The Daily COVID-19 Literature Surveillance Summary

January 12, 2021

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COVID-19 Daily Literature Surveillance

COVID19LST

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

LEVEL OF EVIDENCE

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

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

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

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

How to cite the Levels of Evidence Table

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

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

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

EXECUTIVE SUMMARY

Epidemiology

- What is the best economic way to decrease spread of COVID-19 in college campuses? Public health experts from Brigham and Women's Hospital conducted a modeling study sponsored by the NIH using the Clinical and Economic Analysis of COVID-19 interventions model to analyze the cost-effectiveness of COVID-19 prevention measures on college campuses. In their model, social distancing and mask-wearing precautions dropped infection rates compared to no intervention at relatively low cost. While routine testing reduced infections by 96%, it cost up to ten times more. This model suggests that among college campuses, extensive social distancing measures and wearing masks are the most cost-effective strategies for reducing SARS-CoV-2 transmission, though low-cost routine testing could further reduce infection rates.

Management

- Patients with persistent symptoms after Covid-19 have had a varied experience with the healthcare system. In this retrospective study that interviewed 114 patients with "long Covid" ('post-acute' symptoms persisting beyond 3–4 weeks and 'chronic' symptoms beyond 12 weeks), researchers from the UK consider the characteristics and development of "long Covid." They found that "long Covid" encompasses a variety of symptoms with fluctuating intensity, and patients described differences in the quality of their care experience, with some reporting dismissive providers, difficulty accessing appropriate services, and lack of guidance. The authors suggest that a re-engineering of healthcare services including the employment of online services, is necessary to meet the changing needs of "long Covid" sufferers.

R&D: Diagnosis & Treatments

- Remdesivir is disproportionately being given to acute renal failure patients. Nephrologists and pharmacists from Centre Hospitalier Universitaire de Nice in France evaluated the risk of acute renal failure (ARF) associated with remdesivir compared to hydroxychloroquine, tocilizumab, and lopinavir/ritonavir. They analyzed international pharmacovigilance post-marketing databases with two disproportionality methods, and found a "statistically suggestive disproportionality signal," observing 138 cases of ARF in patients receiving remdesivir where they would have expected nine (ROR: 20.3 [15.7-26.3]; P<0.0001). Authors suggest serum creatinine monitoring is warranted in patients receiving remdesivir treatment for COVID-19.

Mental Health & Resilience Needs

- There has been a surge of firearm sales during COVID-19 that causes concern. In response to a recent cross-sectional survey of 2,870 Californians showing recently increased public concern about violence, firearm and ammunition acquisition and unsafe firearm storage practice (Kravitz-Wirtz et al.), psychiatrists from the University of Pennsylvania fear that this will lead to increased firearm related injury and death, especially amidst increased suicide risk factors (personal loss, isolation, etc.). Authors suggest that establishing and targeting safe firearm storage/training programs, increasing funding for firearm injury prevention research, and focusing suicide prevention efforts, especially among racial and ethnic minority groups who experience disproportionately worse mental health outcomes, is crucial for harm reduction.

TABLE OF CONTENTS

MULTIMORBIDITY, POLYIATROGENESIS, AND COVID-19

Ecks S.. Med Anthropol Q. 2020 Dec 4. doi: 10.1111/maq.12626. Online ahead of print.
Level of Evidence: 5 - Expert Opinion

BLUF

An anthropologist from the University of Edinburgh hypothesizes that polypharmacy in patients with multiple comorbidities may cause iatrogenic harm that contributes to increased morbidity and mortality seen in patients with COVID-19. Furthermore, since preexisting multimorbidity is highly correlated with socioeconomic inequality, lack of integrated management of these medications may be a contributing factor to the higher risk seen in those with pre-existing conditions and lower socioeconomic status, especially in poorer areas within richer countries (Figure 1).

SUMMARY

An Anthropologist from the University of Edinburgh hypothesizes that multimorbidity and polypharmacy are risk factors for COVID-19 infection. He calls to attention the correlation between high gross domestic product (GDP) and COVID-19 mortality, and suggests that regions of poverty within overall richer and more industrialized nations are more likely to be affected by COVID-19. He concludes with a call for further research to better elucidate the relationship between socioeconomic status, multimorbidity and COVID-19 susceptibility.

ABSTRACT

To date, the strongest predictor for dying with COVID-19 is suffering from several chronic disorders prior to the viral infection. Pre-existing multimorbidity is highly correlated with socioeconomic inequality. In turn, having several chronic conditions is closely linked to multiple medication intake, especially in richer countries with good access to biomedical care. Owing to its vertical structure, biomedicine often risks giving multiple treatments in an uncoordinated way. Such lack of integrated care can create complex forms of iatrogenic harm. Multimorbidity is often exacerbated by a pharmaceuticalization of social deprivation in place of integrated care. In this article, I explore the possibility that clusters of over-medication are a contributing factor to higher death rates from COVID-19, especially in poorer areas within richer countries. Anthropological perspectives on the social embeddedness of multimorbidity and multiple medication use can expand our understanding of who is most vulnerable to SARS-CoV-2.

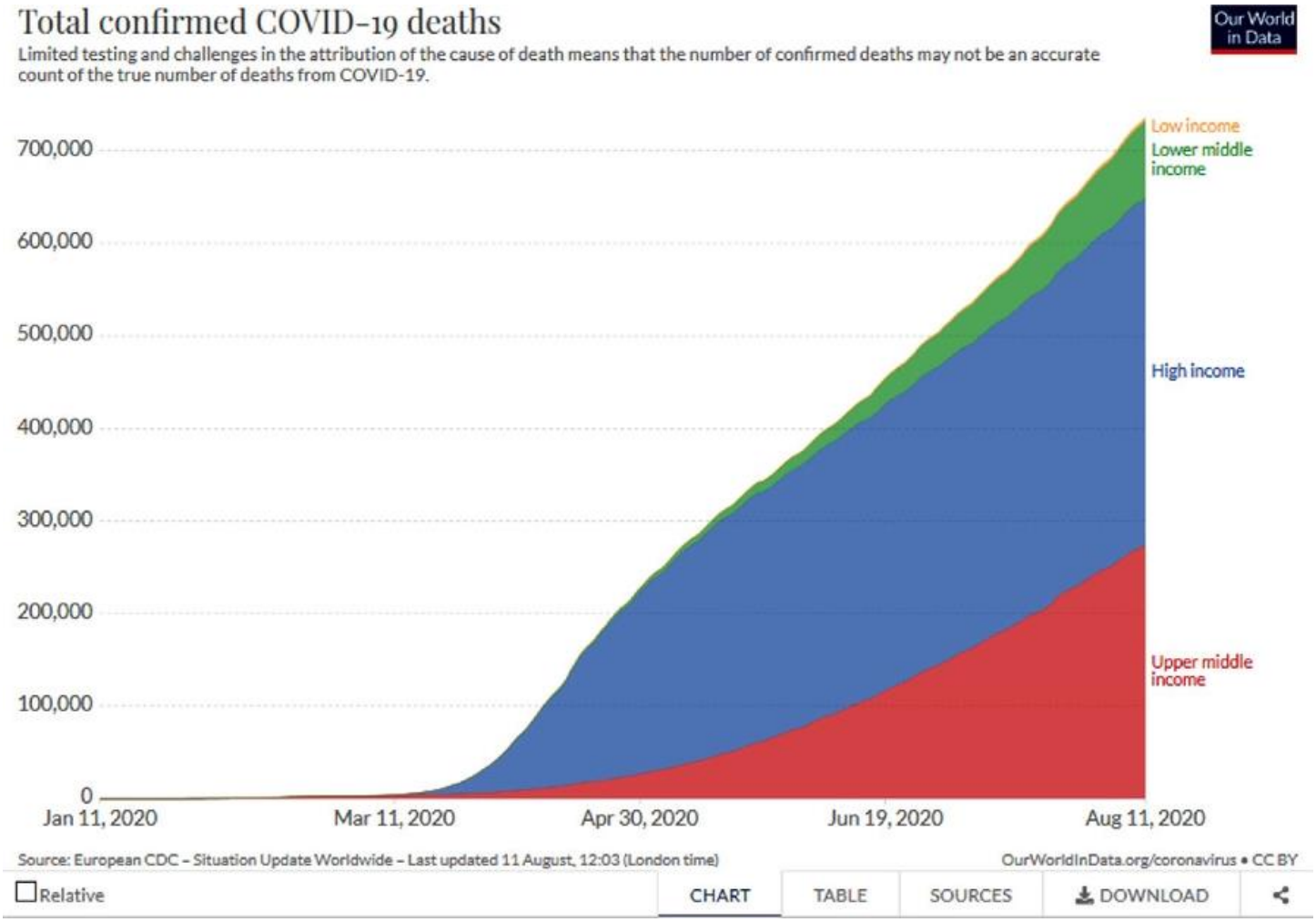


Figure 1. Total confirmed COVID-19 deaths by country GDP.

EPIDEMIOLOGY

CHANGES IN PRETERM BIRTH PHENOTYPES AND STILLBIRTH AT 2 PHILADELPHIA HOSPITALS DURING THE SARS-COV-2 PANDEMIC, MARCH-JUNE 2020

Handley SC, Mullin AM, Elovitz MA, Gerson KD, Montoya-Williams D, Lorch SA, Burris HH.. JAMA. 2021 Jan 5;325(1):87-89. doi: 10.1001/jama.2020.20991.
Level of Evidence: 3 - Local non-random sample

BLUF

Neonatologists from Children's Hospital of Philadelphia and researchers from the Maternal and Child Health Research Center at the Perelman School of Medicine assessed preterm and stillbirth rates at two Philadelphia hospitals from March to June 2020 (pandemic) compared to March to June 2018 and 2019 (pre-pandemic). They found similar pre-pandemic and pandemic rates of preterm (10.5% vs 9.5%), spontaneous preterm (5.7% vs 4.7%), medically indicated preterm (5.4% vs 5.2%), and stillbirths (5.4 per 1000 vs 5.0 per 1000 births)(Table). Because their data conflicts with previously published studies, authors suggest their results may be influenced by local access to healthcare, lockdown measures and other containment measures.

