The Daily COVID-19 Literature Surveillance Summary

October 20, 2020

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COVID-19 Daily Literature Surveillance

COVID19LST

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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

- Clinical features and outcomes of adults with COVID-19 admitted to the hospital based on a systematic review and pooled analysis of the literature of 45 studies (n = 14,358) found the following:
  • the most common symptoms included fever (81.2%), cough (62.9%), fatigue (38.0%) and anorexia/loss of appetite (33.7%;)
  • the most common comorbidities were hypertension (19.1%), cardiovascular disease (17.9%), endocrine disorder (9.3%) and diabetes (9.2%)
  • 27.7% of patients had abnormal chest x-rays; 63% had ground-glass opacities on chest CT
  • Acute respiratory distress syndrome (27.4%), acute cardiac injury (16.2%) and acute kidney injury (12.6%) were the most common adverse outcomes
  • death occurred in 8.2% of patients, 16.3% needed intensive care admission and 11.7% had mechanical ventilation
  • bacterial or secondary infections affected 8.5% of patients and 6.9% developed shock

  These findings reveal the heterogeneous manifestations of COVID-19, although the authors note that these findings may not be generalizable to a wider population and are limited by differences in follow-up.

Understanding the Pathology

- Endotheliopathy is induced by plasma from critically-ill patients and associated with organ failure in severe COVID-19 based on a retrospective cohort study at Lille University Hospital assessing cytotoxicity of plasma from 28 patients (12 ICU and 16 non-ICU) hospitalized with COVID-19. Samples from COVID-19 patients had significantly decreased human pulmonary microvascular endothelial cells (HPMVEC) viability ($p<0.01$) and increased cytotoxicity compared to plasma from 8 healthy donors. The authors suggest their findings bolster the growing body of evidence indicating SARS-CoV-2 induces endothelial damage that contributes to organ dysfunction, respiratory failure, and thrombosis.

Transmission & Prevention

- Regeneration Processes for Filtering Facepiece Respirators (FFRs) in Terms of the Bacteria Inactivation Efficiency and Influences on Filtration Performance were investigated through the ability of microwave irradiation (MWI), UV irradiation (UVI), MWI + UVI, steam, and ethanol. Authors found ethanol unacceptably reduced filtration efficiency while steam and MWI effectively decontaminated FFRs (100% inactivation in 90 min and 30 min, respectively) without sacrificing filtration, though long exposure to MWI did damage fiber morphology. While UVI successfully inactivated surface bacteria, efficiency decreased from outer to inner layers and authors suggest that a combination of UVI and short-duration MWI can best decontaminate used FFRs while maintaining filtration performance.

- Leveraging on the genomics and immunopathology of SARS-CoV-2 for vaccines development has its prospects and challenges according to a literature review covering current data related to genomic organization, genetic mutations, pathophysiology, immune response to SARS-CoV-2, potential vaccine targets (particularly components of the S-protein and ACE-2 receptors), current vaccine trials, and potential animal models for vaccine testing (rhesus macaques, ferrets, mice, and Syrian hamsters). Authors suggest enough promising data exists to synthesize a COVID-19 vaccine in the near future but additional funding is needed to extend trials globally to ensure high performance across diverse population and create a centralized evaluation system to assess safety, efficacy, accessibility, and potency.

- Political partisanship influences behavioral responses to governors' recommendations for COVID-19 prevention in the United States. A team including physicians and communications experts from the University of Pennsylvania used mobility statistics from Safegraph (estimates for time at home), Google search data, and tweets from gubernatorial accounts to evaluate COVID-19 prevention behaviors in 3140 United States counties. Authors found democratic governors tweeted stay-at-home messages earlier than republicans (median 6-7 days before official order vs. 1 day). Additionally, governors' stay-at-home tweets correlated with increased median time spent at home by 3.4% (10.4 minutes/day; $p<0.01$), and democratic counties spent more time at home (4.1% increase vs. 3.1%, $p<0.01$)(Table 2,3), suggesting that political partisanship and governor recommendations had significant impacts on citizens' mobility during the early COVID-19 pandemic.

- With regards to community health workers (CHW) and Covid-19 population health experts from NYU Grossman School of Medicine discuss how CHWs, who are trusted community members also familiar with local health systems, have supported marginalized communities in New York impacted by the COVID-19 pandemic. They review CHWs' various roles (health systems/social services navigators, ability to conduct home visits, health educators, and community advocates,

among others). Because CHWs in New York have performed thousands of services since March 2020 (9600 telephone wellness checks, 600 health coaching sessions, and 3400 enrollments in online patient portals) they argue that investing in such programs could help alleviate the burden of disease in communities disproportionately impacted by COVID-19.

Management

- Anti-androgens may protect against severe COVID-19 outcomes based on results from a prospective cohort study of 77 hospitalized men. The authors found patients taking anti-androgens (dutasteride [n=9], finasteride [n=2], spironolactone [n=1]) were significantly less likely to be admitted to the ICU than men not taking anti-androgens (p=0.0002), even after stratifying for age (p=0.018). Given the reduced risk of experiencing severe COVID-19 (RR: 0.14, 95% CI: 0.02-0.94), they suggest anti-androgens could be utilized therapeutically to improve COVID-19 disease course in men.

- High prevalence of acquired thrombophilia did not have prognosis value in Covid-19 patients based on a prospective cohort study of 89 patients with COVID-19. They found acquired thrombophilia was not significantly associated with increased risk of severe disease (p=0.89), DVT (p=0.71), or mortality (p=0.89). Most (71.9%) patients had antiphospholipid antibodies, and 20.2 % had protein S deficiency, therefore authors suggest thrombophilia does not significantly influence disease course and its presence should not impact management of COVID-19 patients.

Adjusting Practice During COVID-19

- Proof-of-concept calculations to determine the health-adjusted life-year trade-off between intravitreal Anti-VEGF Injections and transmission of COVID-19 were constructed by ophthalmologists in New Zealand through statistical model that weighed risks and benefits of performing anti-VEGF intraocular injections in patients with neovascular age-related macular degeneration (nAMD) during the COVID-19 pandemic. Using health-adjusted life years (HALYs) lost to compare expected disease burden from COVID-19 to visual impairment secondary to nAMD in a variety of theoretical scenarios, authors found expected burden from visual impairment outweighed that from COVID-19 unless the latter's prevalence was very high and suggest continuing anti-VEGF injections during the pandemic minimizes overall HALYs lost.

R&D: Diagnosis & Treatments

- Sensitivity of nasopharyngeal, oropharyngeal, and nasal wash specimens for SARS-CoV-2 detection in the setting of sampling device shortage was explored though a cross-sectional study comparing sensitivities of different samples for detection of ORF1 and E-protein genes via RT-PCR in 29 SARS-CoV-2 positive patients. They found oropharyngeal washes (mean rRT-PCR delta cycle threshold[Ct]:1.24 for ORF1, 1.32 for E-protein; Pearson r: 0.88) and nasal washes (mean delta Ct: 1.77 ORF1,1.73 E-protein; Pearson r: 0.75) demonstrated similar levels of sensitivity compared to nasopharyngeal swabs (current standard of care). They also validated a cell culture medium (Dulbecco's modified Eagle medium) for sample transport (mean delta Ct of 0.67 for E-gene and 0.53 for ORF-1), suggesting that these alternative methods for sample collection can be reliably used in the setting of testing supply shortages.

TABLE OF CONTENTS

BARRIERS AND FACILITATORS OF ADHERENCE TO SOCIAL DISTANCING RECOMMENDATIONS DURING COVID-19 AMONG A LARGE INTERNATIONAL SAMPLE OF ADULTS

Coroiu A, Moran C, Campbell T, Geller AC.. PLoS One. 2020 Oct 7;15(10):e0239795. doi: 10.1371/journal.pone.0239795. eCollection 2020.
Level of Evidence: 3 - Local non-random sample

BLUF

Professionals from Harvard University and University of Calgary conducted a cross-sectional survey (n= 2,013 English-speaking adults primarily within North America and Europe) between March 30 to April 16, 2020 to examine the barriers and facilitators to practicing social-distancing during the COVID-19 pandemic. While survey responses (illustrated below) may be limited by sample selection and participant's attempts to achieve social desirability, these responses can be used to foster adherence to social distancing and to craft policy to remove barriers to social distancing.

SUMMARY

The responses from of the self-reported, cross-sectional survey included:
- Primary motivators for social distancing included protecting others, protecting oneself, and feeling responsibility for the community.
- Reported barriers to social-distancing included high foot traffic on nearby streets, having dependent friends and family, and not trusting government messages about the pandemic (Table 2).
- Adherence to social distancing ranged from 45% for working at home remotely to 90% for avoiding crowded areas, while men and younger individuals showed lower than average adherence (Table 3).

