics pertinent to the finding of arrhythmia.

Pt	Age (yrs)	Arrhythmia	Co-morbidities	HCQ ± AZN	QTc prolonged	Echo findings	SF by Echo (%)	EF by Echo (%)	High Sensitivity Troponin-T (ng/L)	circumstances
1	12	Monomorphic VT	Sickle cell disease	No	No	Mild LV dilation with preserved ventricular function	36	59	<6	None
2	20	Monomorphic VT	Lymphoma, mediastinal mass, pericardial effusion	No	No	Large circumferential pericardial effusion	33	69	10	None
3	13	Sustained Atrial tachycardia	Myocarditis secondary to covid-19	No	No	Mild LV dysfunction	32	49	398	High dose epinephrine and nor-epi drips
4	13	Monomorphic VT	Bloom syndrome, history of testicular cancer	No	No	Mild to moderate LV dysfunction	25	46	<6	None
5	17	Monomorphic VT	Myocarditis secondary to covid-19	No	No	Normal structure and function	31		4013	None
6	16	Monomorphic VT	Acute lymphocytic leukemia, mediastinal mass, pericardial effusion	No	No	Normal structure and function	NA	65	12	HypoMg, HypoK and HypoCa

Key: EF = ejection fraction, SF = shortening fraction, HypoCa = hypocalcemia, HypoK = hypo kalemia, HypoMg = hypo magnesemia.

Journal Pre-proof

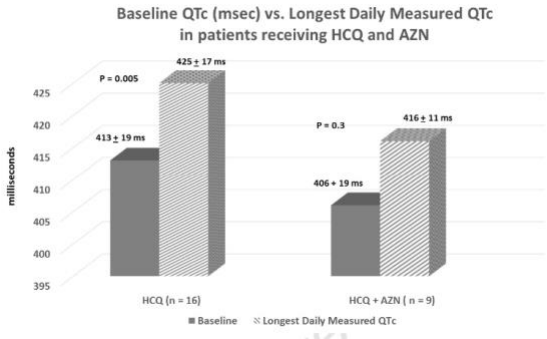


Figure 1. Bar graphs showing QTc prolongation associated with the use of hydroxychloroquine (HCQ) or Azithromycin (AZN). Baseline QTc (solid bars) is compared to the longest daily measured QTc after initiation of therapy (hashed bars) seen during treatment for each treatment strategy. P values for paired T-test comparing baseline and longest daily measured QTc after initiation of therapy values for each group are displayed.

HEMATOLOGY AND ONCOLOGY

CASE OF THE MONTH FROM MEMORIAL SLOAN KETTERING CANCER CENTER, NEW YORK: MANAGING NEWLY-DIAGNOSED METASTATIC TESTICULAR GERM CELL TUMOR IN A COVID-19 POSITIVE PATIENT

Almassi N, Mulhall JP, Funt SA, Sheinfeld J.. BJU Int. 2020 Jul 1. doi: 10.1111/bju.15157. Online ahead of print.
Level of Evidence: Other - Case Report

BLUF

The authors present the case of a 17-year-old COVID-19 positive male with a history of congenital solitary left testis who was recently diagnosed with metastatic testicular germ cell tumor. The decision to pursue surgical management was complicated by the patient's COVID-19 positive status, so radical orchiectomy and chemotherapy were initiated after the patient became COVID-19 negative. This case demonstrates the unique challenges in cancer management that have been introduced by the current pandemic.

ABSTRACT

A 17-year-old young man with history of a congenital solitary left testis presented to our clinic in late April 2020 with left testicular swelling and discomfort over the preceding few weeks. The patient denied unintentional weight loss or nipple tenderness but reported new, mild left-sided back discomfort. His medical history was notable for asthma and a congenitally absent right testis for which he underwent negative surgical exploration in childhood.

FIGURES

Table 1: Comparison of the two management strategies considered in this case.

	Strategy #1	Strategy #2
Description of Management Strategy	Delay treatment until patients tests COVID-19 negative, then proceed with radical orchiectomy and TESE, followed by induction chemotherapy.	Immediate induction chemotherapy, followed by post-chemotherapy surgery (RPLND and left radical orchiectomy)
Treatment Delay?	Yes (until tests COVID-19 negative)	No
Fertility Considerations	Chance of sperm preservation with *ex vivo* TESE at time of radical orchiectomy	Virtually no chance of harvesting viable sperm at post-chemotherapy orchiectomy
Surgical Considerations	Potential increased risk of perioperative morbidity with recent COVID-19 illness (1,2). Surgical delay awaiting negative COVID-19 screening test	Defers surgery to the post-chemotherapy setting, potentially reducing risk of COVID-19 associated morbidity
Chemotherapeutic Considerations	Potential for EPx4 or BEPx3 for IGCCCG good risk disease depending on post-orchiectomy tumor markers	Requires BEPx4 for IGCCCG intermediate risk disease

BEP – Bleomycin, etoposide, cisplatin. EP – etoposide, cisplatin. IGCCCG – International Germ Cell Cancer Collaborative Group. RPLND – retroperitoneal lymph node dissection. TESE – Testicular sperm extraction.