FIGURES

Birth outcome	No. (%) Prepandemic epoch (n = 5907)	No. (%) Pandemic epoch (n = 3007)	Unadjusted *P* value[b]	Adjusted absolute risk difference (95% CI), %[c]
Preterm birth[d]	617 (10.5)	283 (9.5)	.12	−1.1 (−2.4 to 0.2)
Non-Hispanic Black	323 (13.1)	157 (12.4)	.57	−0.7 (−3.0 to 1.5)
Non-Hispanic White	177 (7.9)	73 (6.8)	.26	−1.0 (−2.8 to 0.9)
Other race/ethnicity	117 (9.9)	53 (8.2)	.24	−1.7 (−4.4 to 1.0)
Spontaneous preterm birth[e]	315 (5.7)	135 (4.7)	.09	−0.8 (−1.8 to 0.2)
Non-Hispanic Black	150 (6.6)	77 (6.5)	.99	0.1 (−1.6 to 1.9)
Non-Hispanic White	96 (4.5)	30 (2.9)	.04	−1.4 (−2.8 to −0.1)
Other race/ethnicity	69 (6.1)	28 (4.5)	.16	−1.6 (−3.7 to 0.6)
Medically indicated preterm birth[f]	302 (5.4)	148 (5.2)	.65	−0.3 (−1.4 to 0.6)
Non-Hispanic Black	173 (7.5)	80 (6.7)	.45	−1.0 (−2.7 to 0.8)
Non-Hispanic White	81 (3.8)	43 (4.1)	.70	0.4 (−1.1 to 1.9)
Other race/ethnicity	48 (4.3)	25 (4.0)	.80	−0.3 (−2.3 to 1.7)
Stillbirth (per 1000 births)	32 (0.54)	15 (0.50)	.88	−0.03 (−0.34 to 0.29)
Non-Hispanic Black	25 (1.01)	9 (0.71)	.47	−0.29 (−0.90 to 0.31)
Non-Hispanic White[g]	4 (0.18)	2 (0.19)	.99	
Other race/ethnicity[g]	3 (0.25)	4 (0.61)	.26	

Table: "Birth Outcomes by Race/Ethnicity Before (March-June 2018 and 2019) and During (March-June 2020) the Severe Acute Respiratory Syndrome Coronavirus 2 Pandemic in 2 Philadelphia Hospitals".

COLLEGE CAMPUSES AND COVID-19 MITIGATION: CLINICAL AND ECONOMIC VALUE

Losina E, Leifer V, Millham L, Panella C, Hyle EP, Mohareb AM, Neilan AM, Ciaranello AL, Kazemian P, Freedberg KA.. Ann Intern Med. 2020 Dec 21. doi: 10.7326/M20-6558. Online ahead of print.
Level of Evidence: 5 - Modeling

BLUF

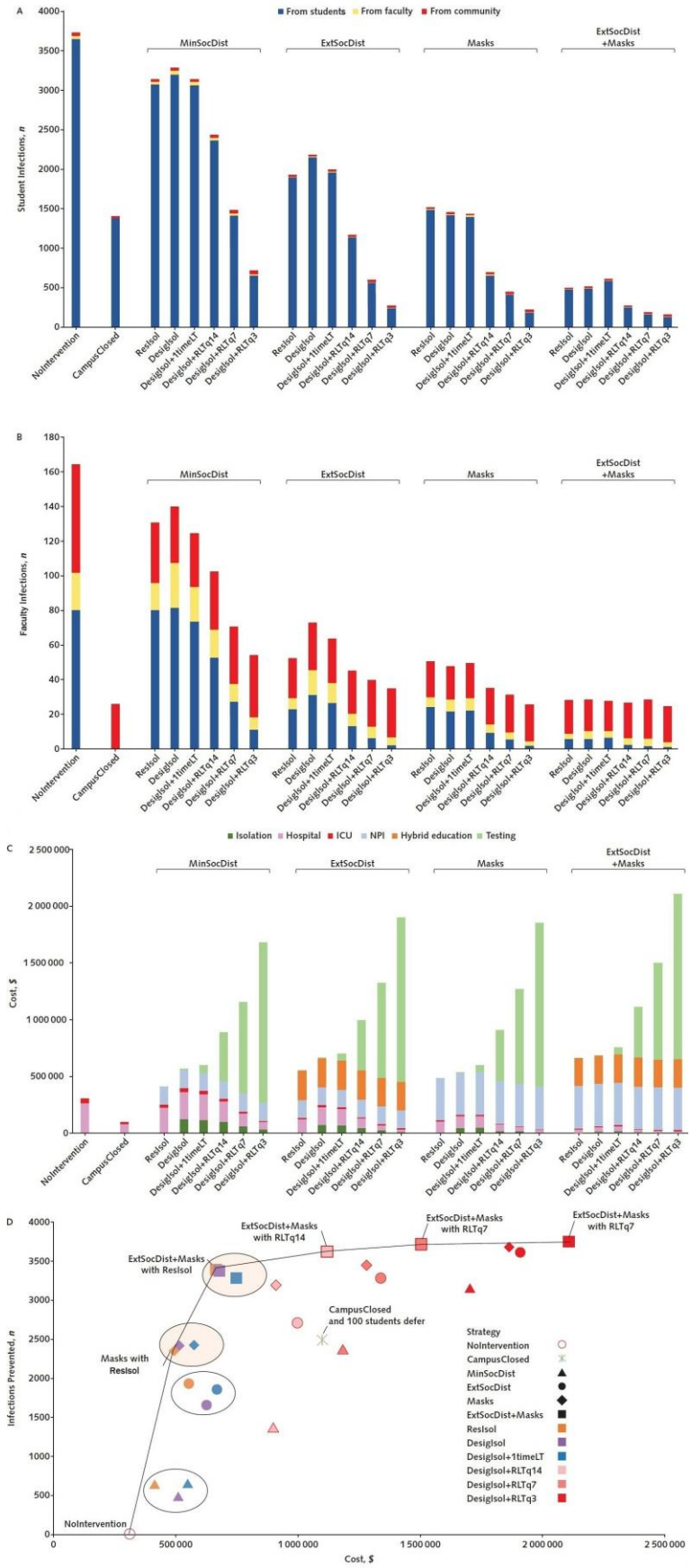
Public health experts from Brigham and Women's Hospital conducted a modeling study sponsored by the NIH using the Clinical and Economic Analysis of COVID-19 interventions model to analyze the cost-effectiveness of COVID-19 prevention measures on college campuses (Table 1). In their model, social distancing and mask-wearing precautions dropped infection rates compared to no intervention at relatively low cost. While routine testing reduced infections by 96%, it cost up to ten times more. This model suggests that among college campuses, extensive social distancing measures and wearing masks are the most cost-effective strategies for reducing SARS-CoV-2 transmission, though low-cost routine testing could further reduce infection rates.

SUMMARY

In a sample of 5000 students and 1000 faculty, the model predicted that 75% (n=3746) of students and 16 (n=164) of faculty would become infected with SARS-CoV-2 without any interventions, while extensive social distancing and mask-wearing ($170 per infection prevented) reduced infections to 10% (n=493) and 3% (n=28), respectively. Routine testing reduced infections by 96% but cost $2010 to $17,210 per infection prevented (Figure)(Table 3).

ABSTRACT

BACKGROUND: Colleges in the United States are determining how to operate safely amid the coronavirus disease 2019 (COVID-19) pandemic. OBJECTIVE: To examine the clinical outcomes, cost, and cost-effectiveness of COVID-19 mitigation strategies on college campuses. DESIGN: The Clinical and Economic Analysis of COVID-19 interventions (CEACOV) model, a dynamic microsimulation model, was used to examine alternative mitigation strategies. The CEACOV model tracks infections accrued by students and faculty, accounting for community transmissions. DATA SOURCES: Data from published literature were used to obtain parameters related to COVID-19 and contact-hours. TARGET POPULATION: Undergraduate students and faculty at U.S. colleges. TIME HORIZON: One semester (105 days). PERSPECTIVE: Modified societal. INTERVENTION: COVID-19 mitigation strategies, including social distancing, masks, and routine laboratory screening. OUTCOME MEASURES: Infections among students and faculty per 5000 students and per 1000 faculty, isolation days, tests, costs, cost per infection prevented, and cost per quality-adjusted life-year (QALY). RESULTS OF BASE-CASE ANALYSIS: Among students, mitigation strategies reduced COVID-19 cases from 3746 with no mitigation to 493 with extensive social distancing and masks, and further to 151 when laboratory testing was added among asymptomatic persons every 3 days. Among faculty, these values were 164, 28, and 25 cases, respectively. Costs ranged from about $0.4 million for minimal social distancing to about $0.9 million to $2.1 million for strategies involving laboratory testing ($10 per test), depending on testing frequency. Extensive social distancing with masks cost $170 per infection prevented ($49 200 per QALY) compared with masks alone. Adding routine laboratory testing increased cost per infection prevented to between $2010 and $17 210 (cost per QALY gained, $811 400 to $2 804 600). RESULTS OF SENSITIVITY ANALYSIS: Results were most sensitive to test costs. LIMITATION: Data are from multiple sources. CONCLUSION: Extensive social distancing with a mandatory mask-wearing policy can prevent most COVID-19 cases on college campuses and is very cost-effective. Routine laboratory testing would prevent 96% of infections and require low-cost tests to be economically attractive. PRIMARY FUNDING SOURCE: National Institutes of Health.



'Figure. Infections, costs, and economic efficiency, by COVID-19 mitigation strategy.'