ABSTRACT

BACKGROUND: Social distancing measures (e.g., avoiding travel, limiting physical contact with people outside of one's household, and maintaining a 1 or 2-metre distance between self and others when in public, depending on the country) are the primary strategies used to prevent transmission of the SARS-Cov-2 virus that causes COVID-19. Given that there is no effective treatment or vaccine for COVID-19, it is important to identify barriers and facilitators to adherence to social distancing to inform ongoing and future public health campaigns. METHOD: This cross-sectional study was conducted online with a convenience sample of English-speaking adults. The survey was administered over the course of three weeks (March 30 -April 16, 2020) when social distancing measures were well-enforced in North America and Europe. Participants were asked to complete measures assessing socio-demographic characteristics, psychological constructs, including motivations to engage in social distancing, prosocial attitudes, distress, and social distancing behaviors. Descriptive (mean, standard deviation, percentage) and inferential statistics (logistic regression) were used to describes endorsement rates for various motivations, rates of adherence to social distancing recommendations, and predictors of adherence. RESULTS: Data were collected from 2013 adults living primarily in North America and Europe. Most frequently endorsed motivations to engage in social distancing (or facilitators) included "I want to protect others" (86%), "I want to protect myself" (84%), and I feel a sense of responsibility to protect our community" (84%). Most frequently endorsed motivations against social distancing (or barriers) included "There are many people walking on the streets in my area" (31%), "I have friends or family who need me to run errands for them" (25%), "I don't trust the messages my government provides about the pandemic" (13%), and "I feel stressed when I am alone or in isolation" (13%). Adherence to social distancing recommendations ranged from 45% for "working from home or remotely" to 90% for "avoiding crowded places/non-essential travel", with men and younger individuals (18-24 years) showing lower adherence compared to women and older individuals. CONCLUSION: This study found that adherence to social distancing recommendations vary depending on the behaviour, with none of the surveyed behaviours showing perfect adherence. Strongest facilitators included wanting to protect the self, feeling a responsibility to protect the community, and being able to work/study remotely; strongest barriers included having friends or family who needed help with running errands and socializing in order to avoid feeling lonely. Future interventions to improve adherence to social distancing measures should couple individual-level strategies targeting key barriers to social distancing identified herein, with effective institutional measures and public health interventions. Public health campaigns should continue to highlight compassionate attitudes towards social distancing.

Crt no	Variable	M (SD)	Never (%)	Sometimes (%)	Often (%)	Always (%)	N/A (%)	Always (%)			p
								Week 1	Week 2	Week 3	
1	Working from home or remotely	3.2 (1.2)	12.0	9.3	9.4	44.8	24.5	46.8	42.3	46.7	-
2	Attending classes virtually or completing coursework remotely	2.7 (1.2)	13.1	9.9	9.2	20.6	47.2	19.4	19.6	24.3	< .001
3	Avoiding non-essential gatherings (social events)	3.9 (0.5)	2.1	1.5	4.9	88.7	2.7	89.6	88.3	88.3	-
4	Avoiding crowded places (concerts, conferences, arenas, festivals)	3.9 (0.4)	0.9	0.7	2.0	90.6	5.8	92.4	88.8	91.6	.03
5	Avoiding going out to restaurants, bars, pubs, coffee shops, etc.	3.9 (0.4)	1.0	1.1	3.6	88.8	5.5	90.6	86.4	91.0	.001
6	Avoiding any non-essential travel (domestic, international)	3.9 (0.4)	1.0	0.9	3.8	90.5	3.7	92.3	87.9	92.9	-
7	Avoiding common greetings that involve close contact (hugs, kisses, handshakes)	3.9 (0.5)	1.3	1.7	6.4	88.1	2.5	90.2	87.2	86.8	-
8	Avoiding making contact with family members who do not typically live with you	3.7 (0.7)	2.8	4.5	14.2	73.6	5.0	73.9	73.2	73.8	-
9	Avoiding socializing in person even with close friends	3.8 (0.6)	1.6	3.0	12.3	82.0	1.0	81.6	81.8	83.1	-
10	Avoiding or limiting contact with people at higher risk or vulnerable populations (for example, older adults, those with at risk conditions or those in poor health)	3.9 (0.5)	1.4	1.8	7.0	85.0	4.8	88.5	84.2	86.0	-
11	Ordering take-out from restaurants (picked up in person)	1.7 (1.0)	54.1	23.1	5.6	8.2	9.0	9.4	7.6	7.9	-
12	Having meals/groceries delivered to your house	1.8 (.1.0)	49.7	27.3	8.8	8.7	5.4	8.5	8.9	8.8	-
13	Keeping a safe distance of at least 6 feet (approximately 2 meters)	3.6 (0.6)	0.5	3.5	28.4	66.2	1.4	66.1	66.6	65.5	.02
14	Isolating myself at home, when sick	3.8 (0.6)	1.4	1.2	2.8	45.9	48.7	45.7	43.3	50.8	.001
15	Avoiding leaving the home, except to go to grocery store or pharmacy	3.6 (0.7)	2.3	7.7	20.5	66.9	2.6	69.3	70.2	57.3	< .001

Note. Response options for each item ranged from 1 ('Never') to 4 ('Always').

Table 3. Descriptive statistics for adherence to social distancing recommendations (N = 2,013)

Crt no.	Variable	N	%
Individual-level Motivations			
1	I want to protect myself	1690	84.0
2	I want to avoid spreading the virus to others	1666	82.8
3	I am concerned about spreading the virus to vulnerable people.	1634	81.2
4	I feel good about myself when I protect others.	934	46.4
5	I feel less stressed when I practice social distancing.	877	43.6
6	I feel more in control when I practice social distancing	822	40.8
7	I don't have a pre-existing medical condition	611	30.4
8	I have an elevated risk for COVID-19	391	19.4
9	*I feel stressed when I am alone or in isolation	268	13.3
10	*I don't trust the messages my government provides about the pandemic	255	12.7
11	*I think it's unlikely I will catch the virus.	159	7.9
12	*I cannot afford to pay for delivery for food or groceries	116	5.8
13	*I don't like to be told what to do.	112	5.6
14	*I believe the best strategy to manage this pandemic is to let the virus run its course.	78	3.9
15	*I think the government is exaggerating the impact of this pandemic.	77	3.8
16	*I think I cannot spread the virus if I am not sick.	39	1.9
17	*I don't have a good internet connection at home	38	1.9
18	*I think this pandemic is not serious.	30	1.5
19	*I believe prayers and religious rituals can protect me from this virus.	29	1.4
20	*I've heard social distancing is not effective at reducing transmission of the virus	22	1.1
Interpersonal-level Motivations			
21	I want to protect others.	1726	85.7
22	I feel a sense of responsibility to protect our community.	1688	83.9
23	I care about the well-being of others.	1634	81.2
24	I have friends or family who are vulnerable to the virus.	1415	70.3
25	I feel connected to others even when I practice social distancing.	1135	56.4
26	I live with someone who is vulnerable to the virus.	569	28.3
27	*I have friends or family who need me to run errands for them.	497	24.7
28	*I socialize with people to avoid feeling lonely.	124	6.2
29	*I don't have friends or family who are vulnerable to the virus.	84	4.2
30	*I believe it's OK to invite people to your home to socialize in small groups.	69	3.4
31	*I believe my actions cannot protect others from contracting the virus.	64	3.2
32	*I believe it's OK to go out and meet with people in small groups.	59	2.9
Organizational-level Motivations			
33	My workplace or school recommended we practice social distancing.	1076	53.5
34	My workplace or school conducts operations remotely	1025	50.9
35	My workplace or school closed down	712	35.4
36	My workplace or school discouraged us from coming in	648	32.2
37	*My workplace has implemented social distancing policies for workers that have to come to work	530	26.3
38	*My work cannot be done remotely.	324	16.1
39	*My workplace requires me to come into work.	224	11.1
40	*My workplace won't pay me if I do not go into work.	93	4.6
41	*My workplace told me that I could lose my job if I do not go into work.	18	0.9
Community-level Motivations			
42	Restaurants in my area are closed for eating-in.	1911	94.9
43	Community centers and recreational facilities in my area are closed.	1897	94.2
44	There are no social events held in person in my area.	1825	90.7
45	My government says I must do social distancing.	1777	88.3
46	My news sources say I should do social distancing.	1675	83.2
47	It is possible to shop online and have items delivered to my house.	1653	82.1
48	There is barely anyone walking outside in my area.	1098	54.5
49	*My place of faith is closed (for example, mosque, temple, church, synagogue).	916	45.5
50	*There are many people walking on the streets in my area.	624	31.0
51	*It is not possible to shop online and get deliveries in my area.	215	10.7
52	*My place of faith is open (for example, mosque, temple, church, synagogue).	71	3.5
53	*There are social events held in person in my area.	36	1.8
54	*Community centers and recreational facilities in my area are open.	31	1.5
55	*Restaurants in my area are open for eating-in	16	0.8

Note. Instructions were to check all that apply.
Motivations "for" were conceptualized as facilitators of social distancing.
* Motivations "against' were conceptualized as barriers to social distancing.

Table 2. Endorsement rates motivations "for" and "against" social distancing (N = 2013).

ADULTS

CLINICAL FEATURES AND OUTCOMES OF ADULTS WITH COVID-19: A SYSTEMATIC REVIEW AND POOLED ANALYSIS OF THE LITERATURE

Bennett S, Tafuro J, Mayer J, Darlington D, Wai Wong C, Muntean EA, Wong N, Mallen C, Shing Kwok C.. Int J Clin Pract. 2020 Sep 23:e13725. doi: 10.1111/ijcp.13725. Online ahead of print.
Level of Evidence: 2 - Systematic review of surveys that allow matching to local circumstances

BLUF

Multiple researchers from the Department of Cardiology, Smart Innovation Hub, School of Primary, Community and Social Care in Stoke-on-Trent and Leicester Royal Infirmary, Leicester, conducted a systematic review of 45 studies (n = 14,358 adult participants) to identify the symptoms, co-morbidities, radiological features and outcomes for adults positive for COVID19 admitted to the hospital. The following observations were obtained:

• the most common symptoms included fever (81.2%), cough (62.9%), fatigue (38.0%) and anorexia/loss of appetite (33.7%; Figure 1, 2)
• the most common comorbidities were hypertension (19.1%), cardiovascular disease (17.9%), endocrine disorder (9.3%) and diabetes (9.2%)
• 27.7% of patients had abnormal chest x-rays; 63% had ground-glass opacities on chest CT
• Acute respiratory distress syndrome (27.4%), acute cardiac injury (16.2%) and acute kidney injury (12.6%) were the most common adverse outcomes
• death occurred in 8.2% of patients, 16.3% needed intensive care admission and 11.7% had mechanical ventilation
• bacterial or secondary infections affected 8.5% of patients and 6.9% developed shock

These findings reveal the heterogeneous manifestations of COVID-19, although the authors note that these findings may not be generalizable to a wider population and are limited by differences in follow-up.