ADJUSTING PRACTICE DURING COVID-19

MITIGATE RISKS OF MEDICATION INTERRUPTION DUE TO COVID-19 FOR ELDERLY WITH CHRONIC DISEASES

Hsiao SH, Chang HM, Kang YT, Chen YH.. Kaohsiung J Med Sci. 2020 Jul 1. doi: 10.1002/kjm2.12263. Online ahead of print.
Level of Evidence: 3 - Non-randomized controlled cohort/follow-up study

BLUF

A prospective interventional study conducted by a multidisciplinary group of researchers at the Kaohsiung Municipal Ta-Tung Hospital (KMTTH) in Taiwan found that the COVID-19 outbreak resulted in elderly patients (defined as age 75 and older) visiting the hospital pharmacy for refills at significantly lower rates compared to pre-pandemic and prior year controls (p=0.002, Table 1). One month after the creation and implementation of an outdoor dispensary for multi-month drug refills at KMTTH, analysis showed that there was now no statistical difference in the number of elderly patients returning for refills on chronic medications, a complete reversal from the month before. These results suggest that the creation of alternative medication delivery mechanisms for citizens most at risk of COVID-19 disease may help prevent nonadherence to medical regimens for chronic disease.

FIGURES

	Before outbreak of SARS-CoV-2			At early stage of outbreak of SARS-CoV-2			After "outdoor dispensary counters" service		
Time period variables	January 1, 2019 to January 22, 2019	January 1, 2020 to January 22, 2020	P value**	January 23, 2019 to February 24, 2019	January 23, 2020 to February 24, 2020	P value**	February 25, 2019 to March 31, 2019	February 25, 2020 to March 31, 2020	Pvalue**
Gender			.714			.272			.227
Male	3762 (47.4%)	3922 (47.1%)		5404 (47.6%)	4733 (48.3%)		5945 (51.7%)	5512 (50.9%)	
Female	4177 (52.6%)	4405 (52.9%)		5954 (52.4%)	5059 (51.7%)		5554 (48.3%)	5319 (49.1%)	
Age			.155			.002****			.272
65-69	2096 (26.4%)	2309 (27.7%)		3056 (26.9%)	2692 (27.5%)		3050 (26.5%)	2909 (26.9%)	
70-74	2027 (25.5%)	2071 (24.9%)		2650 (23.3%)	2453 (25.1%)		2872 (25.0%)	2782 (25.7%)	
75+	3816 (48.1%)	3947 (47.4%)		5652 (49.8%)	4647 (47.5%)		5577 (48.5%)	5140 (47.5%)	
Clinical departments			.094			.083			.888
Internal medicine	4418 (55.6%)	4666 (56.0%)		6448 (56.8%)	5410 (55.2%)		6472 (56.3%)	6127 (56.6%)	
Surgery department	463 (5.8%)	545 (6.5%)		631 (5.6%)	557 (5.7%)		660 (5.7%)	625 (5.8%)	
Other departments	3058 (38.5%)	3116 (37.4%)		4279 (37.7%)	3825 (39.1%)		4367 (38.0%)	4079 (37.7%)	
Straight-line distance between residence and KMTTH (km)			.706			.822			.946
<3 km	4909 (61.8%)	5125 (61.5%)		7084 (62.4%)	6122 (62.5%)		7113 (61.9%)	6695 (61.8%)	
>3 km	3030 (38.2%)	3202 (38.5%)		4274 (37.6%)	3670 (37.5%)		4386 (38.1%)	4136 (38.2%)	

Table 1: Difference analysis of rate of geriatrics back to the hospital for medicines with prescriptions for chronic diseases. *Goodness-of-fit test. **P < .01.

MEDICAL SUBSPECIALTIES

RESUMPTION OF RESPIRATORY OUTPATIENT SERVICES IN THE COVID-19 ERA: EXPERIENCE FROM SOUTHERN ITALY

Crimi C, Impellizzeri P, Campisi R, Spicuzza L, Vancheri C, Crimi N.. Am J Infect Control. 2020 Jul 1:S0196-6553(20)30633-7. doi: 10.1016/j.ajic.2020.06.210. Online ahead of print.
Level of Evidence: Other - Guidelines and Recommendations

BLUF

This report describes the measures taken in Southern Italy to plan for the resumption of the outpatient activity in a respiratory unit during the COVID-19 pandemic. The authors identify the main challenges faced when planning to restart respiratory outpatient clinics and outline potential solutions (Table1). The authors' proposed approach can be utilized by other respiratory clinics that are planning to resume outpatient activity during the COVID-19 pandemic.

SUMMARY

The specific details of the author's proposed model are summarized below:

- Patients are given appointments telephonically and will be instructed to come to the clinic on specific dates. Before entering the clinic, an outpatient triage nurse, while wearing adequate PPE, will screen the patient using a COVID-19 risk assessment questionnaire and obtaining the patient's temperature. If the patient is assigned a high-risk level, the patient will

be referred to the emergency department for nasopharyngeal swab testing, and their respiratory visit will be rescheduled. Patients who are assigned a low-risk level will be given a surgical mask and hand sanitizer and will be able to enter the clinic.

- Pulmonologist evaluation will take place in an exam room with minimal furniture. The physician will be provided adequate PPE, a stethoscope, a portable wireless echography probe for lung ultrasound evaluation, and an oximeter. All equipment and furniture will be wiped down with alcohol solutions between each patient.
- During Pulmonary Function Tests, patients will be placed near the window with a plexiglass wall between the patient and the technician, who will sit in the same direction as the patient to prevent exposure in case the patient coughs or sneezes in the test area.
- Each room will be equipped with adequate ventilation by using natural ventilation and an exhaust fan at the window to increase ventilation and direct airflow (Figure 1).

ABSTRACT

COVID-19 pandemic turned the entire health-care system organization upside-down, suspending elective activities and outpatient services. In Italy, we are entering a second phase of the pandemic and several strategies has been developed to "re-open" the country, some businesses, and also health-care outpatient activities. This manuscript describes the experience of a Southern Italy Respiratory Unit for safely resuming outpatient respiratory services and preventing COVID-19 transmission.