1timeLT = 1-time laboratory testing; CampusClosed = campus remains closed with only online education; COVID-19 =

coronavirus disease 2019; DesigIsol = student isolation in a separate, college-sponsored location; ExtSocDist = extensive social distancing; ICU = intensive care unit; LT = laboratory testing; Masks = mask-wearing policies; MinSocDist = minimal social distancing; NoIntervention = campus operates as it did before COVID-19 without any mitigation interventions; NPI = nonpharmacologic intervention; ResIsol = residence isolation in student dorm room; RLT = routine LT; RLTqX = RLT every X days. A-C. The number and source of infections among students (A) and faculty (B) for each strategy, and total costs (C). On the left are the NoIntervention and CampusClosed strategies. The 4 broad NPI strategies (MinSocDist, ExtSocDist, Masks, and combined ExtSocDist and Masks) are further stratified by the use and frequency of LT, ranging from no LT, where those who report symptoms associated with COVID-19 are asked to isolate in their residence for 10 d; to 1 test for those who report symptoms to confirm placement in isolation; to RLT for all students and faculty at the start of the semester; to RLT among asymptomatic students and faculty at 3-, 7-, or 14-d intervals. Infections decrease as strategies increase in intensity, from MinSocDist to the ExtSocDist+Masks strategy. In each case, adding LT further decreases infections. Among students, most infections are from other students (A). Among faculty, depending on the strategy, most infections are from the community and other faculty (B). In strategies without RLT, hospital and ICU costs account for >50% of total costs (C). In strategies with RLT, testing accounts for >50% of total costs. Cost per test was $10. D. The efficiency frontier (cost per infection prevented) for COVID-19 mitigation strategies. The efficiency frontier represents the relationship between infections prevented (vertical axis) and total costs (horizontal axis). NoIntervention is shown in the open red circle on the lower left. Without RLT or testing at the semester start, regardless of isolation approach, there is clustering (ovals) of strategies involving MinSocDist (triangles), ExtSocDist (circles), Masks (diamonds), and ExtSocDist+Masks (squares). Unshaded ovals represent strategies where masks are not incorporated, and beige ovals represent clustering of strategies where masks are incorporated. More infections are prevented when masks are used. Symbols on the solid black line represent economically efficient strategies. The slope of the solid line represents the incremental cost per infection prevented for each strategy, compared with the next less costly efficient strategy. Testing at 14-, 7-, or 3-d intervals prevents additional infections, but at a substantially increased cost per infection prevented.

Table 3. Cost-Effectiveness of COVID-19 Mitigation Strategies on U.S. College Campuses

Strategy	Isolation Location	Testing	Total Costs, $	Infections Prevented, n*	QALYs Lost, n	Cost per Infection Prevented, $†	Cost per QALY, $†
Efficient mitigation strategies							
No intervention	NA	NA	310 283	0	16.44	–	–
Masks	ResIsol	Self-screen	488 254	2341	6.13	80	17 300
Extensive social distancing + masks	ResIsol	Self-screen	664 015	3389	2.56	170	49 200
Extensive social distancing + masks	DesigIsol	RLTq14	1 118 667	3615	2.00	2010	811 400
Extensive social distancing + masks	DesigIsol	RLTq7	1 504 746	3699	1.88	4600	d
Extensive social distancing + masks	DesigIsol	RLTq3	2 110 595	3735	1.64	17 210	2 804 600
Value of routine screening with laboratory testing, stratified by NPI							
Minimal social distancing							
No intervention	NA	NA	310 283	0	16.44	–	–
Minimal social distancing	ResIsol	Self-screen	414 749	632	13.95	170	41 900
Minimal social distancing	DesigIsol	Self-screen	508 153	481	14.67	D	D
Minimal social distancing	DesigIsol	1-time LT	546 927	640	13.59	d	d
Minimal social distancing	DesigIsol	RLTq14	898 542	1367	11.23	d	d
Minimal social distancing	DesigIsol	RLTq7	1 183 393	2360	7.38	440	117 000
Minimal social distancing	DesigIsol	RLTq3	1 702 406	3143	4.65	660	189 800
Extensive social distancing							
No intervention	NA	NA	310 283	0	16.44	–	–
Extensive social distancing	ResIsol	Self-screen	551 693	1932	7.19	120	26 100
Extensive social distancing	DesigIsol	Self-screen	624 371	1650	8.76	D	D
Extensive social distancing	DesigIsol	1-time LT	667 518	1848	7.90	D	D
Extensive social distancing	DesigIsol	RLTq14	997 635	2698	5.19	580	d
Extensive social distancing	DesigIsol	RLTq7	1 337 494	3275	3.54	590	215 400
Extensive social distancing	DesigIsol	RLTq3	1 909 521	3601	2.47	1750	533 600
Mandatary mask-wearing policy, no mandated social distancing							
No intervention	NA	NA	310 283	0	16.44	–	–
Masks	ResIsol	Self-screen	488 254	2341	6.13	80	17 300
Masks	DesigIsol	Self-screen	512 750	2407	5.79	370	72 300
Masks	DesigIsol	1-time LT	576 108	2423	5.87	d	D
Masks	DesigIsol	RLTq14	909 557	3186	3.47	510	171 300
Masks	DesigIsol	RLTq7	1280 258	3442	2.71	1450	487 000
Masks	DesigIsol	RLTq3	1 863 026	3669	1.87	2560	693 800
Extensive social distancing + masks							
No intervention	NA	NA	310 283	0	16.44	–	–
Extensive social distancing + masks	ResIsol	Self-screen	664 015	3389	2.56	100	25 500
Extensive social distancing + masks	DesigIsol	Self-screen	677 520	3373	2.60	D	D
Extensive social distancing + masks	DesigIsol	1-time LT	747 829	3276	2.81	D	D
Extensive social distancing + masks	DesigIsol	RLTq14	1 118 667	3615	2.00	2010	811 400
Extensive social distancing + masks	DesigIsol	RLTq7	1 504 746	3699	1.88	4600	d
Extensive social distancing + masks	DesigIsol	RLTq3	2 110 595	3735	1.64	17 210	2 804 600

COVID-19 = coronavirus disease 2019; DesigIsol = student isolation in a separate, college-sponsored location; LT = laboratory testing; NA = not applicable; NPI = nonpharmacologic intervention; ResIsol = residence isolation in student dorm room; RLTqX = routine LT every X days; QALY = quality-adjusted life-year.
* Compared with no intervention.
† A strategy is dominated if it is more costly and less effective than another strategy (strong dominance, "D") or some combination of other strategies (weak dominance, "d"). Incremental cost-effectiveness ratios are rounded to $100.

'Table 3.' Cost-Effectiveness of COVID-19 Mitigation Strategies on U.S. College Campuses

Table 1. Input Parameters for an Analysis of COVID-19 Mitigation Strategies on U.S. College Campuses

Parameter	Value			Source
Cohort characteristics				
Cohort size, *n*		105 000		(2); assumption
	Students	Faculty	Community	
Cohort distribution across transmission groups, %	4.76	0.95	94.29	(2); assumption
Age distribution, %				
<20 y	100	0	0	Assumption
20–59 y	0	75	84	Derived from (2) and Supplement references 1, 8, and 10-14
≥60 y	0	25	16	Derived from (2) and Supplement references 1, 8, and 10-14
Initial disease distribution, %				
Susceptible	89	94	81	Derived from Supplement references 2 and 3
Infected incubation	0.5	0.5	1	Derived from Supplement references 2 and 3
Infected asymptomatic	0.5	0.5	1	Derived from Supplement references 2 and 3
Infected mild/moderate symptoms	0	0	1	Derived from Supplement references 2 and 3
Infected severe/critical symptoms	0	0	1	Derived from Supplement references 2 and 3
Recovered	10	5	15	Derived from Supplement references 2 and 3
Infectivity per contact-hour		0.002		Derived from (12)
Transmission rate per day, student-student				
Campus closed		0.142		Product of infectivity and contact-hours
No intervention		0.238		Product of infectivity and contact-hours
Minimal social distancing		0.167		Product of infectivity and contact-hours
Extensive social distancing		0.141		Product of infectivity and contact-hours
Masks		0.128		Product of infectivity, contact-hours and mask efficacy (10)
Extensive social distancing + masks		0.105		Product of infectivity, contact-hours and mask efficacy (10)
Contact-hours*	Students	Faculty	Community	
No intervention				
Students	149.41	1.51	3.86	Derived from (27-33)
Faculty	37.10	10.00	33.50	Derived from (27-33)
Community	0.50	0.30	81.36	Derived from (27-33)
Minimal social distancing				
Students	109.94	1.51	3.86	Derived from (27-33)
Faculty	37.10	10.00	33.50	Derived from (27-33)
Community	0.50	0.30	81.36	Derived from (27-33)
Extensive social distancing				
Students	90.69	0.76	3.86	Derived from (27-33)
Faculty	14.84	8.00	32.79	Derived from (27-33)
Community	0.40	0.30	71.08	Derived from (27-33)
Residence isolation				
Students	31.80	0	0	Assumption
Faculty	0	0	3	Assumption
Community	0	0	3	Assumption
Designated isolation				
Students	3	0	0.5	Assumption
Faculty	0	0	3	Assumption
Community	0	0	3	Assumption
Hospitalization				
Students	0	0	0.5	Assumption
Faculty	0	0	0.5	Assumption
Community	0.5	0.5	0.5	Assumption
Adherence to NPIs				
Masks	0.5	1	0.5	Assumption
Accuracy in symptom reporting	0.5	0.9	NA	Assumption
Adherence to residence isolation	0.6	1	NA	Assumption
Test characteristics				
Sensitivity, %				
Day 1–4 of infection		16.5		Derived from (23)
Day 5–9 of infection		71		Derived from (23)
Day 10-21 of infection		43.5		Derived from (23)
Day >22 of infection		0.0		Derived from (23)
Specificity, %		100		Assumption
Costs, $				
Interventions†				
Minimal social distancing		151 500		Derived from (24); assumption
Extensive social distancing		407 500		Derived from (24, 37); assumption
Masks		370 000		Derived from (24); assumption
Extensive social distancing with masks		620 000		Derived from (24, 37); assumption
Laboratory SARS-CoV-2 diagnostic test (per test)		10		Derived from (25)
Student quarantine room (per day)		30		Derived from (24, 26)
Hospital inpatient cost (per day)		1640		Derived from (34-36)
ICU cost (per day)		2680		Derived from (34-36)

COVID-19 = coronavirus disease 2019; ICU = intensive care unit; NA = not applicable; NPI = nonpharmacologic intervention; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
* For example, a student attending a 1-h discussion session with 10 students will accrue 10 contact-hours.
† Intervention costs were totaled on the basis of which NPIs and mobility restrictions were included. Costs included masks, cleaning, and software costs.