SUMMARY

Additional observations from this review include, but are not limited to, the following:
- Most of the current literature is dominated by studies from China. These studies' generalizability to the global population may be questionable due to reasons such as only sampling individuals who are able to access hospital care into studies, utilization of both Western and traditional medicine practices, etc.
- Cardiovascular diseases are the most common comorbidity in COVID-19 patients. Diabetes, gastrointestinal and respiratory disease occur in fewer than 1 in 10 patients (Figure 3).
- Less than 1/3 of patients have an abnormal chest X-ray while the majority undergoing further imaging have bilateral changes and ground-glass opacities on CT scan (Figure 4).
- Acute respiratory distress syndrome (ARDS), acute cardiac injury and acute kidney injury requiring intensive care admission and mechanical ventilation was noted in many patients. Death occurred in 8.2% of hospitalized patients. (Figure 5).
-Several of the limitations of this review include restricted sample population to adult hospital patients with COVID-19, difficulties in assessing mortality rate following discharge, inconsistent reporting among studies, limited long-term follow-up, and not accounting for the impact of lockdown, self-isolation, and community treatment.

ABSTRACT

BACKGROUND: The 2019 coronavirus disease (COVID-19) has become a global pandemic and the published literature describing the virus has grown exponentially. METHODS: We conducted a systematic review of the literature to identify the symptoms, comorbidities present, radiological features and outcomes for adults testing positive for COVID-19 admitted to hospital. The results across multiple studies were numerically pooled to yield total estimated. RESULTS: A total of 45 studies were included in this review with 14,358 adult participants (average age 51 years, male 51%). The pooled findings suggest that the most common symptom among patients was fever (81.2%) followed by cough (62.9%), fatigue (38.0%) and anorexia/loss of appetite (33.7%). The comorbidities that were most prevalent among patients with the virus were

hypertension (19.1%), cardiovascular disease (17.9%), endocrine disorder (9.3%) and diabetes (9.2%). Abnormal chest X-ray findings were present in 27.7% of patients and ground-glass opacity was demonstrated on chest CT in 63.0% of patients. The most frequent adverse outcomes were acute respiratory distress syndrome (27.4%), acute cardiac injury (16.2%) and acute kidney injury (12.6%). Death occurred in 8.2% of patients and 16.3% required intensive care admission and 11.7% had mechanical ventilation. Bacterial or secondary infections affected 8.5% of patients and 6.9% developed shock. CONCLUSIONS: COVID-19 most commonly presents with fever, cough, fatigue and anorexia among patients with existing hypertension and cardiovascular disease. It is important as serious adverse outcomes can develop such as acute respiratory distress syndrome, acute cardiac injury, acute kidney injury and death.

FIGURES

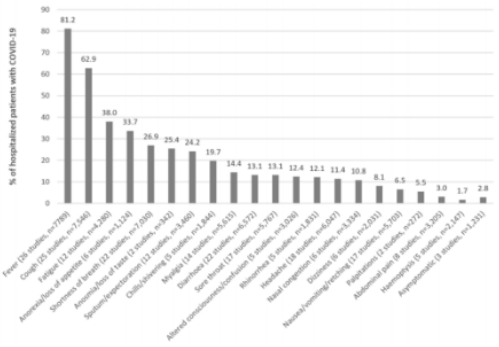


Figure 1

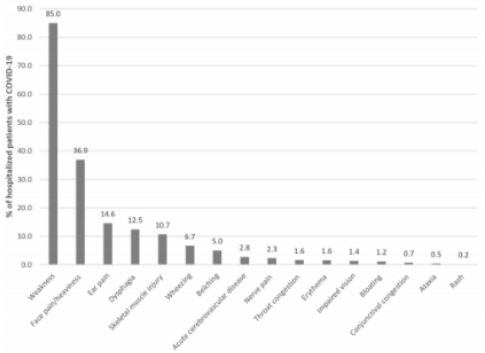


Figure 2

Figure 1: Most common symptoms via collective pooling from studies hospitalized patients with COVID-19

Figure 2: Other symptoms commonly reported but only from single studies for hospitalized patients with COVID-19

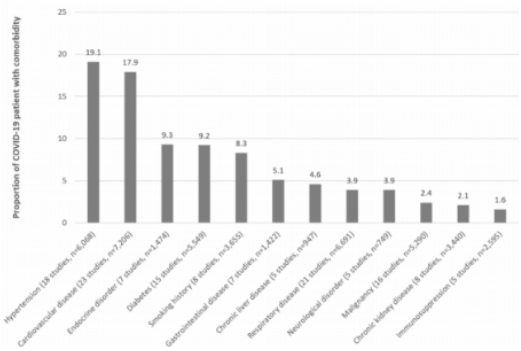


Figure 3

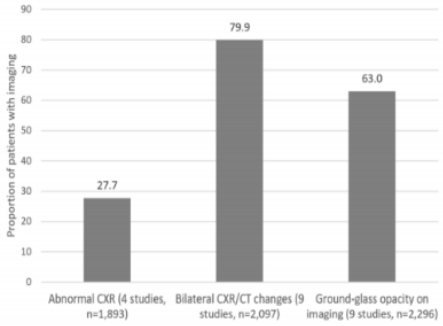


Figure 4

Figure 3: Proportion of COVID-19 patients with co-morbidities

Figure 4: Proportion of COVID-19 patients with abnormal chest x-ray and CT scans

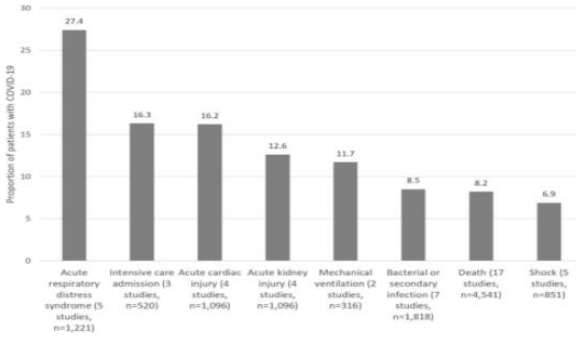


Figure 5

Figure 5: Proportion of COVID-19 patients with adverse outcomes

UNDERSTANDING THE PATHOLOGY

IN VITRO

ENDOTHELIOPATHY IS INDUCED BY PLASMA FROM CRITICALLY-ILL PATIENTS AND ASSOCIATED WITH ORGAN FAILURE IN SEVERE COVID-19

Rauch A, Dupont A, Goutay J, Caplan M, Staessens S, Moussa M, Jeanpierre E, Corseaux D, Lefevre G, Lassalle F, Faure K, Lambert M, Duhamel A, Labreuche J, Garrigue D, De Meyer SF, Staels B, Van Belle E, Vincent F, Kipnis E, Lenting P, Poissy J, Susen S; Lille Covid Research Network(LICORNE).. Circulation. 2020 Sep 24. doi: 10.1161/CIRCULATIONAHA.120.050907. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

A multidisciplinary group of French physicians conducted a retrospective cohort study at Lille University Hospital assessing cytotoxicity of plasma from 28 patients (12 ICU and 16 non-ICU) hospitalized with COVID-19 between March 30-April 8, 2020. Samples from COVID-19 patients had significantly decreased human pulmonary microvascular endothelial cells (HPMVEC) viability ($p<0.01$) and increased cytotoxicity compared to plasma from 8 healthy donors (Figure 1). The authors suggest their findings bolster the growing body of evidence indicating SARS-CoV-2 induces endothelial damage that contributes to organ dysfunction, respiratory failure, and thrombosis.