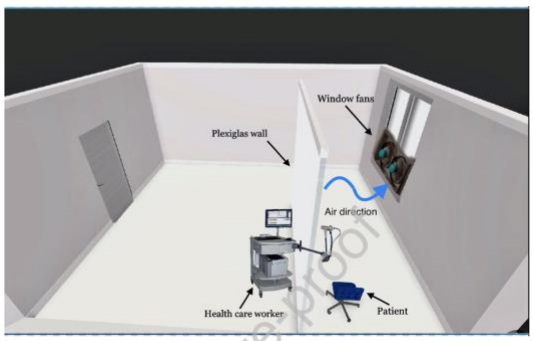
FIGURES

Table 1. Problems and possible solutions for resuming respiratory outpatient clinics.

Challenges	Identified Solutions
Physical distancing	One patient at a specific date/time
COVID-19 infection control	COVID-19 risk assessment questionnaire Body temperature detection
HCW protection	PPE + Hand washing
Airborne / Droplet transmission	HCW sitting in the same direction as the patient during PFTs Plexiglas wall between HCW and the patient
Poorly ventilated room	Natural ventilation + Window exhaust fan
Contact transmission	Cleaning of the equipment and surfaces

COVID-19, Coronavirus 2019; HCW, health-care worker; PPE, personal protective equipment; PFTs, pulmonary function tests.

Figure 1. 3D image of spirometry room design.



CARDIOLOGY

ECHOCARDIOGRAPHIC CHARACTERISTICS OF SUBJECTS WITH COVID-19: A CASE SERIES

Vera-Pineda R, Francisco Carrizales-Sepulveda E, Camacho-Ortiz A, Nuzzolo-Shihadeh L, Cruz-Ramos F, Ordaz-Farias A, Benavides-Gonzalez MA, Carranza-Villegas G.. Cardiol Res. 2020 Aug;11(4):260-265. doi: 10.14740/cr1084. Epub 2020 Jun 3. Level of Evidence: 4 - Case-series

BLUF

A case series by authors at University Hospital, Mexico explored echocardiographic features in four COVID-19 patients (Table 1), with cases classified as severe (n=1) and critical (n=3), all with acute respiratory distress syndrome (ARDS). Transthoracic echocardiography (TTE) was performed and found that of the four cases all had altered ventricular function including left ventricular dysfunction, three had elevated creatine kinase and creatine kinase myocardial band (Table 1), one had a mobile 12x10 mm vegetation attached to the septal leaflet of the tricuspid valve with severe tricuspid regurgitation (Figure 1a), two had reduced ejection fraction, and those available for global longitudinal strain (GLS) analysis (n=3) showed signs of dysfunction (Table 2, Figure 1b). At the conclusion of the study two cases had expired, one remained intubated in the ICU, and one was discharged home after 13 days. The authors suggest that acute cardiac injury is an independent risk factor for mortality in patients with COVID-19 and further research regarding echocardiographic characteristics in this population can be useful in prompt interpretation of disease.

ABSTRACT

Although coronavirus disease 2019 (COVID-19) manifests in most cases with respiratory symptoms, other presentations can occur. Direct damage to the cardiovascular system has been reported and recently, acute myocardial injury has been identified as a risk factor for mortality. Transthoracic echocardiography is a non-invasive tool that allows the detection of myocardial damage with validated markers (left ventricular ejection fraction and global longitudinal strain). Herein, we present the echocardiographic findings in four patients with COVID-19. All cases had acute respiratory distress syndrome (100%). Three out of four had elevated levels of creatine kinase and creatine kinase myocardial band. One case had ventricular concentric remodeling (25%). All cases (100%) had altered ventricular function: two had a reduced ejection fraction (50%) and, of those available for global longitudinal strain analysis, all had abnormal global longitudinal strain (100%). One case was found to have a tricuspid vegetation of 12 x 10 mm with no other manifestation of endocarditis. All of our cases had left ventricular dysfunction as assessed by echocardiography. One of our patients had a vegetation in the tricuspid valve. Two of our cases had a reduced ejection fraction. The importance of acute cardiac injury in COVID-19 has recently been established. A recent study found it to be an independent risk factor for mortality in patients with this disease. Information regarding echocardiographic characteristics of this population is scarce. Further research to elucidate the impact of these characteristics on morbidity and mortality is urgently needed.

FIGURES

Table 1

Baseline Clinical and Laboratory Characteristics

Variable	Case 1	Case 2	Case 3	Case 4
Gender	Male	Male	Male	Male
Age (years)	76	64	66	26
Comorbidities	Prostate cancer	HIV	None	None
White blood cell count, /μL	11.2	8.6	14.3	8.1
Lymphocytes, /μL	0.306	0.483	0.563	1.4
Serum creatinine, mg/dL	0.9	0.9	5.3	0.8
Aminotransferase				
Aspartate, U/L	44	96	99	68
Alanine, U/L	40	108	43	85
Albumin, g/dL	2.1	2	2.7	3.4
hs-CRP, mg/dL	27	20.6	23.1	11.3
ARDS	Yes	Yes	Yes	Yes
PaO_2/FiO_2 ratio	59	66	180	258
Cardiac injury markers				
hs-TpnI, ng/L	2.8	5.4	5.6	1.4
CK, U/L	721	868	517	50
CK-MB, U/L	29	35.3	26.5	n/a
LDH, U/L	312	259	424	317