'Table 1.' Input Parameters for an Analysis of COVID-19 Mitigation Strategies on U.S. College Campuses

ADULTS

ASSESSMENT OF MUSCULOSKELETAL PAIN, FATIGUE AND GRIP STRENGTH IN HOSPITALIZED PATIENTS WITH COVID-19

Tuzun S, Keles A, Okutan D, Yildiran T, Palamar D.. Eur J Phys Rehabil Med. 2021 Jan 4. doi: 10.23736/S1973-9087.20.06563-6. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

Members of the Department of Physical Medicine and Rehabilitation at Istanbul University-Cerrahpaşa (IUC) Cerrahpaşa Pandemic Clinic in Turkey assessed 150 adult patients hospitalized with COVID-19 (see summary) for musculoskeletal symptoms between May 15 and June 30, 2020. Muskuloskeletal symptoms were extremely common with 85% experiencing fatigue, 68% myalgia, 43% arthlagia, and 22% back pain. Those with severe disease had a significantly higher Chalder Fatigue Score (p= .048; Table 4) compared to those with non-severe disease (see summary). Authors suggest that musculoskeletal symptoms are common among COVID-19 patients and should be factored into the rehabilitation of recovering patients.

SUMMARY

Authors used the disease severity 2007 IDSA/ITS guidelines for community acquired pneumonia to classify patients into 103 non-severe and 47 severe cases.

Myalgia was stratified by a numerical rating scale: those with severe disease had a mean score of 7.21 (6.21 – 8.13) and those with non-severe disease had a mean score of 7.19 (6.71 - 7.68). LDH (p: 0.03) and CRP (p:0.027) were both higher in fatigued patients (Table 7).

ABSTRACT

BACKGROUND: Although there are some retrospective studies to present musculoskeletal findings of the COVID-19, still the muscle strength and fatigue has not been studied in detail. AIM: To reveal the symptoms of musculoskeletal system in COVID-19 patients, to evaluate myalgia, arthralgia and physical/mental fatigue, to assess handgrip muscle strength, and to examine the relations of these parameters with the severity and laboratory values of the disease. DESIGN: This study was designed as a cross-sectional, single-center case series. SETTING: This study took place from May 15,2020, to June 30, 2020 at the Istanbul University-Cerrahpasa, Cerrahpasa Pandemia Services. POPULATION: Hospitalized 150 adults with laboratory and radiological confirmation of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) according to WHO interim guidance were included in the study. METHODS: The disease severity 2007 idsa/ats guidelines for community acquired pneumonia was used. Myalgia severity was assessed by numerical rating scale (NRS). Visual analog scale and Chalder Fatigue Scale (CFS) were used for fatigue severity determination. Handgrip strength (HGS) was measured by Jamar hand dynamometer. RESULTS: 103 patients (68.7%) were non-severe and 47 patients (31.3%) were severe. The most common musculoskeletal symptom was fatigue (133 [85.3%]), followed by myalgia (102 [68.0%]), arthralgia (65 [43.3%]) and back pain (33 [22.0%]). Arthralgia, which was mostly notable at wrist (25 [16.7%]), ankle (24 [16.0%]) and knee (23 [15.3%]) joints, was significantly higher among the severe group. Severe myalgia was prevalent among myalgia sufferers regardless of COVID-19 severity. The physical fatigue severity score was significantly higher in severe cases, whereas this difference was not significant in mental fatigue score. Female patients with severe infection had "lower" grip strength, whereas grip strength among males did not differ significantly between non-severe and severe COVID-19 cases. Nevertheless the mean values in both genders and in age decades were below the specified normative values. CRP, ferritin, and LDH levels were significantly higher in women with "lower" grip strength compared to the "normal" group. CONCLUSIONS: Aside from other multi-systemic symptoms, musculoskeletal symptoms are quite common in patients with COVID-19. Patients have severe ischemic myalgia regardless of disease activity. Although there is a muscle weakness in all patients, the loss of muscle function is more of a problem among women in connection with disease severity. Muscular involvement in coronavirus disease is a triangle of myalgia, physical fatigue, and muscle weakness. CLINICAL REHABILITATION IMPACT: Muscle involvement in COVID-19 patients does not mean only myalgia but also a combination of physical fatigue and muscle weakness, and this should be considered in planning the rehabilitation strategies of COVID-19 patients.

Table IV. Evaluation of Fatigue with Chalder Fatigue Scale and VAS-F †				
	Freq. (%)			
	Non-severe	Severe	Total	

	(n= 103)		(n= 47)		(n= 150)		
Characteristic	***No***	**%**	**No**	**%**	**No**	**%**	***P-Value***
Chalder Fatigue Scale (Bimodal)							
Non-Fatigue	*24*	23.3	6	12.8	30	20.0	0.135
Fatigue	*79*	76.7	41	87.2	120	80.0	
Mean (Confidence Interval) or Median (Range)							
Physical Fatigue VAS, median	7 (1 - 10)		8 (3 - 10)		8 (1- 10)		0.075
Phys. Fatigue VAS, mean (bootstrap CI)	6.94 (6.43 - 7.41)		7.70 (7.09 - 8.26)		7.20 (6.76 - 7.59)		0.048*
Mental Fatigue VAS, median	6 (0 - 10)		7.5 (0 - 10)		7 (0 - 10)		0.318
Ment. Fatigue VAS, mean (bootstrap CI)	5.64 (4.89 - 6.34)		6.41 (5.41 - 7.35)		5.89 (5.27 - 6.55)		0.215
† VAS-F: Visual Analog Scale to Evaluate, Fatigue Severity							

Table VII. Laboratory Findings vs Musculoskeletal Symptoms

	Mean (Bootstrap CI) or Freq. (%)																			
	Myalgia NO (n= 48)		Myalgia YES (n=102)		Total (n= 150)			Arthralgia NO (n=85)		Arthralgia YES (n=65)		Total (n= 150)			Fatigue NO (n= 17)		Fatigue YES (n=133)		Total (n= 150)		
Lab Findings	**Value**	**%**	**Value**	**%**	**Value**	**%**	***P-Value***	**Value**	**%**	**Value**	**%**	**Value**	**%**	***P-Value***	**Value**	**%**	**Value**	**%**	**Value**	**%**	***P-Value***
LDH (IU/L)	354 (310 - 395)		323 (293 - 360)		333 (307 - 358)		0.287	347 (315 - 386)		315 (280 - 353)		333 (307 - 358)		0.245	286 (255 - 318)		339 (311 - 371)		333 (307 - 358)		0.030*
(high ≥ 250). freq.	35	72.9	57	55.9	92	61.3	0.045*	54	63.5	38	58.5	92	61.3	0.528	13	76.5	79	59.4	92	61.3	0.173
CK (IU/L)	194 (127 - 293)		171 (139 - 210)		178 (145 - 216)		0.658	186 (136 - 244)		168 (127 - 219)		178 (145 - 216)		0.649	144 (104 - 192)		183 (144 - 227)		178 (145 - 216)		0.235
(high ≥ 170). freq.	14	29.2	24	23.5	38	25.3	0.459	22	25.9	16	24.6	38	25.3	0.860	5	29.4	33	24.8	38	25.3	0.768
Troponin T (ng/ml)	0.044 (0.017 – 0.092)		0.015 (0.009 – 0.024)		0.024 (0.014 – 0.040)		0.381	0.033 (0.017 - 0.056)		0.014 (0.006 - 0.028)		0.024 (0.014 - 0.040)		0.341	0.018 (0.011 - 0.026)		0.025 (0.013 - 0.043)		0.024 (0.014 - 0.040)		0.467
(high ≥ 0.014). freq.	24	50.0	22	21.6	46	30.7	<0.001*	39	45.9	7	10.8	46	30.7	<0.001*	8	47.1	38	28.6	46	30.7	0.120
Lymphocyte (count/mcL)	1377 (1133 - 1640)		1274 (1157 - 1400)		1307 (1200 - 1418)		0.532	1305 (1143 - 1499)		1309 (1143 - 1486)		1307 (1200 - 1418)		0.963	1488 (1150 - 1882)		1283 (1154 - 1424)		1307 (1200 - 1418)		0.296
(low < 1100). freq.	20	41.7	33	32.4	53	35.3	0.266	33	38.8	20	30.8	53	35.3	0.306	5	29.4	48	36.1	53	35.3	0.588
CRP (mg/L)	59.38 (41.58 – 79.90)		75.48 (55.42 – 100.57)		70.33 (55.96 – 86.92)		0.306	62.46 (50.04 - 75.77)		80.61 (52.24 - 118.09)		70.33 (55.96 - 86.92)		0.702	37.76 (22.21 - 56.82)		74.49 (58.50 - 91.70)		70.33 (55.96 - 86.92)		0.027*
(high ≥ 5). freq.	41	85.4	82	80.4	123	82.0	0.455	71	83.5	52	80.0	123	82.0	0.577	15	88.2	108	81.2	123	82.0	0.739
Ferritin (ng/ml)	588.56 (412.65 – 800.27)		390.42 (309.98 – 480.57)		453.83 (377.75 – 550.41)		0.062	512.49 (406.14 - 629.01)		377.11 (264.60 - 505.71)		453.83 (377.75 - 550.41)		0.109	342.83 (220.82 - 493.92)		468.01 (384.16 - 554.97)		453.83 (377.75 - 550.41)		0.154
(high ≥ 400). freq.	21	43.8	35	34.3	56	37.3	0.265	37	43.5	19	29.2	56	37.3	0.073	5	29.4	51	38.3	56	37.3	0.473
Procalcitonin (ng/ml)	1.581 (0.159 - 3.392)		1.326 (0.255 - 2.684)		1.407 (0.452 - 2.551)		0.851	2.139 (0.471 - 4.324)		0.450 (0.118 - 0.964)		1.407 (0.452 - 2.551)		0.146	0.095 (0.068 - 0.121)		1.575 (0.469 - 3.010)		1.407 (0.452 - 2.551)		0.856
(high ≥ 0.500). freq.	4	8.3	12	11.8	16	10.7	0.525	10	11.8	6	9.2	16	10.7	0.618	0	0.0	16	12.0	16	10.7	0.218
D-DIMER (mg/L)	2.47 (1.32 - 3.92)		3.19 (1.63 - 5.25)		2.96 (1.86 - 4.23)		0.559	2.74 (1.62 - 4.10)		3.23 (1.62 - 5.35)		2.96 (1.86 - 4.23)		0.771	0.92 (0.59 - 1.30)		3.22 (1.93 - 4.65)		2.96 (1.86 - 4.23)		0.086
(high ≥ 0.50). freq.	31	64.6	76	74.5	107	71.3	0.210	57	67.1	50	76.9	107	71.3	0.186	9	52.9	98	73.7	107	71.3	0.090