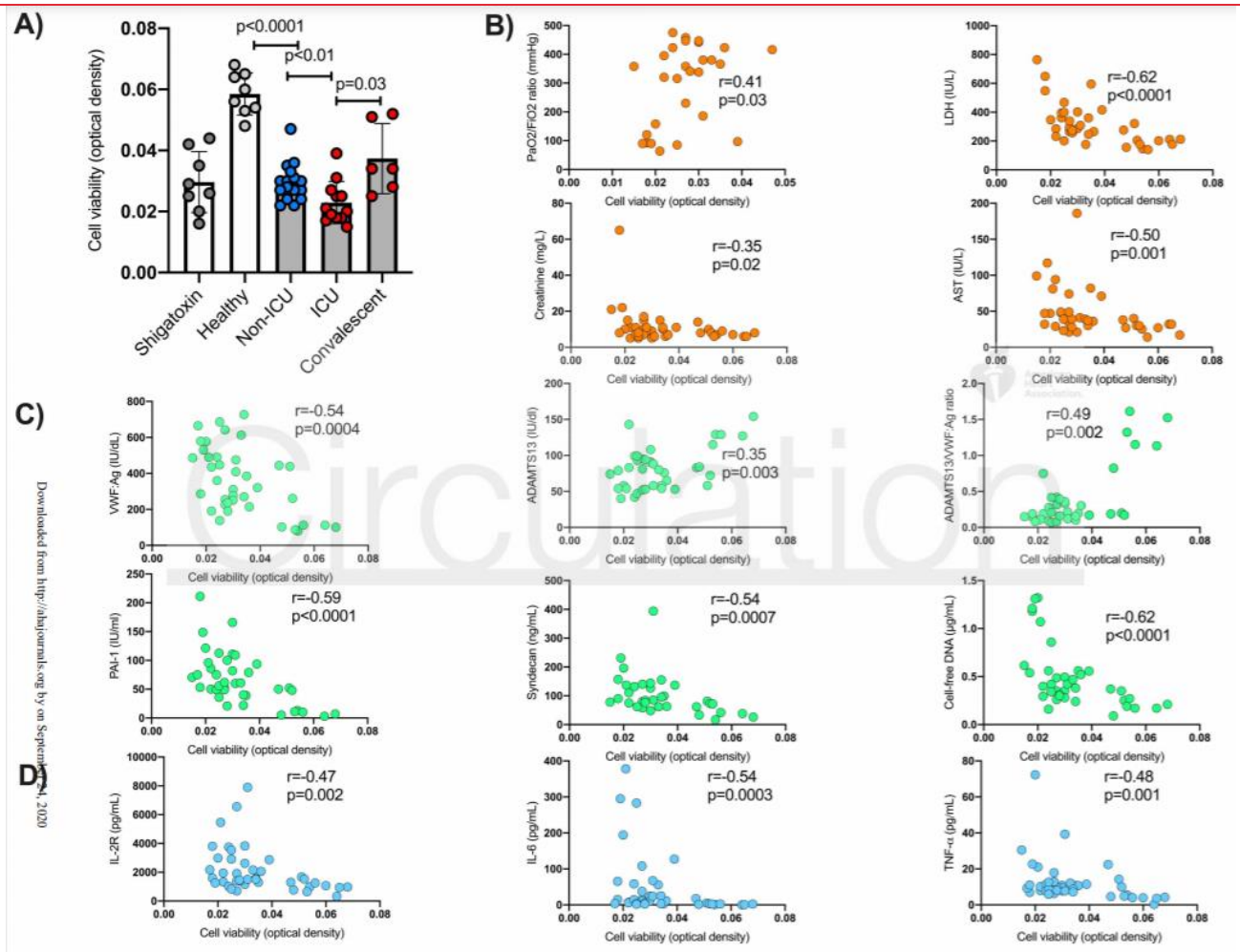


Figure 1: Endothelial cell cytotoxicity induced by plasma sampled from critically-ill and convalescent COVID-19 patients.'The cytotoxicity of platelet-poor plasma samples (obtained after a double centrifugation of citrate tubes at 2500g for 15 min at room temperature) from COVID-19 patients and controls on HPMVEC was evaluated with a colorimetric assay using 4-[3-(4-iodophenyl)-2-(4-nitrophenyl)-2H-5-tetrazolio]-1.3-benzene disulfonate (WST-1), which in viable cells is cleaved by mitochondrial dehydrogenases. After incubation, the cells were washed with PBS and incubated with WST-1 (Roche, Basel, Switzerland) at a dilution of 1:10 (10 µL) for 2 h at 37°C. Absorbance was measured using a multi-well plate reader (Synergy HTX multi-mode plate reader, BioTek Instruments, Highland Park, VT, USA) at 450 nm with a reference wavelength of 620 nm. As a positive control for endothelial cell injury, Shiga toxin 145 (Sigma-Aldrich, Saint Quentin Fallavier, France) was spiked in plasma from healthy adults (10 µg/mL final concentration) and incubated at 37°C for 15 min, before addition to HPMVECs. Experiments were performed in triplicates for each patient sample. (A) HPMVEC viability after exposure to plasma sampled in healthy subjects (n=8), in non-ICU (n=16), ICU (n=12) upon admission and in 6 convalescent COVID-19 patients sampled after ICU discharge (21±7 days). Datapoints represent individual sample measurements, whereas horizontal bars show the mean (+/-SD). Comparisons between groups were done using the Mann-Whitney U test, except for comparison between ICU and convalescent patients where we used Wilcoxon signed-rank test on matched pairs (n=6). Correlations between HPMVEC viability and (B) markers of organ dysfunction: the PaO2/FiO2 ratio, widely used as an indicator of oxygenation requirements, LDH, Creatinine and AST; (C) parameters related to endothelial dysfunction and tissue injury: VWF:Ag, ADAMTS13, ADAMTS13:VWF ratio, PAI-1, syndecan-1 and cell-free DNA and (D) plasma cytokine concentrations: IL-2R, IL-6 and TNF-α. Correlations were evaluated with the Spearman's rank-correlation statistical test. No adjustment for multiple comparisons was done and the result should be interpreted as hypothesis generating. AST: Aspartate Transaminase, HPMVEC: human pulmonary microvascular endothelial cells, ICU: intensive care unit, IL-2R: soluble interleukin-2 receptor, LDH: lactate dehydrogenase, PAI-1: plasminogen activator inhibitor-1, VWF: Ag: von Willebrand factor antigen

DEVELOPMENTS IN TRANSMISSION & PREVENTION

UNDETECTABLE VIRAL RNA IN OOCYTES FROM SARS-COV-2 POSITIVE WOMEN

Barragan M, Guillén JJ, Martin-Palomino N, Rodriguez A, Vassena R.. Hum Reprod. 2020 Sep 30:deaa284. doi: 10.1093/humrep/deaa284. Online ahead of print.
Level of Evidence: 4 - Case-series

BLUF

Fertility specialists from Spain describe two cases of asymptomatic women who underwent ovarian stimulation and were RT-PCR positive for SARS-CoV-2 on the day of oocyte collection in February and March 2020. Authors found that the N gene of SARS-CoV-2 was undetectable by whole transcriptome amplification and PCR testing in all 16 oocyte RNA samples from both donors. They suggest vertical transmission via oocyte is unlikely and that oocytes collected for assisted reproductive technology treatment during the pandemic do not pose an infectious risk to staff handling samples, though they acknowledge limited generalizability from this small sample.

ABSTRACT

A central concern for the safe provision of ART during the current coronavirus disease 2019 (CODIV-19) pandemic is the possibility of vertical transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection through gametes and preimplantation embryos. Unfortunately, data on SARS-CoV-2 viral presence in oocytes of infected individuals are not available to date. We describe the case of two women who underwent controlled ovarian stimulation and tested positive to SARS-CoV-2 infection by PCR on the day of oocyte collection. The viral RNA for gene N was undetectable in all the oocytes analyzed from the two women.

EVALUATION OF REGENERATION PROCESSES FOR FILTERING FACEPIECE RESPIRATORS IN TERMS OF THE BACTERIA INACTIVATION EFFICIENCY AND INFLUENCES ON FILTRATION PERFORMANCE

He W, Guo Y, Gao H, Liu J, Yue Y, Wang J.. ACS Nano. 2020 Sep 25. doi: 10.1021/acsnano.0c04782. Online ahead of print.
Level of Evidence: Other - Mechanism-based reasoning

BLUF

Engineers in Liaoning, China and Switzerland investigated the ability of microwave irradiation (MWI), UV irradiation (UVI), MWI + UVI, steam, and ethanol (Table 3) to regenerate filtering facepiece respirators (FFRs) by loading FFRs with model bacteria, decontaminating them, assessing filtration efficiency, then counting bacterial colonies in the outer, middle, and inner mask layers (Figure 1). Authors found ethanol unacceptably reduced filtration efficiency while steam and MWI effectively decontaminated FFRs (100% inactivation in 90 min and 30 min, respectively) without sacrificing filtration, though long exposure to MWI did damage fiber morphology (Table 1). While UVI successfully inactivated surface bacteria, efficiency decreased from outer to inner layers and authors suggest that a combination of UVI and short-duration MWI can best decontaminate used FFRs while maintaining filtration performance.

ABSTRACT

The regeneration of filtering facepiece respirators (FFRs) is of critical importance because of the severe shortage of FFRs during large-scale outbreaks of respiratory epidemics, such as COVID-19. Comprehensive experiments regarding FFR regeneration were performed in this study with model bacteria to illustrate the decontamination performance of the regeneration processes. The results showed that it is dangerous to use a contaminated FFR without any microbe inactivation treatment because the bacteria can live for more than 8 hours. The filtration efficiency and surface electrostatic potential of 75% ethanol-treated FFRs were significantly reduced, and a most penetrating particle size of 200 nm was observed. Steam and microwave irradiation showed promising decontamination performances, achieving 100% inactivation in 90 min and 30 min, respectively. The filtration efficiencies of steam-treated FFRs for 50 and 100 nm particles decreased from 98.86% and 99.51% to 97.58% and 98.79%, respectively. Ultraviolet irradiation (UVI) effectively inactivated the surface bacteria with a short treatment of 5 min and did not affect the filtration performance. However, the UV dose reaching different layers of the FFP2 mask sample gradually decreased from the outermost layer to the innermost layer, while the model bacteria on the second and

third layers could not be killed completely. UVI+MWI and steam were recommended to effectively decontaminate the used respirators and still maintain the respirators' filtration efficiency. The present work provides a comprehensive evaluation for FFR regeneration in terms of the filtration efficiencies for 50-500 nm particles, the electrostatic properties, mechanical properties and decontamination effects.

FIGURES

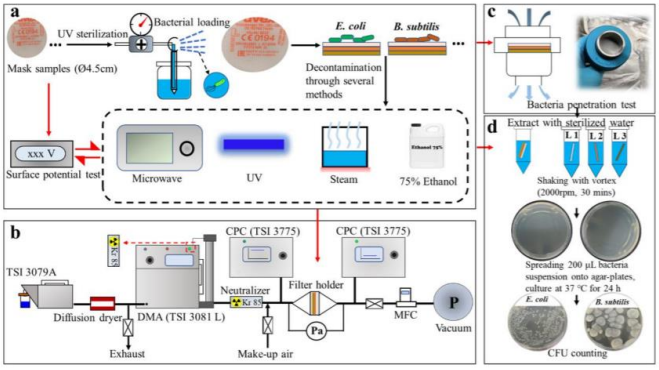


Fig. 1. Experimental setup and procedure for FFR regeneration: a) Bacterial loading and bacteria inactivation treatment. b) Setup for the particle filtration test. c) Setup for the bacteria penetration test. d) Procedure of colony-forming unit counting. L1, L2 and L3 represent the outermost layer, middle layer, and innermost layer, respectively.