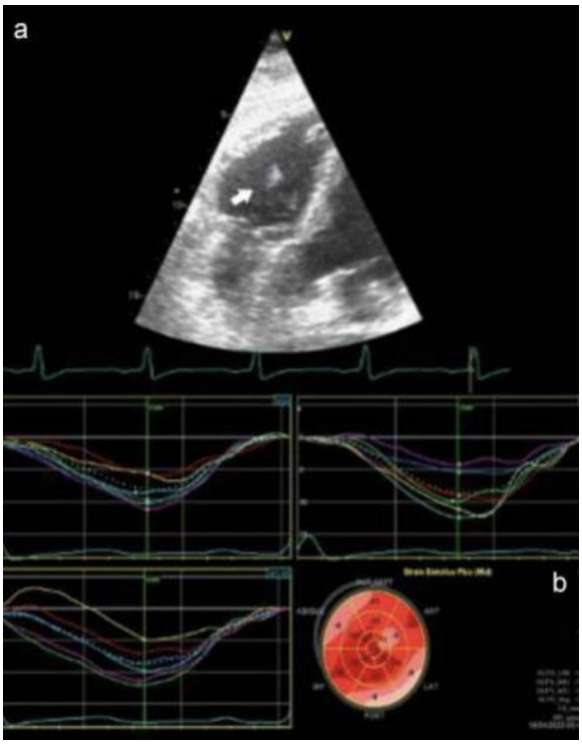
hs-CRP: high-sensitivity C-reactive protein; ARDS: acute respiratory distress syndrome; hs-TpnI: high-sensitivity troponin I; CK: creatine kinase; CK-MB: creatine kinase myocardial band; LDH: lactate dehydrogenase.

Table 2

Echocardiographic characteristics and Recommended Reference Values

Variable	Case 1	Case 2	Case 3	Case 4	Reference value
LV septal thickness, cm	0.8	1.2	1.1	0.7	0.6 - 1
Posterior wall thickness, cm	0.8	1.1	0.8	0.9	0.6 - 1
LV indexed mass, g/m^2	80.7	56.5	81.4	73.6	49 - 115
Relative wall thickness	0.31	0.47	0.32	0.37	0.24 - 0.42
V6dVI MOD BP	38	76	n/a	83	62 - 150
V6vVI MOD BP	25	26	n/a	56	21 - 61
LVEF, %	35	66	65	33	52 - 72
Left atrial indexed volume, mL/m^2	21.8	15.4		11.1	< 34
Average GLS, %	-14	-18	n/a	-14	< -18.5%
Aplax GLS, %	-12	-18	n/a	-14	< -18.5%
a4C GLS, %	-13	-18	n/a	-13	< -18.5%
a2C GLS, %	-15	-19	n/a	-14	< -18.5%
TAPSE, mm	25	26	20	20	> 18
S wave, cm/s	0.18	0.7	0.18	0.12	> 0.095
RV basal diameter, mm	33	34	47	39	25 - 41
RV mid-cavity diameter, mm	29	22	45	34	19 - 35
MV E wave velocity, m/s	0.5	0.83	0.54	0.38	> 50
MV deceleration time, ms	210	218	185	147	> 200
E/A ratio	0.63	1.03	0.69	0.44	≥ 0.8
Septal e' velocity, m/s	0.05	0.08	0.07	0.1	> 7
Lateral e' velocity, m/s	0.1	0.09	0.1	0.1	> 10
E/e' ratio	6.6	9.66	6.27	3.78	< 10

Data are shown as frequencies (%) and median (min. - max.) or mean ± SD. LV: left ventricular; LVEF: LV ejection fraction; GLS: global longitudinal strain; a4C: apical four-chamber view; APLAX: apical long axis view; a2C: apical two-chamber view; TAPSE: tricuspid annulus plane systolic excursion; RV: right ventricular; MV: mitral valve; n/a: not available.



OBGYN

PROTECTION CHALLENGES OF PREGNANT WOMEN AGAINST VERTICAL TRANSMISSION DURING COVID-19 EPIDEMIC: A NARRATIVE REVIEW

Hasnain M, Pasha MF, Ghani I, Budiarto R.. Am J Infect Control. 2020 Jul 1:S0196-6553(20)30365-5. doi: 10.1016/j.ajic.2020.06.206. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

A literature review conducted by researchers in Malaysia analyzed 12 articles published between 1 December 2019 and 15 April 2020 related to challenges of pregnancy during the COVID-19 pandemic. Healthcare systems at large, lack of availability to reproductive medicine, risks of COVID-19 vertical transmission (from pregnant person to baby), and increased susceptibility during pregnancy were reviewed (Table 1). Authors suggest vertical transmission is unlikely (Ashokka et al; Liu et al); special attention should be given during earlier stages of pregnancy due to increased risk of immune compromise, and the non-availability of health systems to pregnant persons creates a higher rate of complications. Authors advocate for

education and innovation on availability of reproductive medicine, highlighting its role in reducing pregnancy complication risk during the COVID-19 pandemic.

SUMMARY

Additional review findings related to COVID-19 and pregnancy:
- Studies have shown SARS-CoV-2 is not detected in breast milk, amniotic fluid, or cord blood.
- Due to COVID-19 disease effects on kidneys and testicles, impact on the placenta cannot be ruled out.
- In emergency cases, the cesarean method of delivery with the use of biosafety measures is suggested (Chen et al).
- Italy recommended cancellation of transfers of frozen or fresh embryos (La Marca et al).
- Immune system disorders may occur if persons are infected at earlier stages of pregnancy.
- Per case fatality rate among pregnant persons with COVID-19 were lower and outcomes of pregnancies among pregnant persons with COVID-19 in Canada remained well but there was an increase in preterm labor, as suggested by Elwood et al.

ABSTRACT

This paper presents a narrative review study of five popular data repositories focusing on challenges of pregnant women protection during the COVID-19 pandemic. The study concludes that the likelihood of a vertical transmission of COVID-19 infection from pregnant women to neonates was not observed. Nevertheless, it remains a serious risk for them during their earlier stage of pregnancy, thus, special attention from health professionals has been recommended.