HIV AND SARS-COV-2 CO-INFECTION: CROSS-SECTIONAL FINDINGS FROM A GERMAN 'HOTSPOT'

Noe S, Schabaz F, Heldwein S, Mayer W, Ruecker K, Tiller FW, von Krosigk A, Wiese C, Balogh A, Gersbacher E, Jonsson-Oldenbuettel C, Jaeger H, Wolf E; ArcHIV study group... Infection. 2021 Jan 2. doi: 10.1007/s15010-020-01564-8. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

Physicians from the HIV Research and Clinical Care Centre in Munich, Germany tested 500 people living with HIV (PLWH) to determine the seroprevalence of Anti-SARS-CoV-2 IgG antibodies between May 29 and July 15, 2020. Among the 500 participants (Table 1), 22 tested positive initially via recomWell SARS-CoV-2 IgG ELISA and 9 were confirmed positive via recomLine SARS-CoV-2 IgG immunoassay (Table 2), indicating a prevalence of 1.5% (CI 95%: 0.7; 3.1) after accounting for test sensitivity (see summary). This study suggests confirmatory testing is necessary to identify SARS-CoV-2 cases and that the rate of SARS-CoV-2 among PLWH is not excessively higher than that of the general population.

SUMMARY

Further stratified, it was found of the 292 patients living in Munich, 7 were confirmed positive for antibodies (Figure 1) placing the seroprevalence at 2.2% (CI 95%:1.1; 3.9). Of these, 3 had been diagnosed with COVID-19 (1.0% prevalence) compared to a diagnostic prevalence of 0.4% in the general Munich population.

ABSTRACT

PURPOSE: This study aimed to determine the proportion of people living with HIV with anti-SARS-CoV-2 IgG antibodies in a sample from a large single HIV center in Munich, Germany, after the first phase of the coronavirus pandemic and to infer the prevalence of SARS-CoV-2 co-infection in people living with HIV. METHODS: Prospective sub-study of the ongoing ArcHIV cohort between May and July 2020. Anti-SARS-CoV-2 IgG antibodies were measured using the recomWell SARS-CoV-2 IgG ELISA (Mikrogen, Neuried, Germany); positive and borderline results were re-tested using the recomLine SARS-CoV-2 IgG immunoassay (Mikrogen, Neuried, Germany). Demographic and medical data were extracted from the electronic patient files. RESULTS: Overall, 500 people living with HIV were included in the study (83% male, median age 51 years). Three participants had been diagnosed with COVID-19 prior to study inclusion. Of those, nine were confirmed positive for SARS-CoV-2 IgG antibodies, resulting in an estimated seroprevalence (accounting for sensitivity and specificity of the test) of 1.5% (CI 95%: 0.69; 3.13) for the entire study sample, and 2.2% (CI 95%: 1.1; 3.9) for the subset of the Munich citizens. There were no marked differences for people living with HIV with and without SARS-CoV-2 co-infection. CONCLUSION: The seroprevalence of SARS-CoV-2 co-infection in people living with HIV as found in our study does not seem to exceed previous reports from general populations of 'hot-sport' areas; comparative data from the Munich population can be expected to be published soon. Our data also highlight, once more, the need to do confirmatory testing on positive samples to minimize the impact of false-positive results.

Table 1 Demographic data of 500 PLWH included in this study in comparison to the PLWH population, defined as all PLWH attending the study site within the previous year

	Study sample ($n=500$)	(CI 95%)	PLWH population ($n=2728$)
Age [years], mean (SD)	50 (11)	[49–51]	48, (13)
Missing, n	0		0
Male, *n* (%)	415 (83)	[79.4–86.1]	2173 (79.7)
Missing, *n*	0		0
Munich citizens, *n* (%)	292 (58.4)	[53.7–62.5]	1595 (58.5)
Missing, *n*	0		0
Homosexual transmission, *n* (%)	232 (46.4)	[49.1–58.0]	997 (50.2)
Missing, *n*	0		741
ART naive, *n* (%)	7 (1.4)	[0.6–3.0]	15 (0.8)*
Missing, *n*	0		741
Patients with viral load < 50 copies/mL, *n* (%)	466 (93.2)	[90.5–95.2]	2499 (91.6)
Missing, *n*	0		0

Asterisks marking population parameters differing significantly from the sample estimates on a $\alpha=0.05$ level

Table 2 Comparison of characteristics between the groups of PLWH with confirmed positive and negative anti-SARS-CoV-2 serostatus

	Serostatus		*p* value
	Positive ($n=9$)	Negative ($n=491$)	
Age, years, median (IQR)	41 (38;57)	51 (42;57)	0.296
Male sex, %	100.0	82.7	0.369
Munich citizens, %	77.8	57.8	0.316
Homosexual transmission risk, %	55.6	53.6	1.000
Caucasian ethnicity, %	77.8	87.6	0.316
African ethnicity, %	11.1	5.5	0.407
HIV-RNA level below 50 copies/mL, %	88.9	93.3	0.472
CD4 cells [cells/µL], median (IQR)	790.0	714.0	0.244
CD4 cell count [cells/µL], median (IQR)	(615;1220)	(553;923)	

Due to the marked differences in the sizes of both groups, frequencies are only displayed as percentages instead of absolute numbers. Asterisks marking *p* values < 0.05

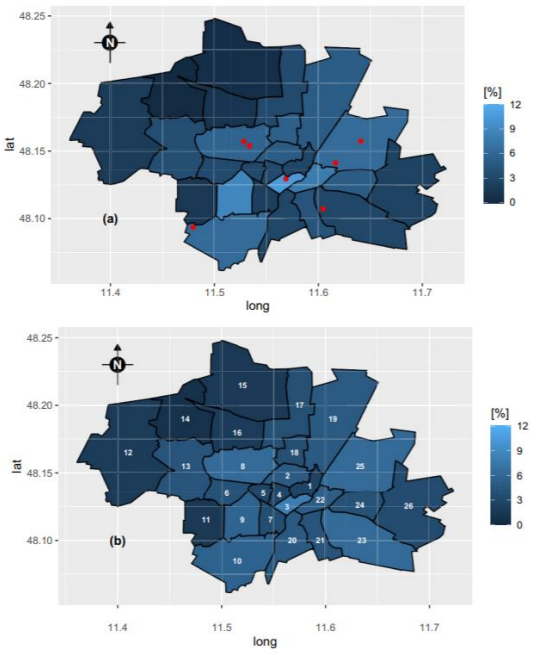


Fig. 1 Comparison of the percentage of PLWH in each district from (**a**) the study sample and (**b**) the overall PLWH population from the study site in Munich. Red dots in (**a**) are indicating the residence of PLWH with confirmed positive tests for anti-SARS-CoV-2 antibodies in the study sample. Numbers in (**b**) are referring to the different districts

PEDIATRICS

ARTERITIS AND LARGE VESSEL OCCLUSIVE STROKES IN CHILDREN FOLLOWING COVID-19 INFECTION

Appavu B, Deng D, Dowling MM, Garg S, Mangum T, Boerwinkle V, Abruzzo T.. Pediatrics. 2020 Dec 4:e2020023440. doi: 10.1542/peds.2020-023440. Online ahead of print.
Level of Evidence: 5 - Case Report

BLUF

Pediatric neurologists and pathologists from the University of Arizona and University of Texas Southwestern describe two children who experienced arterial ischemic strokes due to large vessel occlusion 3-4 weeks after SARS-CoV-2 infection. Upon imaging, both patients presented with cerebral arteritis, which authors hypothesize is due to anti-IgG autoimmunity. The authors suggest large vessel arteritis and arterial ischemic stroke may complicate COVID-19 infection in previously healthy children, and these symptoms may overlap but not fulfill criteria for other complications such as multisystem inflammatory syndrome in children (MIS-C) or Focal Cerebral Arteriopathy (FCA). Recognition of this condition may facilitate early intervention, which is essential to improving outcomes in these children.

SUMMARY

Case 1: An 8-year-old female with a National Institute of Health Stroke Scale (NIHSS) score of 15 presented with COVID-19 symptoms along with iron deficiency anemia for which she received a transfusion. Imaging showed infarctions of the middle cerebral artery (MCA) and proximal left M1 occlusion, treated with thrombectomy. SARS-CoV-2 infection was confirmed by the presence of anti-SARS-CoV-2 IgG along with increased inflammatory markers.