Table 1. The average surface potential (AVG) of regenerated circular FFRs samples *via* the MWI, UVI and steam decontamination methods and the *p-value* of the *t*-test.

	MWI			UVI			Steam exposure		
	AVG (V)	Uncertainty	*p-value*	AVG (V)	Uncertainty	*p-value*	AVG (V)	Uncertainty	*p-value*
FFP 1	868.4	82.8	0.055	1152.4	168.5	0.338	777.6	276.1	0.046
FFP 2	1098	286.8	0.058	1413.8	443.4	0.497	1067.4	198.9	0.029
FFP 3	1347.6	147.1	0.142	1595.8	238.8	0.403	1105.2	126.9	0.021
Surgical masks	265.2	83.5	0.494	247.6	51.9	0.279	247.6	46.8	0.266

Table 3 Summary of the treatment methods for the FFR samples

Treatment	Experimental conditions and parameters
Microwave	Household microwave oven (Wave 300, Mio Star, Switzerland) with a revolving glass carousel and an output power of 400 W; treatment time: 4 min × 1 cycle, 4 min × 2 cycles, 5 min × 2 cycles, 5 min × 4 cycles, 5 min × 6 cycles; FFR circular samples were placed on a plastic petri dish; the glass carousel was cooled to room temperature before the next trial.
UV	FFR circular samples were treated with UV in a biosafety cabinet with a UV sterilization lamp (BVL - 315.G, wavelength - 254 nm, Vilber Lourmat, France). Treatment time: 5 min (126 mJ/cm^2), 10 min (252 mJ/cm^2) and 15 min (378 mJ/cm^2).
UV + Microwave	UV: 5 min (126 mJ/cm^2); microwave treatment time: 4 min × 1 cycle, 4 min × 2 cycles, 4 min × 3 cycles with an output power of 400 W.
Steam	FFR circular samples were steamed for 30, 60 and 90 minutes above boiling water. After the steam treatment, the samples were kept in a biosafety cabinet and air-dried completely.
Ethanol	FFR circular samples were immersed in 75% ethanol for 2 minutes, then kept in a biosafety cabinet and air-dried completely.

LEVERAGING ON THE GENOMICS AND IMMUNOPATHOLOGY OF SARS-COV-2 FOR VACCINES DEVELOPMENT: PROSPECTS AND CHALLENGES

Abdullahi IN, Emeribe AU, Adekola HA, Abubakar SD, Dangana A, Shuwa HA, Nwoba ST, Mustapha JO, Haruna MT, Olowookere KA, Animasaun OS, Ugwu CE, Onoja SO, Gadama AS, Mohammed M, Daneji IM, Amadu DO, Ghamba PE, Onukegbe NB, Shehu MS, Isomah C, Babayo A, Ahmad AE.. Hum Vaccin Immunother. 2020 Sep 16:1-18. doi: 10.1080/21645515.2020.1812313. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

Immunology experts in Nigeria reviewed literature pertaining to SARS-CoV-2 vaccine development, covering current data related to genomic organization (Figure 1), genetic mutations (Table 1), pathophysiology, immune response to SARS-CoV-2, potential vaccine targets (particularly components of the S-protein and ACE-2 receptors), current vaccine trials (Table 3), and potential animal models for vaccine testing (rhesus macaques, ferrets, mice, and Syrian hamsters). Authors suggest enough promising data exists to synthesize a COVID-19 vaccine in the near future but additional funding is needed to extend trials globally to ensure high performance across diverse population and create a centralized evaluation system to assess safety, efficacy, accessibility, and potency.

ABSTRACT

The incidence and case-fatality rates (CFRs) of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection, the etiological agent for Coronavirus Disease 2019 (COVID-19), have been rising unabated. Even though the entire world has been implementing infection prevention and control measures, the pandemic continues to spread. It has been widely accepted that preventive vaccination strategies are the public health measures for countering this pandemic. This study critically reviews the latest scientific advancement in genomics, replication pattern, pathogenesis, and immunopathology of SARS-CoV-2 infection and how these concepts could be used in the development of vaccines. We also offer a detailed discussion on the anticipated potency, efficacy, safety, and pharmaco-economic issues that are and will be associated with candidate COVID-19 vaccines.

FIGURES

Figure 1. Genomic organization of SARS-CoV-2. UTR = Untranslated Region: ORF = Open Reading frame: M = Membrane protein: N = Nucleocapsid: E = Envelop protein: S= Spike protein

Table 1. SARS-CoV-2 Genetic Mutations and their Implications on Vaccine development.

Citation	Study Design	Observed Mutations	Key Findings and Significance in Vaccine Intervention
Tang *et al.*[27]	Population genetic analyses of 103 SARS-CoV-2 genomes	Receptor binding the domain of the S protein	In the discovery of the L and S types of SARS-CoV-2, the L type was reportedly evolutionarily aggressive and more contagious than the S type. This biotype variation might consequently affect the efficacy of candidate vaccine if a monovalent vaccine against either is produced. Therefore, polyvalent vaccines should be produced to act against both virus biotypes.
Angelleti *et al.*[29]	Fast-unconstrained Bayesian approximation and Homology modelling	NSP2 and NSP3	Mutations occurring on NSP2 and NSP3 could have significantly influenced the pathogenesis and transmission of the virus. Thus, structural analogues of the NSPs could be used for vaccines that elicit neutralizing antibodies which can effectively bind to the SARS-CoV-2 NSPs.
Yao *et al.*[30]	Functional characterizations of 11 patient-derived viral isolates.	Intrapersonal variation and 6 different mutations in S protein	A mutation on the S protein could substantially change the pathogenicity of the virus. Therefore, production multiepitope based peptide vaccines against the S protein of SARS-CoV-2 should be considered.
Jin *et al.*[31]	Phylogenetic analysis and Heat mapping of 788 confirmed COVID-19 patients.	Furin cleavage site mutation on S protein	FCS mutation may represent an essential SARSCoV-2 evolution site. Vaccines targeted at the binding of Furin could reduce pathogenesis of SARS-CoV-2 in lungs of infected humans.
Holland *et al.*[32]	Genomic characterization of a 27 amino acid in -frame deletion in accessory protein	An 81-nucleotide deletion in SARS-CoV-2 ORF7a	The occurrence of phylogenetically distinct mutants indicating independent transmissions patterns. Since mutation is occurring slowly, vaccines made from original strains could still significantly confer immunity against distinct mutants.
Van Dorp *et al.*[33]	Curation of dataset of 7666 public genome and genomic diversity analysis	NSP6, NSP11, NSP13, Spike protein	There is a chance of continuous adaptation measures in the SARS-COV-2 genome. However, vaccines would be used prophylactically while targeting different sites on the viral structure so that significant immune response could be elicited against SARS-COV-2.
Pachetti *et al.*[25]	220 genomic sequences analysis from database derived from COVID-19 patients	8 novel recurrent mutations of SARS-CoV-2 RdRp	Development of multi-epitope vaccines would significantly inhibit SARS-CoV-2 viruses with recurrent RdRp mutations reported in this study. Furthermore, similar structural analogues which could act as polyvalent RdRp inhibitors can be considered.
Happi *et al* [155].	Genome annotation and Mutation Analysis	D614G in S protein	The occurrence of D614G mutation inS protein has been linked to increased transmission rate and pathogenicity as well as immuno-evasion. Hence, vaccine platforms that elicit broadly neutralizing antibodies against both D614G and D614 should be considered.

Table 3. Overview of Some Ongoing COVID-19 Vaccine Trials.

Developer	Candidate	Vaccine Characteristics	Status	Comments
University of Oxford	ChAdOx1 (AZD1222)	Non-replicating viral vector	ISRCTN[Phase III ISRCTN89951424 NIH[Phase I/II NCT04324606 EUCTR[Phase I/II 2020-001072-15 EUCTR[Phase II/III 2020-001228-32	Strategy has shown to provide strong immune responses. Success depends on the choice of vector and immune-inducing protein of interest [111]
Sinovac Biotech	PiCoVacc	Inactivated SARS-COV2 plus alum	NIH[Phase III NCT04456595 NIH[Phase I/II NCT04352608	Generally safe. Some previous inactivated vaccines suffered from ineffectiveness and worse outcome [112]
CanSino Biologicals/ Beijing Institute of Biotechnology	Ad5-nCoV	Adenovirus type 5 vector that expresses S protein	NIH[Phase I NCT04313127 ChiCTR[Phase II ChiCTR2000031781 ChiCTR[Phase I ChiCTR2000030906	Strategy has shown to provide strong immune responses. Success depends on the choice of vector and immune-inducing protein of interest.[111]
Moderna/NAID	mRNA-1273	LNP-encapsulated mRNA vaccine encoding S protein	NIH[Phase III NCT04470427	Easy and quick to design. Looks promising First of its type and its utility has not yet been determined.[113]
Wuhan Institute of Biological Products/ Sinopharm	Inactivated virus	Inactivated SARS-COV2 in Vero cells	ChiCTR[Phase III ChiCTR2000034780	Generally safe Some previous inactivated vaccines suffered from ineffectiveness and worse outcome [112]
Beijing Institute of Biological Products/ Sinopharm	Inactivated virus	Inactivated SARS-COV2 in Vero cells	ChiCTR[Phase III ChiCTR2000034780	Generally safe. Some previous inactivated vaccines suffered from ineffectiveness and worse outcome [112]
BioNTech/Fosun Pharma/Pfizer	BNT162	RNA vaccine containing 3 LNP-mRNAs	EUCTR[Phase I/II 2020-001038-36 Phase I/II NCT04368728	Easy and quick to design. Looks promising. First of its type and its utility has not yet been determined.[113]
Inovio Pharmaceuticals	INO-4800	DNA plasmid encoding S protein delivered by electroporation	NIH[Phase I/II NCT04336410 NCT04447781	Easy and quick to design. Looks promising. First of its type and its utility has not yet been determined [114]
Shenzhen Geno-Immune Medical Institute	LV-SMENP-DC	DCs modified with lentiviral vector expressing synthetic minigene based on domains of selected viral proteins; administered with antigen-specific CTLs	NIH[Phase I NCT04276896	Strategy has shown to provide strong immune responses. Success depends on the choice of vector and immune-inducing protein of interest.[111]
Shenzhen Geno-Immune Medical Institute	Pathogen-specific aAPC	aAPCs modified with lentiviral vector expressing synthetic minigene based on domains of selected viral proteins	NIH[Phase I NCT04299724	Strategy has shown to provide strong immune responses. Success depends on the choice of vector and immune-inducing protein of interest.[111]
Novavax	NVX-CoV2373	Full length recombinant SARA-CoV-2 glycoprotein nanoparticle vaccine adjuvanted with Matrix M	NIH[Phase I/II NCT04368988	Focuses on antigenic part of virus and hence cannot cause infection May not stimulate a strong response. Usually needs an adjuvant [115]
Clover Biopharmaceuticals	SCB-2019	Dead vaccine with genetically engineered Native like Trimeric subunit Spike Protein	NIH[Phase I NCT04405908	Generally safe Some previous inactivated vaccines suffered from ineffectiveness and worse outcome.[112] Focuses on antigenic part of virus and hence cannot cause infection. May not stimulate a strong immunologic response. Usually needs an adjuvant.[116]