FIGURES

Table 1

Main features of the included studies

Main Feature	Disadvantages	Consequences	Preferred solution	Target countries
Healthcare system	• Lack of healthcare system resources. • Delayed access to a healthcare system	• Stillbirths, • Preterm Deliveries • Maternal Mortality and Respiratory Complications	• Cesarean delivery	• Singapore • China
Medicine unavailability	• The challenging risk for countries with a higher mortality rate	• Shortage of Reproductive medicine	• To ensure the availability of reproductive medicines	• Italy, USA, and Mexico
Higher susceptibility	• Increase in the transmission of COVID-19 infection • The risk for pregnant women, and their family newborns	• Cardiovascular and Hypertension Disease. • Preterm Deliveries • Shortness of breathing, Vomiting, Higher heart rate, Diffuse rashes, and moaning • Increase in preterm labor cases	• Recommended more top-care of both pregnant women and their neonates in intensive care units • Particular recommendations for antepartum, intrapartum and postpartum care	• China • China • Canada and China
COVID-19 vertical transmission	• Potential risks of transmission • Foreign fetal antigen challenges	• Variation in hormones • Severe disorder in the immune system	• Special care of pregnant women at the first and second trimester of pregnancy • Vaccine for pregnant women is especially recommended	• Singapore • China • China • China • China

PSYCHIATRY

PRACTICAL LESSONS LEARNED FOR ASSESSING AND TREATING BIPOLAR DISORDER VIA TELEHEALTH MODALITIES DURING THE COVID-19 PANDEMIC

Burgess C, Miller C, Franz A, Abel EA, Gyulai L, Osser D, Smith EG, Connolly S, Krawczyk L, Bauer M, Godleski L.. Bipolar Disord. 2020 Jul 1. doi: 10.1111/bdi.12969. Online ahead of print.
Level of Evidence: Other - Guidelines and Recommendations

BLUF

The authors discuss the challenges in treating bipolar disorder via Telehealth and provide recommendations. Assessing certain aspects of speech, affect and psychomotor agitation can be complicated by lag, audio quality, and poor lighting. Giving the patient specific instructions may help alleviate these challenges. The authors also encourage clinicians to pan their rooms for patients with paranoia to lessen suspicion of other people watching the session.

ABSTRACT

We briefly frame challenges and steps to overcoming those challenges in delivering care for patients with bipolar disorder via telehealth or telephone during COVID-19. Telehealth provides an invaluable opportunity to provide care for patients even under circumstances of social isolation. The issues discussed in this debate are intended to guide and assist clinicians, both in assessment and intervention, in adjusting to the use of virtual care for patients with bipolar disorder.

OROPHARYNGEAL SECRETION AS ALTERNATIVE FOR SARS-COV-2 DETECTION

Yu C, Li L, Tuersun Y, Zhao X, Feng Q, Zhang T, Tay FR, Ma J.. J Dent Res. 2020 Jul 2:22034520940292. doi: 10.1177/0022034520940292. Online ahead of print.
Level of Evidence: 3 - Non -randomized controlled cohort/follow-up study

BLUF

A prospective cohort study conducted at Tongji Hospital found improved accuracy of SARS-CoV-2 nucleic acid testing via oropharyngeal secretions (OS) as opposed to nasopharyngeal sampling (NPS), with false negative rates of 14% and 59%, respectively (Table 2). This suggests the potential use of OS sampling as a key screening and diagnostic tool for detection of SARS-CoV-2 in the future; however further research is needed given the very small sample size of this study.

ABSTRACT

This study aimed to determine if sampling of oropharyngeal secretions (OSs) helps improves detection of SARS-CoV-2 RNA by nucleic acid amplification testing of potential patients with COVID-19. The first prospective study consisted of 75 patients with COVID-19 who were ready for discharge and who had 2 consecutive negative results per nucleic acid amplification testing (NAAT) of viral samples retrieved with nasopharyngeal swabs (NPSs). Because of detection of potential false negatives in that cohort, the NAAT results of paired OS and NPS samples from 50 additional recruits with COVID-19 during their recovery stage were used in a second prospective study to compare the diagnostic values of the 2 viral RNA sampling methods. For identification of the frequency of inconsistency between the sampling methods, the McNemar's test was used for difference analysis and the kappa statistic for consistency analysis. OSs obtained from 2 of the 75 participants in the first study yielded positive results for SARS-CoV-2 nucleic acid. Both were male and aged >60 y. Subsequent chemiluminescence enzyme immunoassays indicated that they were positive for the SARS-CoV-2 IgM and IgG antibodies. For parallel NAAT of OS and NPS samples in the second study, McNemar's test indicated that the difference between the frequencies of inconsistent parts of OS and NPS was statistically significant (P = 0.021). Cohen's kappa coefficient for OS and NPS was 0.244, which is indicative of fair consistency. The NPS test has a risk of sending home more patients (59%) who still have the infection, while the OS test will make such an error in fewer patients (14%). Although OS sampling improves the accuracy of SARS-CoV-2 nucleic acid testing, it has to be emphasized that this conclusion is based on a very small sample size. Detection of viral RNA from a patient's secretions is not confirmative of viral infectivity.

FIGURES

Table 3. Comparison of Each Test with "the Ground Truth."