Case 2: A 16-year-old male with a NIHSS score of 19 presented with global aphasia and right hemiparesis. Imaging demonstrated a complete left MCA infarction, irregularity of left M1 suggesting arteritis, and occlusion of left MCA bifurcation. The patient had a positive nasopharyngeal PCR test 30 days prior to the stroke as well as elevated inflammatory markers on admission.

EXPRESSION OF SARS-COV-2 ENTRY FACTORS IN HUMAN ORAL TISSUE

Sawa Y, Ibaragi S, Okui T, Yamashita J, Ikebe T, Harada H.. J Anat. 2021 Jan 9. doi: 10.1111/joa.13391. Online ahead of print.
Level of Evidence: 5 - Mechanism-based reasoning

BLUF

Oral and maxillofacial surgeons from Japan analyzed the distribution of cells expressing the SARS-CoV-2 entry factors angiotensin-converting enzyme 2 (ACE2) and transmembrane serine protease 2 (TMPRSS2) in oral cell samples from 8 human volunteers and various tissue samples from 5 mice. The lingual and buccal mucosa of humans strongly expressed ACE2 and TMPR22 (Figure 2), with mouse tissue specimens demonstrating expression in the kidney, small intestine, tongue, and submandibular gland (Figure 1). Authors suggest the oral cavity is an important attachment point for SARS-CoV-2 before it infects other parts of the body and underscore the importance of masks for infection control.

ABSTRACT

The distribution of cells expressing SARS-CoV-2 entry factor angiotensin-converting enzyme 2 (ACE2) and transmembrane serine protease 2 (TMPRSS2) in human oral tissues were tested. The investigation was conducted with normal flesh tissue and paraffin-embedded specimens. The ACE2 and TMPRSS2 expression was detected with all subjects in the normal mucosa of the keratinized stratified squamous epithelia of the tongue and non-keratinized stratified squamous epithelia of the lip and cheek. It was found that ACE2 is expressed in the cytoplasm and on the cell membrane mainly in the stratum granulosum of the epithelia while the TMPRSS2 is strongly expressed on the cell membrane mainly in the stratum granulosum and stratum spinosum, but not in the stratum basale. Antibodies' reactions for ACE2 and TMPRSS2 were not observed in the nuclei or keratin layer. The expression of ACE2 and TMPRSS2 in the oral epithelia appears to be general, and the expression was also observed in the mucous and serous acini of the labial glands. The SARS-CoV-2 may transiently attach to the oral mucosa and the minor salivary glands which are present under all of the oral mucosa. The oral cavity can be considered an important organ for SARS-CoV-2 attachment and may provide a preventive medical avenue to guard against COVID-19 by preventing saliva from scattering.

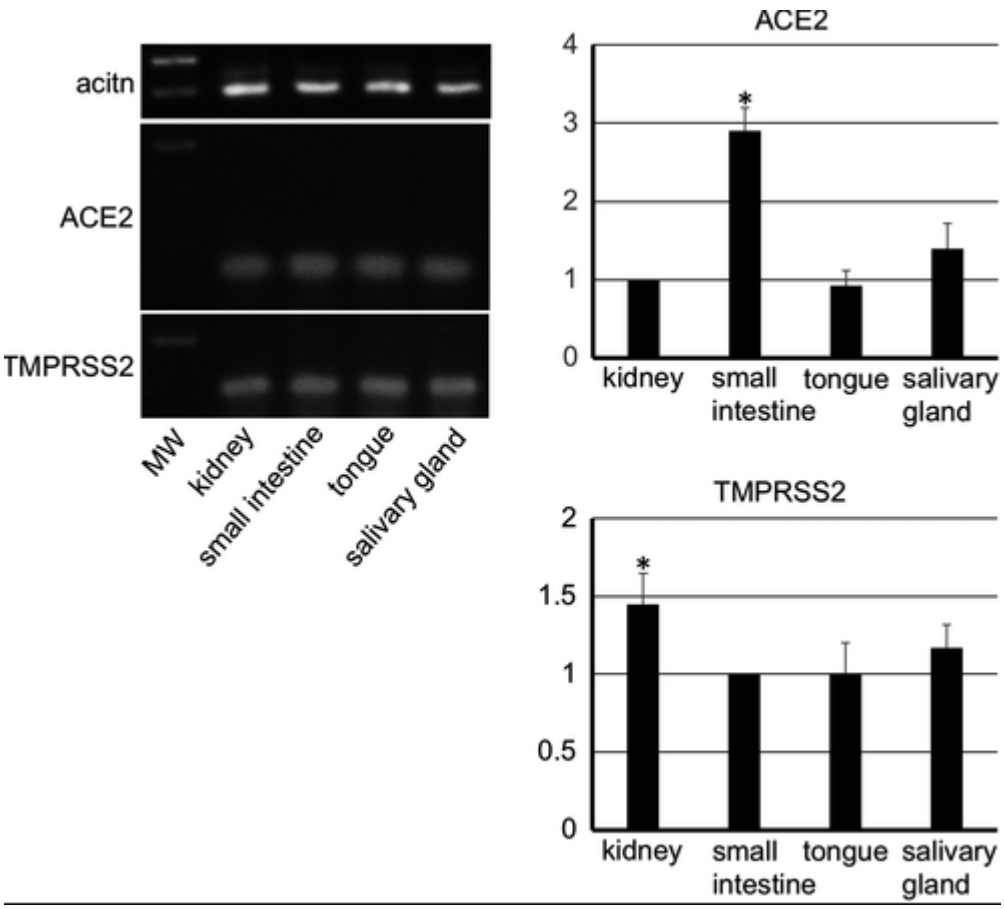


Figure 1: RT-PCR analysis for mouse tissue. The RT-PCR analysis for the mouse tissue shows that there are cells expressing ACE2 and TMPRSS2 in the submandibular gland, tongue, small intestine, and kidney. The real time-PCR analysis shows that the gene expression of ACE2 in the small intestine and TMPRSS2 in the kidney was significantly stronger than in other tissues. Target gene cDNA were normalized to β-actin cDNA. The relative gene expression was expressed as arbitrary units according to the following formula: cDNA amounts of experimental samples/cDNA amounts of samples determined as controls (ACE2: kidney, TMPRSS2: small intestine). Values are means ± SD. *Significantly different in ANOVA ($p < 0.01$)

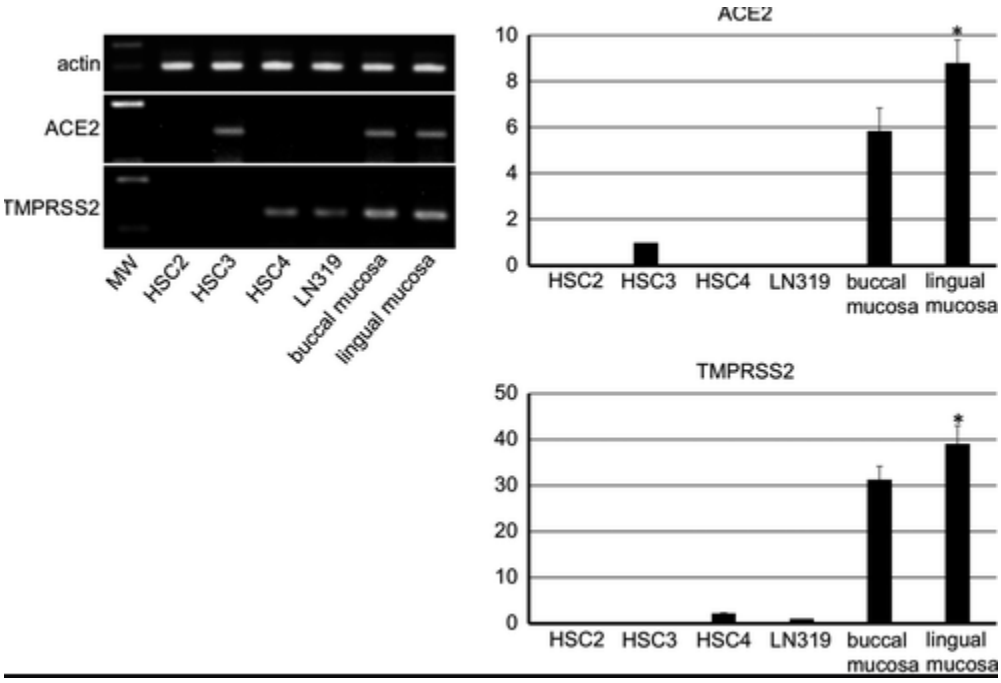


Figure 2: RT-PCR analysis for human tissue and cells. The RT-PCR analysis for the human tissue of the lingual mucosa and buccal mucosa including normal keratinocytes shows that there are cells expressing ACE2 and TMPRSS2. In human epithelial-like oral cancer cell lines, the reaction product of RT-PCR for ACE2 mRNA was detected in HSC3 but not in HSC2 or HSC4. The reaction product for TMPRSS2 mRNA was detected in HSC4 but not in HSC2 or HSC4. In the human glioma cell line LN319, the reaction product for ACE2 mRNA was not detected while the reaction product for TMPRSS2 mRNA was detected. The real time-PCR analysis shows that a strong expression of ACE2 and TMPRSS2 genes are present in the lingual and buccal mucosa, and the gene expression of both ACE2 and TMPRSS2 was significantly stronger in the lingual mucosa than in buccal mucosa or cell line controls. Target gene cDNA were normalized to β-actin cDNA. The relative gene expression was expressed as arbitrary units according to the following formula: cDNA amounts of experimental samples/cDNA amounts of samples determined as controls (ACE2: HSC3, TMPRSS2: LN319). Values are means ± SD of 5 data. *Significantly different in ANOVA ($p < 0.01$)

MANAGEMENT

PERSISTENT SYMPTOMS AFTER COVID-19: QUALITATIVE STUDY OF 114 "LONG COVID" PATIENTS AND DRAFT QUALITY PRINCIPLES FOR SERVICES

Ladds E, Rushforth A, Wieringa S, Taylor S, Rayner C, Husain L, Greenhalgh T.. BMC Health Serv Res. 2020 Dec 20;20(1):1144. doi: 10.1186/s12913-020-06001-y.
Level of Evidence: 3 - Local non-random sample

BLUF

In this retrospective study that interviewed 114 patients with "long Covid" ('post-acute' symptoms persisting beyond 3–4 weeks and 'chronic' symptoms beyond 12 weeks), researchers from the UK consider the characteristics and development of "long Covid." They found that "long Covid" encompasses a variety of symptoms with fluctuating intensity, and patients described differences in the quality of their care experience, with some reporting dismissive providers, difficulty accessing appropriate services, and lack of guidance. The authors suggest that a re-engineering of healthcare services including the employment of online services, is necessary to meet the changing needs of "long Covid" sufferers.