Table 3. (Continued).

Developer	Candidate	Vaccine Characteristics	Status	Comments
Imperial College London	LNP-nCoVsaRNA	saRNA gene-based vaccine	ISRCTN[Phase I ISRCTN17072692	Easy and quick to design. Looks promising First of its type and its utility has not yet been determined.[113]
CureVac	CVnCoV	mRNA-based vaccine	NIH[Phase I NCT04449276	Easy and quick to design. Looks promising. First of its type and its utility has not yet been determined.[114]
Genexine/Binex/ GenNBio/Int. Vaccine Inst./Korea Advanced Inst. Of Science & Technology (KAIST)/ Pohang Univ. of Science and Technology (POSTECH)	GX-19	DNA-based vaccine	NIH[Phase I/II NCT04445389	Easy and Quick to design. Looks promising First of its type and its utility has not yet been determined.[114]
Vaxine Pty Ltd/Medytox	COVAX-19	Recombinant spike protein with Advax™ adjuvant	NIH[Phase I NCT04453852	Focuses on antigenic part of virus and hence can cause infection May not stimulate a strong response. Usually nee an adjuvant.[116]
Walvax Biotechnology/ People's Liberation Army (PLA) Academy of Military Sciences/ Suzhou Abogen Biosciences	ARCoV	Gene-based vaccine (mRNA)	ChiCTR[Phase I ChiCTR2000034112	Easy and quick to design. Looks promising First of its type and its utility has not yet been determined.[114]
Natl. Gamaleya Research Center for Epidemiology and Microbiology (Russia)	-	Vector virus vaccine (adenovirus)	NIH[Phase I NCT04436471 NCT04437875	Strategy has shown to provide strong immune responses. Success depends on the choice of vector and immune-inducing protein of interest.[111]
Anhui Zhifei Longcom Biopharmaceutical/ Institute of Microbiology, Chinese Academy of Sciences	-	Subunit vaccine (recombinant antigen and adjuvant)	NIH[Phase II NCT04466085	Focuses on antigenic part of virus and hence can cause infection May not stimulate a strong response. Usually nee an adjuvant.[116]
University of Queensland/ GSK/Dynavax	-	Dead vaccine with genetically engineered molecular clamp stabilized spike protein and adjuvant	*Phase I NCT04405908	Generally safe Some previous inactivated vaccines suffered from ineffectiveness and worse outcome.[112]
Arcturus Therapeutics/ Duke-NUS	LUNAR-COV19	mRNA-based vaccine	*Phase I/II NCT04480957	Easy and Quick to design. Looks promising First of its type and its utility has not yet been determined.[114]
MIGAL (The Galilee Research Institute) and MigVax	-	Oral *E. coli*-based protein expression system of S and N proteins	*Preclinical: Planned for summer 2020	Focuses on antigenic part of virus and hence can cause infection May not stimulate a strong response. Usually nee an adjuvant.[116]
ReiThera/Leukocare/ Univercells (Italy/ Germany/Belgium)	-	Replication defective Simian Adenovirus (GRAd) encoding SARS-CoV-2 S	*Preclinical: Planned for summer 2020 in Italy	Strategy has shown to provide strong immune responses. Success depends on the choice of vector and immune-inducing protein of interest.[111]
Sanofi Pasteur/GSK	-	Dead vaccine with genetically engineered (baculovirus) virus antigen and adjuvant	*Preclinical	Generally safe Some previous inactivated vaccines suffered from ineffectiveness and worse outcome.[112]

Table 3. (Continued).

Developer	Candidate	Vaccine Characteristics	Status	Comments
Janssen (Johnson & Johnson)	Ad26	Non-replicating viral vector	*Phase I/II NCT04436276	Strategy has shown to provide strong immune responses. Success depends on the choice of vector and immune-inducing protein of interest.[111]
OpenCorona Consortium (Karolinska Institute, University of Gießen and partners)	-	DNA-based vaccine with electroporation	*Preclinical: Planned for 2021	Easy and Quick to design. Looks promising First of its type and its utility has not yet been determined.[114]

NIH[US National Library of Medicine – clinicaltrials.gov
ChiCTR[Chinese Clinical Trial Registry – chictr.org.cn
EUCTR[EU Clinical Trials Register – clinicaltrialsregister.eu
ISRCTN[ISRCTN Registry – isrctn.com
* Pre-clinical – Data obtained from vfa [104] and WHO [97]
Chinese Clinical Trial Registry (ChiCTR). http://www.chictr.org.cn/abouten.aspx
EU Clinical Trials Register. https://www.clinicaltrialsregister.eu
ISRCTN Registry. http://www.isrctn.com/
Note: Vaccine trial is an ongoing clinical process. Hence, data and phase of evaluations presented in table 3 might change with time.

POLITICAL PARTISANSHIP INFLUENCES BEHAVIORAL RESPONSES TO GOVERNORS' RECOMMENDATIONS FOR COVID-19 PREVENTION IN THE UNITED STATES

Grossman G, Kim S, Rexer JM, Thirumurthy H.. Proc Natl Acad Sci U S A. 2020 Sep 15:202007835. doi: 10.1073/pnas.2007835117. Online ahead of print.
Level of Evidence: 3 - Non-randomized controlled cohort/follow-up study

BLUF

A team including physicians and communications experts from the University of Pennsylvania used mobility statistics from Safegraph (estimates for time at home), Google search data, and tweets from gubernatorial accounts from March 1-31, 2020 to evaluate COVID-19 prevention behaviors in 3140 United States counties. Authors found democratic governors tweeted stay-at-home messages earlier than republicans (median 6-7 days before official order vs. 1 day)(Figure 1). Additionally, governors' stay-at-home tweets correlated with increased median time spent at home by 3.4% (10.4 minutes/day; p<0.01), and democratic counties spent more time at home (4.1% increase vs. 3.1%, p<0.01)(Table 2,3), suggesting that political partisanship and governor recommendations had significant impacts on citizens' mobility during the early COVID-19 pandemic.

ABSTRACT

Voluntary physical distancing is essential for preventing the spread of COVID-19. We assessed the role of political partisanship in individuals' compliance with physical distancing recommendations of political leaders using data on mobility from a sample of mobile phones in 3,100 counties in the United States during March 2020, county-level partisan preferences, information about the political affiliation of state governors, and the timing of their communications about COVID-19 prevention. Regression analyses examined how political preferences influenced the association between governors' COVID-19 communications and residents' mobility patterns. Governors' recommendations for residents to stay at home preceded stay-at-home orders and led to a significant reduction in mobility that was comparable to the effect of the orders themselves. Effects were larger in Democratic- than in Republican-leaning counties, a pattern more pronounced under Republican governors. Democratic-leaning counties also responded more strongly to recommendations from Republican than from Democratic governors. Political partisanship influences citizens' decisions to voluntarily engage in physical distancing in response to communications by their governor.

FIGURES

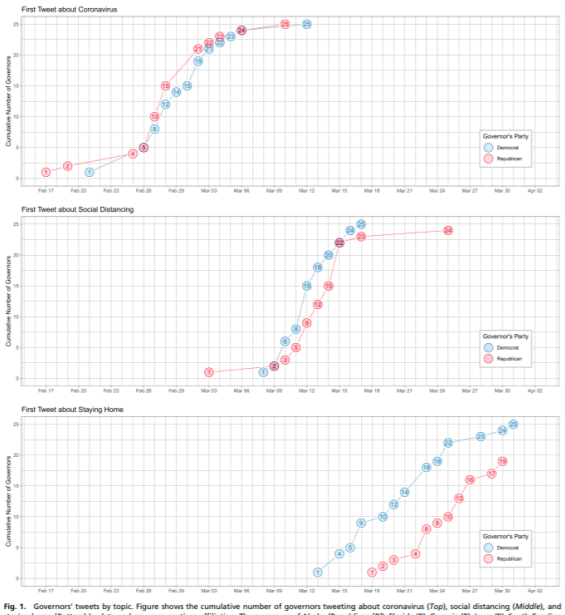


Fig. 1. Governors' tweets by topic. Figure shows the cumulative number of governors tweeting about coronavirus (*Top*), social distancing (*Middle*), and staying home (*Bottom*) by date and governor partisan affiliation. The governors of Alaska (Republican [R]), Florida (R), Georgia (R), Iowa (R), South Carolina (R), and South Dakota (R) did not tweet about staying home (shelter-in-place) during this time period.