	Ground Truth+	Ground Truth–	Total
OS[a]			
OS+	19	0	19
OS–	3	28	31
Total	22	28	50
NPS[b]			
NPS+	9	0	9
NPS–	13	28	41
Total	22	28	50

[a]Sensitivity: 19/22 = 86%. Youden's index: (19/22 + 100%) – 1 = 86%. Agreement rate: (19 + 28)/50 = 94%. Negative predictive value: 28/31 = 90%. Negative likelihood ratio: (1 – 19/22)/100% = 14%.
[b]Sensitivity: 9/22 = 41%. Youden's index: (9/22 + 100%) – 1 = 41%. Agreement rate: (9 + 28)/50 = 74%. Negative predictive value: 28/41 = 68%. Negative likelihood ratio: (1 – 9/22)/100% = 59%.

"Ground truth" defined as:
True positive: patients tested positive by either of the 2 diagnostic tests (OS and NPS)
True negative: patients tested negative by both tests

DEEP THROAT SALIVA AS AN ALTERNATIVE DIAGNOSTIC SPECIMEN TYPE FOR THE DETECTION OF SARS-COV-2

Leung EC, Chow VC, Lee MK, Lai RW.. J Med Virol. 2020 Jul 4. doi: 10.1002/jmv.26258. Online ahead of print.
Level of Evidence: 4 - Case-control studies, or "poor or non-independent reference standard

BLUF

A retrospective, matched-pairs study conducted in Hong Kong from February to March 2020 found that the results of COVID-19 tests from patient-collected deep throat saliva (i.e. the posterior oropharyngeal region; n=95 patients) were comparable to results from nasopharyngeal swabs (Table 1; n= 62 patients). Overall agreement between the tests was 78.9% (kappa value=0.5). Although further investigation with a larger sampling of patients is needed, these findings suggest that patient-collected saliva from the posterior oropharyngeal region could be used to test for COVID-19.

ABSTRACT

Nasopharyngeal swabs (NPS) are widely accepted as specimens for the detection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in the current pandemic of Coronavirus disease 2019 (COVID-19). However, the collection procedures for NPS specimens causes sneezing and coughing in most patients, which generate droplets or aerosol particles that are hazardous to the healthcare workers collecting these specimens. In this study, 95 patient-matched paired deep throat saliva (DTS) and NPS specimens from 62 patients were analysed. Samples were tested for SARS-CoV-2 by reverse-transcription polymerase chain reaction (RT-PCR). The rates of detection for DTS (53.7%) and NPS (47.4%) samples were comparable (P = 0.13). It is important to note that the patients should be clearly instructed or supervised during DTS collection. In conclusion, SARS-CoV-2 detection by RT-PCR was equivalent in DTS and NPS specimens. This article is protected by copyright. All rights reserved.

FIGURES

	Paired samples (n = 95)	
	DTS[a]	NPS[b]
No. of RT-PCR positive sample (%)	51 (53.7)	45 (47.4)
No. of RT-PCR negative sample (%)	44 (46.3)	50 (52.6)
Overall agreement (95% CI[c])	78.9% (69.1% - 86.4%)	
Kappa (95% CI)	0.58 (0.42 – 0.74)	
P[d]	0.13	

[a]Deep throat saliva; [b]Nasopharyngeal swab; [c]Confidence internal; [d]*P*-value from Pearson's chi-square comparison

Table I: Clinical performance comparison between DTS and NPS for detecting SARS-CoV-2.

A SARS-COV-2 CORONAVIRUS NUCLEOCAPSID ANTIGEN-DETECTING HALF-STRIP LATERAL FLOW ASSAY TOWARDS THE DEVELOPMENT OF POINT OF CARE TESTS USING COMMERCIALLY AVAILABLE REAGENTS

Grant BD, Anderson CE, Williford JR, Alonzo LF, Glukhova VA, Boyle DS, Weigl BH, Nichols KP.. Anal Chem. 2020 Jul 1. doi: 10.1021/acs.analchem.0c01975. Online ahead of print.
Level of Evidence: 5 - Mechanism-based reasoning

BLUF

In this article, the authors describe the development of a half strip lateral flow assay (LFA) designed to detect the nucleocapsid protein (N protein) of SARS-CoV-2 with a latex bead conjugate, antibody biotinylation, and nitrocellulose (Figure 1). The half strip they produced was found to have a limit of detection of 0.65 ng/ mL when tested with the Genemedi sourced N protein and 3.03 ng/mL for the Genscript sourced N protein (Figure 2). The authors are hopeful that this work can support development of a functional LFA that can be used clinically for rapid antigen detection for SARS-CoV-2, noting that the analytical sensitivity on blood and nasal samples still needs to be determined to enable clinical application.

ABSTRACT

The SARS-CoV-2 pandemic has created an unprecedented need for rapid diagnostic testing to enable the efficient treatment and mitigation of COVID-19. The primary diagnostic tool currently employed is reverse transcription polymerase chain reaction (RT-PCR), which can have good sensitivity and excellent specificity. Unfortunately, implementation costs and

logistical problems with reagents during the global SARS-CoV-2 pandemic have hindered its universal on demand adoption. Lateral flow assays (LFAs) represent a class of diagnostic that, if sufficiently clinically sensitive, may fill many of the gaps in the current RT-PCR testing regime, especially in low- and middle-income countries (LMICs). To date, many serology LFAs have been developed, though none meet the performance requirements necessary for diagnostic use cases, primarily due to the relatively long delay between infection and seroconversion. However, based on previously reported results from SARS-CoV-1, antigen-based SARS-CoV-2 assays may have significantly better clinical sensitivity than serology assays. To date, only a very small number of antigen-detecting LFAs have been developed. Development of a half-strip LFA is a useful first step in the development of any LFA format. In this paper we present a half-strip LFA using commercially available antibodies for the detection of SARS-CoV-2. We have tested this LFA in buffer and measured an LOD of 0.65 ng/ mL (95% CI of 0.53 to 0.77 ng/mL) ng/mL with recombinant antigen using an optical reader with sensitivity equivalent to a visual read. Further development, including evaluating the appropriate sample matrix, will be required for this assay approach to be made useful in a point of care setting, though this half-strip LFA may serve as a useful starting point for others developing similar tests.