ABSTRACT

BACKGROUND: Approximately 10% of patients with Covid-19 experience symptoms beyond 3-4 weeks. Patients call this "long Covid". We sought to document such patients' lived experience, including accessing and receiving healthcare and ideas for improving services. METHODS: We held 55 individual interviews and 8 focus groups (n = 59) with people recruited from UK-based long Covid patient support groups, social media and snowballing. We restricted some focus groups to health professionals since they had already self-organised into online communities. Participants were invited to tell their stories and comment on others' stories. Data were audiotaped, transcribed, anonymised and coded using NVIVO. Analysis incorporated sociological theories of illness, healing, peer support, clinical relationships, access, and service redesign. RESULTS: Of 114 participants aged 27-73 years, 80 were female. Eighty-four were White British, 13 Asian, 8 White Other, 5 Black, and 4 mixed ethnicity. Thirty-two were doctors and 19 other health professionals. Thirty-one had attended hospital, of whom 8 had been admitted. Analysis revealed a confusing illness with many, varied and often relapsing-remitting symptoms and uncertain prognosis; a heavy sense of loss and stigma; difficulty accessing and navigating services; difficulty being taken seriously and achieving a diagnosis; disjointed and siloed care (including inability to access specialist services); variation in standards (e.g. inconsistent criteria for seeing, investigating and referring patients); variable quality of the therapeutic relationship (some participants felt well supported while others felt "fobbed off"); and possible critical events (e.g. deterioration after being unable to access services). Emotionally significant aspects of participants' experiences informed ideas for improving services. CONCLUSION: Suggested quality principles for a long Covid service include ensuring access to care, reducing burden of illness, taking clinical responsibility and providing continuity of care, multi-disciplinary rehabilitation, evidence-based investigation and management, and further development of the knowledge base and clinical services. TRIAL REGISTRATION: NCT04435041.

OBGYN

ACUTE PANCREATITIS IN A PREGNANT PATIENT WITH CORONAVIRUS DISEASE 2019 (COVID-19)

Narang K, Szymanski LM, Kane SV, Rose CH.. Obstet Gynecol. 2020 Dec 22;Publish Ahead of Print. doi: 10.1097/AOG.0000000000004287. Online ahead of print.
Level of Evidence: 5 - Case report

BLUF

A case report of a 20-year-old COVID-19-positive pregnant patient at Mayo Clinic in Rochester, Minnesota who presented with respiratory decompensation then subsequently developed viral pancreatitis, suggesting pregnant patients in the setting of COVID-19 may present with additional viral manifestations and are at risk for serious complications.

SUMMARY

Authors from the Department of Obstetrics and Gynecology, Mayo Clinic, Rochester, Minnesota present a case report of a 20-year-old COVID-19 positive patient at 33 weeks gestation who presented to their facility with acute respiratory decompensation and was admitted to the ICU. Although respiratory symptoms improved initially, on day 3 of hospitalization she developed severe epigastric pain with concomitant elevated lipase (916 units/L) and amylase (396 units/L), and was diagnosed viral pancreatitis was made, given her lack of additional risk factors such as alcohol use disorder, hypertriglyceridemia, or autoimmune conditions. On day 5-6, she again began to acutely deteriorate and went into preterm labor, subsequently delivering a healthy male child, who was SARS-CoV-2 negative. The patient's condition improved drastically after delivery, and she was discharged home on day 3 postpartum. This case exhibits the variation in clinical symptoms, presentations, and difficulties of COVID-19 in pregnant populations, and displays the importance of recognition of rare complications, such as viral pancreatitis.

ABSTRACT

BACKGROUND: Pregnant women with coronavirus disease 2019 (COVID-19) infection are at risk for a variety of COVID-19 complications. CASE: We report a case of acute pancreatitis in a pregnant patient hospitalized for COVID-19 pneumonia. Comprehensive evaluation ruled out other etiologies of acute pancreatitis. Preterm labor developed at 33 5/7 weeks of gestation, and the patient delivered a liveborn male neonate; neonatal severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) screening was negative. The patient improved significantly postpartum and was discharged home on postpartum day 3. CONCLUSION: Coronavirus disease 2019 may present in pregnancy with a myriad of clinical symptoms other than respiratory. Acute pancreatitis represents an infrequent complication of primary COVID-19 infection.

REMDESIVIR AND ACUTE RENAL FAILURE: A POTENTIAL SAFETY SIGNAL FROM DISPROPORTIONALITY ANALYSIS OF THE WHO SAFETY DATABASE

Gérard A, Laurain A, Fresse A, Parassol N, Muzzone M, Rocher F, Esnault VLM, Drici MD.. Clin Pharmacol Ther. 2020 Dec 19. doi: 10.1002/cpt.2145. Online ahead of print.

Level of Evidence: 3 - 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.)

BLUF

Nephrologists and pharmacists from Centre Hospitalier Universitaire de Nice in France evaluated the risk of acute renal failure (ARF) associated with remdesivir compared to hydroxychloroquine, tocilizumab, and lopinavir/ritonavir. They analyzed international pharmacovigilance postmarketing databases with two disproportionality methods, and found a "statistically suggestive disproportionality signal," observing 138 cases of ARF in patients receiving remdesivir where they would have expected nine (ROR: 20.3 [15.7-26.3]; P<0.0001)(Table 2). Authors suggest serum creatinine monitoring is warranted in patients receiving remdesivir treatment for COVID-19.

ABSTRACT

Remdesivir is approved for emergency use by the Food and Drug Administration (FDA) and authorized conditionally by the European Medicines Agency (EMA) for patients with Coronavirus disease 2019 (COVID-19). Its benefit-risk ratio is still being explored since data in the field are rather scant. A decrease of the creatinine clearance associated with remdesivir has been inconstantly reported in clinical trials with unclear relevance. Despite these uncertainties, we searched for a potential signal of acute renal failure (ARF) in pharmacovigilance postmarketing data. An analysis of the international pharmacovigilance postmarketing databases (VigiBase) of the World Health Organization (WHO) was performed, using two disproportionality methods. Reporting odds ratio (ROR) compared the number of ARF cases reported with remdesivir, with those reported with other drugs prescribed in comparable situations of COVID-19 (hydroxychloroquine, tocilizumab, lopinavir/ritonavir). The combination of the terms "acute renal failure" and "remdesivir" yielded a statistically significant disproportionality signal with 138 observed cases instead of the 9 expected. ROR of ARF with remdesivir was 20-fold (20.3; CI 0.95 [15.7-26.3], p<0.0001]) that of comparative drugs. Based on ARF cases reported in VigiBase , and despite the caveats inherent to COVID-19 circumstances, we detected a statistically significant pharmacovigilance signal of nephrotoxicity associated with remdesivir, deserving a thorough qualitative assessment of all available data. Meanwhile, as recommended in its Summary of Product Characteristics, assessment of COVID-19 patients' renal function should prevail before and during treatment with remdesivir in COVID-19.

FIGURES

Exposure	Cases of ARF	Non-cases	ROR [95% condence interval]
Comparator drugs[b]	138	7385	/
Remdesivir	138	363	20.3 [15.7-26.3] (P<0.0001)

Table 2: Reporting Odds ratio for the SMQ (Standardized MedDRA Version 23.0 query) "acute renal failure" (ARF, broad) associated with remdesivir. (Comparative drugs: hydroxychloroquine, tocilizumab, lopinavir/ritonavir)

PSYCHOLOGICAL IMPACTS OF COVID-19 DURING THE FIRST NATIONWIDE LOCKDOWN IN VIETNAM: WEB-BASED, CROSS-SECTIONAL SURVEY STUDY

Ngoc Cong Duong K, Nguyen Le Bao T, Thi Lan Nguyen P, Vo Van T, Phung Lam T, Pham Gia A, Anuratpanich L, Vo Van B..
JMIR Form Res. 2020 Dec 15;4(12):e24776. doi: 10.2196/24776.
Level of Evidence: 3 - Local non-random sample

BLUF

Physicians and scientists from Thailand and Vietnam conducted a web-based cross sectional survey from April 10th - April 15th, 2020, and used the Event Scale-Revised (IES-R) and Depression, Anxiety, and Stress Scale-21 (DASS-21) to assess the psychological (depression, anxiety, and stress) impacts of the first nationwide lockdown in Vietnam due to COVID-19. From 1385 total respondents, the researchers found that 35.9% reported psychological distress, 23.5% reported depression, 22.3% reported stress and 14.1% reported anxiety. This study illustrates the need for health policy and medical interventions to mitigate the psychological effects of the COVID-19 pandemics and lockdowns.

SUMMARY

Several other prominent findings in this study include the following:
- Those who self reported average physical health had higher depression, anxiety, stress and higher scores on both IES-R and DASS-21 scales. Similarly, those who reported bad or very bad health had more severe depression, anxiety, and stress compared to those with self-reported good or very good health.
- Unemployment and presence of a chronic disease were related to a higher risk of depression.
- 96.4% of respondents were confident about their doctor's expertise in diagnosing and treating COVID-19.