Table 2. Governors' tweets, partisanship, and mobility

Panel A: Full sample				
Outcome	Median minutes at home		Log minutes at home	
Post stay-at-home message	10.409***	15.694***	0.034***	0.031**
	(3.542)	(4.697)	(0.009)	(0.014)
Post stay-at-home message × Trump vote margin		−1.679**		0.001
		(0.707)		(0.002)
Observations R^2	94,690	94,690	94,690	94,690
	0.984	0.984	0.997	0.997
County fixed effect (FE)	Yes	Yes	Yes	Yes
Day FE	Yes	Yes	Yes	Yes
Demographics × Day FE	Yes	Yes	Yes	Yes
Trump margin × Day FE	Yes	Yes	Yes	Yes
COVID controls	Yes	Yes	Yes	Yes
Other tweets	Yes	Yes	Yes	Yes
Orders	Yes	Yes	Yes	Yes
Panel B: By county party				
Outcome	Median time at home		Log time at home	
County party	Dem	Rep	Dem	Rep
Post stay-at-home message	21.217***	9.956***	0.041*	0.031***
	(7.634)	(3.243)	(0.020)	(0.009)
Observations R^2	14,708	79,982	14,708	79,982
	0.985	0.984	0.997	0.998
County FE	Yes	Yes	Yes	Yes
Day FE	Yes	Yes	Yes	Yes
Demographics × Day FE	Yes	Yes	Yes	Yes
Trump margin × Day FE	Yes	Yes	Yes	Yes
COVID controls	Yes	Yes	Yes	Yes
Other tweets	Yes	Yes	Yes	Yes
Orders	Yes	Yes	Yes	Yes
Panel C: Triple interactions				
Outcome	Median time at home	Log time at home		
Interaction	Continuous vote margin	Binary	Continuous vote margin	Binary
Post stay-at-home message	12.728**	9.978	0.009	−0.011
	(6.094)	(6.395)	(0.013)	(0.023)
Post stay-at-home message × Republican governor	6.464	23.380**	0.055**	0.115***
	(8.096)	(11.329)	(0.021)	(0.030)
Post stay-at-home message × Trump vote margin	0.964		0.008***	
	(1.033)		(0.003)	
Post stay-at-home message × Republican governor × Trump vote margin	−4.460***		−0.014***	
	(1.271)		(0.004)	
Post stay-at-home message × Republican county		7.000		0.051**
		(4.540)		(0.022)
Post stay-at-home message × Republican governor × Republican county		−42.820***		−0.138***
		(10.124)		(0.031)
Republican county × Day FE	No	Yes	No	Yes
Trump margin × Day FE	Yes	No	Yes	No
Republican governor × Day FE	Yes	Yes	Yes	Yes
Republican county × Republican governor × Day FE	No	Yes	No	Yes
Trump margin × Republican governor × Day FE	Yes	No	Yes	No
COVID controls	Yes	Yes	Yes	Yes
Other tweets	Yes	Yes	Yes	Yes
Orders	Yes	Yes	Yes	Yes
Observations R^2	94,690	94,690	94,690	94,690
	0.984	0.984	0.997	0.997

Standard errors in parentheses clustered at the state level. Sample is 96,690 county-days over the period 1 March to 31 March 2020. Treatment indicator equals 1 for all days after the governor of state *s* issues a tweet encouraging citizens to stay home. "Trump vote margin" is county *i*'s vote margin for President Trump in the 2016 election. Republican counties are those in which Trump's vote margin in 2016 was greater than zero. County-level demographic controls are median age, log household income, population density, share of population over 65 y, share Black, share Hispanic, and share male. "COVID controls" include controls for county-level COVID cases and state-level COVID deaths. "Other tweets" includes controls for post-COVID and social distancing related tweets. "Orders" includes controls for whether the state has issued the following types of orders: emergency declarations, banning large gatherings, school closures, restaurant/bar closures, nonessential business closures, and stay-at-home orders. $^{***}P < 0.01$, $^{**}P < 0.05$, $^{*}P < 0.1$.

Table 3. Governors' tweets and stay-at-home orders

Outcome	Median time at home			Log time at home		
County party	All (1)	Dem (2)	Rep (3)	All (4)	Dem (5)	Rep (6)
Post stay home message	10.409***	21.217***	9.956***	0.034***	0.041*	0.031***
	(3.542)	(7.634)	(3.243)	(0.009)	(0.020)	(0.009)
Post stay home order	8.425*	4.554	9.503**	−0.001	−0.017	0.004
	(4.380)	(9.457)	(4.239)	(0.014)	(0.023)	(0.014)
$\beta_1 - \beta_2$	1.984	16.663	0.453	0.036	0.057	0.026
	(5.558)	(14.167)	(5.095)	(0.016)	(0.031)	(0.015)
Observations R^2	94690	14708	79982	94690	14708	79982
	0.984	0.985	0.984	0.997	0.997	0.998
County FE	Yes	Yes	Yes	Yes	Yes	Yes
Day FE	Yes	Yes	Yes	Yes	Yes	Yes
Demographics × Day FE	Yes	Yes	Yes	Yes	Yes	Yes
Trump margin × Day FE	Yes	Yes	Yes	Yes	Yes	Yes
COVID controls	Yes	Yes	Yes	Yes	Yes	Yes
Other tweets	Yes	Yes	Yes	Yes	Yes	Yes

Sample is 94,690 county-days between 1 March and 31 March 2020. Treatment indicator equals 1 for all days after the governor of state *s* issues a tweet about staying home. "Trump vote margin" is county *i*'s vote margin for Donald Trump in the 2016 presidential election. Republican counties are those in which Trump's vote margin in 2016 was greater than zero. County-level demographic controls are median age, log household income, population density, share of population over 65 y, share Black, share Hispanic, and share male. "COVID controls" account for county-level confirmed positive cases and state-level COVID-19 deaths. "Other tweets" includes controls for post-COVID and social distancing related tweets. Standard errors clustered at the state level. $\beta_1 - \beta_2$ is the difference between messaging and stay at home order coefficients. $^{***}P < 0.01$, $^{**}P < 0.05$, $^{*}P < 0.1$.

COMMUNITY HEALTH WORKERS AND COVID-19 - ADDRESSING SOCIAL DETERMINANTS OF HEALTH IN TIMES OF CRISIS AND BEYOND

Peretz PJ, Islam N, Matiz LA.. N Engl J Med. 2020 Sep 23. doi: 10.1056/NEJMp2022641. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

Population health experts from NYU Grossman School of Medicine discuss how community health workers (CHW), trusted community members also familiar with local health systems, have supported marginalized communities in New York impacted by the COVID-19 pandemic since March 2020. They review CHWs' various roles (health systems/social services navigators, ability to conduct home visits, health educators, and community advocates, among others)(Table 1). Because CHWs in New York have performed thousands of services since March 2020 (9600 telephone wellness checks, 600 health coaching sessions, and 3400 enrollments in online patient portals) they argue that investing in such programs could help alleviate the burden of disease in communities disproportionately impacted by COVID-19.

FIGURES

Examples of Ways in Which CHWs Have Addressed Intermediary Social Determinants during the Pandemic in New York City.*

Social Determinant of Health	CHW Strategies and Approaches	Example
Food availability	Connect patients to pantries and food-distribution sites; enroll them in SNAP benefits. Organize food tables and food drives in partnership with community- and faith-based organizations.	The undocumented-immigrant parent of a child with special needs successfully obtained access to a hospital's mobile food pantry. An immigrant community member expressed shame and fear of stigma associated with food assistance; after a supportive discussion, a CHW arranged for delivery directly to the patient's home.
Employment	Support patients and connect them to vocational training. Educate community members on unemployment resources and help them navigate complex filing systems.	A patient couldn't obtain access to the state's unemployment website; a CHW coached her through the application-submission process. An immigrant community member working as a taxi driver couldn't obtain access to unemployment benefits because of having independent-contractor status; a CHW connected the community member to a local worker center that helped clarify eligibility for benefits.
Housing	Connect patients to rent assistance and help with the transition out of shelters and other congregate settings.	A community member was desperate to leave the shelter system; a CHW successfully advocated for permanent placement by repeatedly calling the case manager during the peak of the pandemic.
Access to health care	Facilitate prescription refills; connect patients to primary care providers and mental health resources. Help patients navigate health systems by advocating for interpreter services, accompanying patients during in-person or televisits, or facilitating enrollment in health insurance.	A patient was nearly out of medication and was unable to obtain access to telehealth services; a CHW connected her to her provider to obtain refills and worked with a local pharmacy to have medication delivered to her home. CHWs created a linguistically tailored guide on televisits and virtual health education sessions for community members with limited English proficiency.
Immigration and documentation status	Navigate resources for undocumented immigrants.	A patient was concerned about obtaining access to unemployment benefits because of her immigration status; a CHW connected her to a local community-based immigration resource to safely explore options.

* CHW denotes community health worker, and SNAP Supplemental Nutrition Assistance Program.