FIGURES

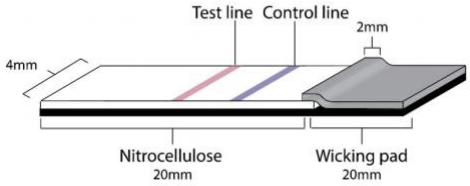


Figure 1. A half-strip was constructed using 20 mm of a nitrocellulose analytical membrane, and 20 mm of wicking pad. Notably, as a half strip, no sample preparation, or sample pad, is included in this version of this assay.

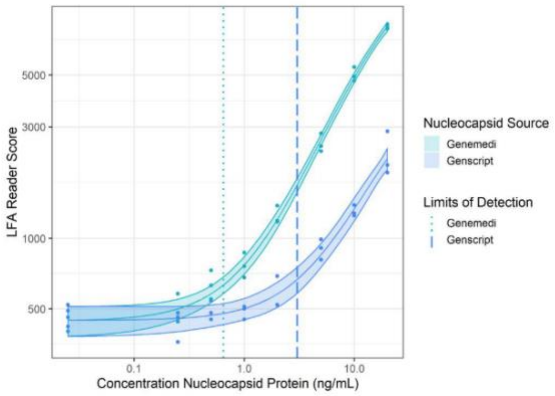


Figure 2. The dose response curve for a half-strip LFA using nucleocapsid protein from two commercially available sources, as measured using a commercially available optical LFA reader. The limit of detection the Genemedi N protein was 0.65 ng/ mL (95% CI of 0.53 to 0.77 ng/mL) and for the Genscript N protein was 3.03 ng/mL (95% CI of 0.00 to 7.44 ng/mL).

DEVELOPMENTS IN TREATMENTS

SYSTEMATIC REVIEW AND META-ANALYSIS OF THE EFFICACY OF NANOSCALE MATERIALS AGAINST CORONAVIRUSES-POSSIBLE POTENTIAL ANTIVIRAL AGENTS FOR SARS-COV-2

Alizadeh F, Khodavandi A.. IEEE Trans Nanobioscience. 2020 Jul;19(3):485-497. doi: 10.1109/TNB.2020.2997257.
Level of Evidence: 3 - Non-randomized controlled cohort/follow-up study

BLUF

A systematic review conducted in Iran on March 4, 2020 by the Islamic Azad University reviewed 21 studies and found that nanoscale materials (such as spike protein micelles) demonstrated efficacy against coronaviruses (MERS-CoV and SARS-CoV) in both in-vitro models (RR: 1.84, 95% CI: 1.57, 2.15) and animal models (RR: 1.66, 95% CI: 1.36, 2.02). Since SARS-CoV-2 is similar to other coronaviruses, these findings suggest that these materials could potentially be utilized to treat COVID-19

patients. The relative risk of each individual study is charted in Figures 2 and 3 while the size and morphology of the nanomaterials used against each coronavirus are demonstrated in Table 3.

ABSTRACT

The available antiviral agents and their potential for the management of coronavirus disease 2019 (COVID-19) outbreak are important interventions. A systematic review and meta-analysis was performed to summarize the available evidence on the efficacy of nanoscale materials against coronaviruses in vitro and in animal models. PubMed, Scopus and Wiley Online Library databases were searched up to 4 March 2020. Studies that developed the efficacy of nanoscale materials against coronaviruses were included. Two reviewers independently extracted study characteristics and assessed risk of bias and applicability in the included studies. Meta-analyses were conducted to determine the overall inhibition efficacy of nanoscale materials against coronaviruses. A total of 21 studies were identified. Positive association was found between efficacy of nanoscale materials and coronaviruses in vitro and in animal models. The inhibition efficacy of nanoscale materials against coronavirus in vitro and in animal models were 1.84 (95% CI: 1.57, 2.15) and 1.66 (95% CI: 1.36, 2.02), respectively. Results of subgroup analysis of selected studies revealed that the nanoscale materials with spherical morphology were found to be more antiviral activity than the other morphologies against Middle East respiratory syndrome-coronavirus (MERS-CoV) and severe acute respiratory syndrome coronavirus (SARS-CoV). Using systematic review and meta-analysis, our results indicate that nanoscale materials are positive affect against coronaviruses. We might clarify the possible potential for the use of nanoscale materials for SARS-CoV-2.

FIGURES

TABLE III

SUMMARY OF THE SUBGROUP META-ANALYSIS OF THE INHIBITION EFFICACY OF NANOSCALE MATERIALS AGAINST CORONAVIRUSES AND CORRELATION OF PROBABLE EFFECTIVE FACTORS (SIZE AND MORPHOLOGY OF NANOSCALE MATERIALS)

Subgroup analysis	No. of studies	Mean	Std. Dev.	MCSE	OR (95% Cr. I)
MERS-CoV [21], [28]-[32], [34], [36]					
Size of nanoscale materials					
≤50 nm [30], [31], [34], [36]	4	1.634	1.890	0.055	1.058 (0.178-6.842)
>50 nm [21], [28], [29], [31], [32]	5	Reference level	-	-	-
Morphology of nanoscale materials					
Spherical [29]-[31], [32], [34], [36]	6	1.935	2.356	0.069	1.230 (0.210-8.143)
Others [21], [28]	2	Reference level	-	-	-
SARS-CoV [27], [36]-[40]					
Size of nanoscale materials					
≤50 nm [27], [36], [38], [40]	4	1.652	1.903	0.054	1.055 (0.178-6.637)
>50 nm [37], [39]	3	Reference level	-	-	-
Morphology of nanoscale materials					
Spherical [27], [36]-[39]	5	2.099	2.877	0.073	1.390 (0.214-8.607)
Others [40]	1	Reference level	-	-	-