ABSTRACT

BACKGROUND: The first nationwide lockdown due to the Coronavirus disease 2019 (COVID-19) pandemic has been imposed in Vietnam between April 1 and 15, 2020. Nevertheless, there has been limited information on the impact of COVID-19 to society's psychological health. OBJECTIVE: This study aimed to estimate the prevalence of psychological issues and identify the factors associated with the psychological impact of COVID-19 during the first nationwide lockdown among the general population in Vietnam. METHODS: We employed a cross-sectional study design with convenience sampling. A self-administered, online survey was used to collect data and assess psychological distress, depression, anxiety, and stress of participants from April 10 to 15, 2020. The Impact of Event Scale-Revised (IES-R) and the Depression, Anxiety, and Stress Scale (DASS-21) were utilized to assess psychological distress, depression, anxiety, and stress of participants during COVID-19 social distancing. The associated factors were explored by using regression analysis. RESULTS: A total of 1,385 respondents completed the survey. There were 35.9%, 23.5%, 14.1%, and 22.3% who suffered from psychological distress, depression, anxiety, and stress, respectively. Those respondents who evaluated their physical health as average had higher IES-R score, DASS-21 depression, anxiety and stress than those in good/very good health status (beta-coefficient regression (B) = 9.16, 95% Confidence Interval (CI), 6.43 to 11.89), B = 5.85, 95% CI, 4.49 to 7.21, B = 3.64, 95% CI, 2.64 to 4.63, and B = 5.19, 95% CI, 3.83 to 6.56, respectively). Those who were in bad or very bad health condition suffered more severe depression, anxiety and stress (B = 9.57, 95% CI, 4.54 to 14.59, B = 7.24, 95% CI, 3.55 to 10.9, and B = 10.60, 95% CI, 5.56 to 15.65, respectively). Unemployment was more likely associated with depression and stress (B = 3.34, 95% CI, 1.68 to 5.01, and B = 2.34, 95% CI, 0.84 to 3.85). Regarding concerns about COVID-19, more than half (54.5%) expressed concern on their children aged below 18 years, which increased their IES-R score and DASS-21 stress score (B = 7.81, 95% CI, 4.98 to 10.64, and B = 1.75, 95% CI, 0.27 to 3.24, respectively). Majority (94.6%) were confident on the doctor's expertise in COVID-19 diagnosis and treatment, which was positively associated with less distress caused by the outbreak (B = -7.84, 95% CI, -14.58 to -1.11). CONCLUSIONS: The findings highlight the impacts on mental health of COVID-19 during the nationwide lockdown among the general population in Vietnam. The study provides useful evidence for policy decision-makers to develop and implement interventions to mitigate these impacts. CLINICALTRIAL:

INTERSECTION OF SURGING FIREARM SALES AND COVID-19, PSYCHOLOGICAL DISTRESS, AND HEALTH DISPARITIES IN THE US-A CALL FOR ACTION

Hoskins K, Beidas RS.. JAMA Netw Open. 2021 Jan 4;4(1):e2034017. doi: 10.1001/jamanetworkopen.2020.34017.
Level of Evidence: 5 - Expert Opinion

BLUF

In response to a recent cross-sectional survey of 2,870 Californians showing recently increased public concern about violence, firearm and ammunition acquisition and unsafe firearm storage practice (Kravitz-Wirtz et al.), psychiatrists from the University of Pennsylvania fear that this will lead to increased firearm related injury and death, especially amidst increased suicide risk factors (personal loss, isolation, etc.). Authors suggest that establishing and targeting safe firearm storage/training programs, increasing funding for firearm injury prevention research, and focusing suicide prevention efforts, especially among racial and ethnic minority groups who experience disproportionately worse mental health outcomes, is crucial for harm reduction.

A SCIENTOMETRIC OVERVIEW OF CORD-19

Colavizza G, Costas R, Traag VA, van Eck NJ, van Leeuwen T, Waltman L.. PLoS One. 2021 Jan 7;16(1):e0244839. doi: 10.1371/journal.pone.0244839. eCollection 2021.
Level of Evidence: 5 - Modeling

BLUF

An in-depth analysis conducted by computer scientists from the University of Amsterdam evaluated the July 1, 2020 version of the COVID-19 open research dataset (CORD-19) which contains 169,821 articles covering literature pertaining to the COVID-19 pandemic. Included literature covered a wide range of topics (coronaviruses, viral molecular biology, treatments, public health, and clinical medicine, among others). Using topic modeling (Figure 5) and citation network clustering analysis (Figure 8), they found 63.1% of articles and 68.8% of 2020 articles had received social media attention as measured by Altmetric (Table 1). Authors suggest that CORD-19 provides a broad and cohesive coverage of relevant publications and is a useful tool for researchers looking for COVID-19 literature.

ABSTRACT

As the COVID-19 pandemic unfolds, researchers from all disciplines are coming together and contributing their expertise. CORD-19, a dataset of COVID-19 and coronavirus publications, has been made available alongside calls to help mine the information it contains and to create tools to search it more effectively. We analyse the delineation of the publications included in CORD-19 from a scientometric perspective. Based on a comparison to the Web of Science database, we find that CORD-19 provides an almost complete coverage of research on COVID-19 and coronaviruses. CORD-19 contains not only research that deals directly with COVID-19 and coronaviruses, but also research on viruses in general. Publications from CORD-19 focus mostly on a few well-defined research areas, in particular: coronaviruses (primarily SARS-CoV, MERS-CoV and SARS-CoV-2); public health and viral epidemics; molecular biology of viruses; influenza and other families of viruses; immunology and antivirals; clinical medicine. CORD-19 publications that appeared in 2020, especially editorials and letters, are disproportionately popular on social media. While we fully endorse the CORD-19 initiative, it is important to be aware that CORD-19 extends beyond research on COVID-19 and coronaviruses.

FIGURES

Table 1. Coverage of CORD-19 publications by Altmetric.

	CORD-19 publications	In Altmetric	Share in Altmetric
All	140, 302	88, 570	63.1%
2020	52, 440	36, 058	68.8%

https://doi.org/10.1371/journal.pone.0244839.t001

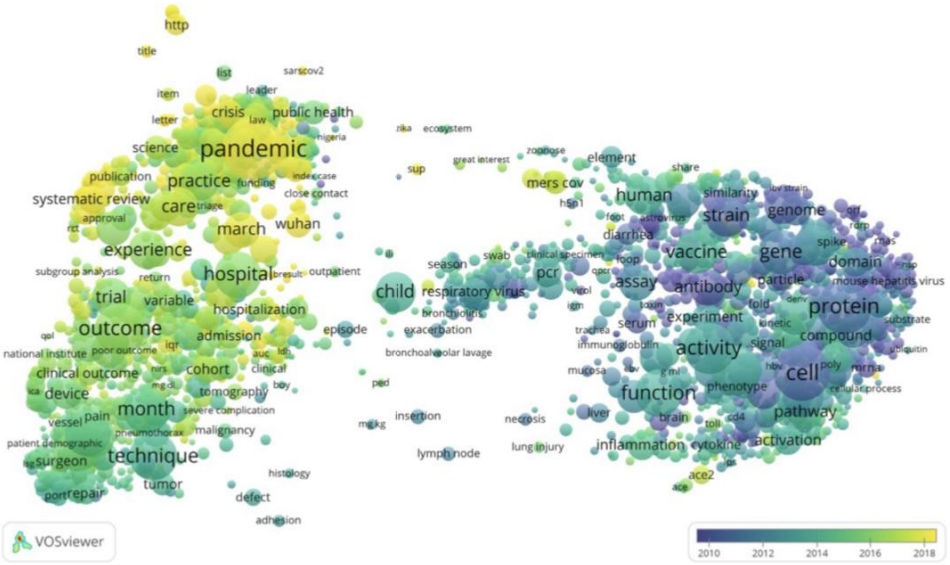
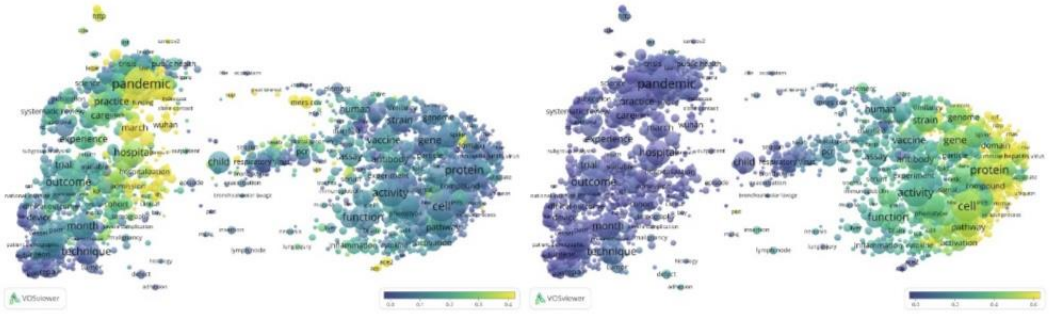


Fig 5. Term map highlighting temporal trends in the contents of CORD-19. Also compare with the topic words in the S1 Appendix.

https://doi.org/10.1371/journal.pone.0244839.g005



(a) Largest cluster (b) Second largest cluster

Fig 8. Top level citation network clustering. The color of a term reflects the percentage of publications in which the term occurs that belong to a specific cluster. For example, in (a), 46% of the publications that include the term "pandemic" belong to the largest cluster, whereas only 6% of the publications that include the term "protein" belong to this cluster. In (b), only 2% of the publications that include the term "pandemic" belong to the second largest cluster, whereas 54% of the publications that include the term "protein" belong to this cluster. Compare with Fig A.6 in S1 Appendix. (a) Largest cluster (b) Second largest cluster.

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