Middle East respiratory syndrome coronavirus= MERS-CoV; Monte-Carlo standard error= MCSE; Odds ratio= OR; Severe acute respiratory syndrome= SARS-CoV; 95 % credible interval=95% Cr. I; 95% Cr. I= 2.5%-97.5%. The size of more than 50 nm and other morphologies of nanoscale materials considered as reference levels for meta-analysis of the model.

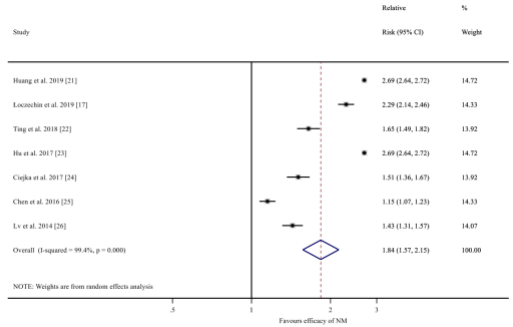


Fig. 2. Forrest plot: summary estimate of the inhibition efficacy of nanoscale materials against coronavirus *in vitro*. NM: nanoscale materials.

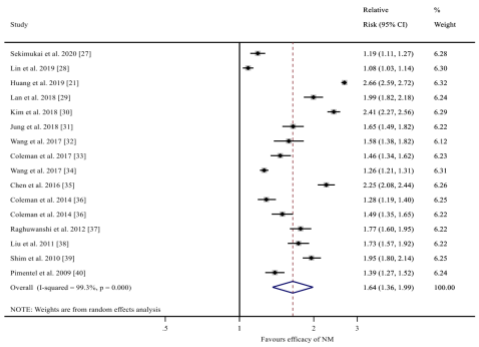


Fig. 3. Forrest plot: summary estimate of the inhibition efficacy of nanoscale materials against coronavirus in the animal model. NM: nanoscale materials.

ANXIETY AND DEPRESSION SCORES IN MATERNITY HEALTHCARE WORKERS DURING THE COVID-19 PANDEMIC

Corbett GA, Milne SJ, Mohan S, Reagu S, Farrell T, Lindow SW, Hehir MP, O'Connell MP.. Int J Gynaecol Obstet. 2020 Jul 2. doi: 10.1002/ijgo.13279. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

A prospective survey was conducted with Healthcare Workers (HCWs) at a tertiary hospital in Dublin, Ireland, which collected self-reported scores of the GAD and PHQ-9 surveys to assess levels of anxiety and depression. 240/600 (40%) of hospital staff completed the questionnaire, with 20.3% of respondents showing moderate to severe depression and 21% with moderate to severe anxiety, with additional demographics shown in Table 1. This study contributes to mounting evidence that the COVID-19 pandemic has had a significant negative psychological effect on healthcare workers (HCW) as they continue to serve patients, and recognition of this data can be helpful in providing the necessary aid to care for HCWs during this strenuous time.

ABSTRACT

While Severe-Acute-Respiratory-Syndrome-CoronaVirus-2 (SARSCoV-2/Covid-19) causes physical morbidity for healthcare workers (HCWs), Covid-19 also carries psychological morbidity for HCWs. This morbidity translates to anxiety and depressive symptomatology. To this end, we assessed anxiety and depression among HCWs during Covid-19 pandemic.

FIGURES

Table 1: Baseline demographics of participants who completed the survey, with responses and variation in GAD-7 and PHQ-9 scores with baseline characteristics

GAD-7 Scores	Baseline demographics	n	Median	Range	P Value
Gender	Female	175	5.00	0-21	**0.027**
	Male	22	2.00	0-20	
Age	18-25 years	9	9.00	0-12	**0.000**
	25-40 years	110	5.5	0-21	
	40-50 years	64	3.50	0-21	
	50-60 years	50	3.00	0-21	
	Over 60 years	7	1.00	0-10	
Underlying Health Conditions	Yes	44	5.5	0-21	0.454
	No	195	5.00	0-21	
Role	Midwife / Nurse	87	4.00	0-21	**0.001**
	Doctor	36	3.00	0-14	
	Laboratory Staff	22	5.00	0-17	
	Clerical / Administrative staff	53	7.00	0-21	
	Support Staff	42	4.0	0-21	
PHQ-9 Scores	**Baseline demographics**	**n**	**Median**	**Range**	**P Value**
Gender	Female	175	4.00	0-24	0.144
	Male	22	3.00	0-20	
Age	18-25 years	9	9.00	0-14	**0.001**
	25-40 years	110	4.00	0-24	
	40-50 years	64	3.00	0-18	
	50-60 years	50	4.00	0-19	
	Over 60 years	7	0.50	0-4	
Underlying Health Conditions	Yes	44	4.00	0-21	0.322
	No	195	4.00	0-24	
Role	Midwife / Nurse	87	3.00	0-24	**0.010**
	Doctor	36	2.00	0-15	
	Laboratory Staff	22	5.00	0-15	
	Clerical / Administrative staff	53	6.00	0-24	
	Support Staff	42	4.50	0-21	

Table 1: Baseline demographics of participants who completed the survey, with responses and variation in GAD-7 and PHQ-9 scores with baseline characteristics.

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