ANTI-ANDROGENS MAY PROTECT AGAINST SEVERE COVID-19 OUTCOMES: RESULTS FROM A PROSPECTIVE COHORT STUDY OF 77 HOSPITALIZED MEN

Goren A, Wambier CG, Herrera S, McCoy J, Vaño-Galván S, Gioia F, Comeche B, Ron R, Serrano-Villar S, Ramos PM, Cadegiani FA, Kovacevic M, Tosti A, Shapiro J, Sinclair R.. J Eur Acad Dermatol Venereol. 2020 Sep 25. doi: 10.1111/jdv.16953. Online ahead of print.
Level of Evidence: 3 - Non-randomized controlled cohort/follow-up study

BLUF

A multidisciplinary, international team of physicians collaborated on a prospective cohort study of 77 men hospitalized with COVID-19 (Table 1) in Madrid, Spain from late March to early May 2020. The authors found patients taking anti-androgens (dutasteride [n=9], finasteride [n=2], spironolactone [n=1]) were significantly less likely to be admitted to the ICU than men not taking anti-androgens (p=0.0002), even after stratifying for age (p=0.018)(Figure 1). Given the reduced risk of experiencing severe COVID-19 (RR: 0.14, 95% CI: 0.02-0.94), they suggest anti-androgens could be utilized therapeutically to improve COVID-19 disease course in men.

ABSTRACT

The COVID-19 pandemic has disproportionally affected men.1 Men infected with SARS-CoV-2 are more than twice as likely to be admitted to the intensive care unit (ICU).2 This disparity in ICU admissions suggests the important role of androgens in COVID-19 severity.3 Previously, we reported that among 122 men hospitalized due to COVID-19, 79% were diagnosed with androgenetic alopecia (AGA),4 which is commonly treated with anti-androgens. Anti-androgens commonly used in the treatment of AGA such as finasteride, dutasteride, spironolactone, and bicalutamide could improve outcomes among men infected by SARS-CoV-2.

FIGURES

Table I. Characteristics of the anti-androgen group, and non-anti-androgen groups.

	Anti-Androgen Group	non-Anti-Androgen Group	Aged Matched non-Anti-Androgen Group
Subjects	n=12	n=65	n=36
Age	80.6 (+/-8.2)	66.4 (+/-12.2)	75.3 (+/-8.2)
Intensive Care Unit Rate	**1 (8.3%)**	**38 (58.5%)**	**17 (47.2%)**
		p=0.0014	**p=0.018**
Deaths	1 (8.3%)	4 (6.2%)	2 (5.6%)
		p=0.58	p=1.00
Comorbidities			
Prostate Cancer	0 (0%)	1 (1.5%)	1 (2.8%)
		p=1.00	p=1.00
Benign Prostate Hyperplasia	**11 (91.7%)**	**10 (15.4%)**	**9 (25%)**
		p=0.000001	**p=0.000069**
Hypertension	8 (66.7%)	30 (46.2%)	21 (58.3%)
		p=0.22	p=0.74
Immunosuppression	0 (0%)	8 (12.3%)	4 (11.1%)
		p=0.34	p=0.559667
Cardiovascular	**8 (66.7%)**	**18 (27.7%)**	13 (36.1%)
		p=0.017	p=0.095
Neurological	3 (25%)	13 (20%)	10 (27.8%)
		p=0.71	p=1.00
Endocrine (mainly Diabetes Mellitus)	6 (50%)	26 (40%)	20 (55.6%)
		p=0.54	p=0.75
Respiratory	2 (16.7%)	11 (16.9%)	8 (22.2%)
		p=1.00	p=1.00
Renal	2 (16.7%)	5 (7.7%)	4 (11.1%)
		p=0.75	p=0.63

Bold: Statistically significant difference between groups (p<0.05).

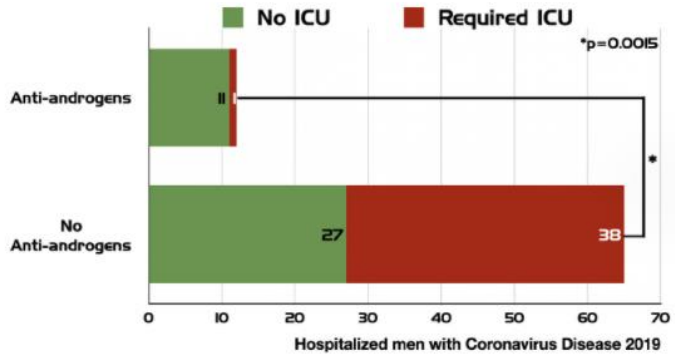


Figure 1: Hospital Outcomes. Prospective cohort of 77 men hospitalized due to severe COVID-19 in Madrid, Spain. Individuals were categorized by use of anti-androgens for at least 6 months before hospital admission, and followed for 60 days. The relative risk for intensive care unit (ICU) admission for individuals taking anti-androgens was 0.14 (95% confidence interval: 0.02-0.94).

NEUROLOGY

INTRAVENOUS IMMUNOGLOBULIN THERAPY IN COVID-19-RELATED ENCEPHALOPATHY

Muccioli L, Pensato U, Bernabè G, Ferri L, Tappatà M, Volpi L, Cani I, Henry OJ, Ceccaroni F, Cevoli S, Stofella G, Pasini E, Fornaro G, Tonon C, Vidale S, Liguori R, Tinuper P, Michelucci R, Cortelli P, Bisulli F.. J Neurol. 2020 Oct 8. doi: 10.1007/s00415-020-10248-0. Online ahead of print.
Level of Evidence: 4 - Case-series, case-control studies, or historically controlled studies

BLUF

Investigators mainly from the University of Bologna and the IRCCS Istituto delle Scienze Neurologiche di Bologna (Italy) performed a retrospective case series with 5 COVID-19 patients who developed encephalopathy and were treated with intravenous immunoglobulin (IVIg) therapy. The IVIg therapy (0.4g/kg/day) was commenced 29.8 days on average after encephalopathy onset and lead to complete electroclinical recovery in each patient, with initial improvement of neuropsychiatric symptoms occurring at a mean of 3.4 days (Table 1, Table 2). While these findings are limited by size of the case series, the improvement of the patients without any safety issue is significant and warrants further investigation for IVIg therapy in COVID-19-related encephalopathy.

ABSTRACT

OBJECTIVE: To report on efficacy and safety of intravenous immunoglobulin (IVIg) therapy in a case series of patients with COVID-19-related encephalopathy. METHODS: We retrospectively collected data on all patients with COVID-19 hospitalized at two Italian hospitals who developed encephalopathy during disease course and were treated with IVIg. RESULTS: Five patients (two females, mean age 66.8 years) developed encephalopathy after a mean of 12.6 days, since the onset of respiratory/constitutional symptoms related to COVID-19. Four patients suffered severe respiratory distress, three of which required invasive mechanical ventilation. Neurological manifestations included impaired consciousness, agitation, delirium, pyramidal and extrapyramidal signs. EEG demonstrated diffuse slowing in all patients. Brain MRI showed non-specific findings. CSF analysis revealed normal cell count and protein levels. In all subjects, RT-PCR for SARS-CoV-2 in CSF tested negative. IVIg at 0.4 g/kg/die was commenced 29.8 days (mean, range: 19-55 days) after encephalopathy onset, leading to complete electroclinical recovery in all patients, with an initial improvement of neuropsychiatric symptoms observed in 3.4 days (mean, range: 1-10 days). No adverse events related to IVIg were observed. CONCLUSIONS: Our preliminary findings suggest that IVIg may represent a safe and effective treatment for COVID-19-associated encephalopathy. Clinical efficacy may be driven by the anti-inflammatory action of IVIg, associated with its anti-cytokine qualities.

FIGURES

Pt	Age (y), Sex	Comorbidities	COVID-19 onset (day)[a,b]	Worst P/F (day)[a]	IVIg treatment (0.4 g/kg/d) (start, end)[a]	Clinical Response (initial, complete)[a]	Other immuno-therapies (start, end)[a]	Last f.up (day)[a]
1	54, F	None	−5	130 (+3)	+18, +21	+19, +21	Tocilizumab 400 mg (+0) Low-dose steroids (+3, +17)	+90
2	75, M	Type 2 DM, hyper-tension, ischemic heart disease, previous stroke	0	114 (+12)	+26, +30	+28, +34	Tocilizumab 400 mg (+33) Low-dose steroids (+21, +36)	+115
3	69, F	Bipolar disorder, MCI, iatrogenic parkinsonism, type 2 DM	−15	345 (+14)	+28, +32	+30, +38	MP 1 g/die (+13, +17)	+86
4	69, M	Hypertensive cardi-opathy	−23	81 (−14)	+22, +27	+24, +28		+70
5	67, M	Type 2 DM, hypertension	−20	79 (−8)	+55, +60	+65, +75	Tocilizumab 400 mg (−8)	+105

DM diabetes mellitus, *MCI* mild cognitive impairment, *MP* methylprednysolone

[a]We referred to encephalopathy onset as day "0", and to all events occurred previously or subsequently as minus or plus "day", respectively

[b]Onset of constitutional or respiratory symptoms such as fever, cough, dyspnea

Table 1 Demographics, comorbidities and disease course

Pt	Neurological manifestations	EEG (D)	MRI (D)	CSF (D)
1	Irritability, quadriparesis with pyramidal signs, akinetic mutism, agitated delirium, frontal release reflexes	Diffuse slowing at 6–7 Hz (+15)	Fronto-parietal white matter hyper-intensity (+16)	Cells: 0/μL Proteins: 26 mg/dL Qalb: 4 (+17)
2	Confusion, disorientation, global memory deficits	Diffuse slowing at 4–5 Hz (+21)	Previous right fronto-parietal stroke (+22)	Cells: 1 WBC/μL Proteins: 60 mg/dL Qalb: 17.8 (+25)
3	Apraxia, mixed delirium, pyramidal signs, frontal release reflexes, extrapyramidal signs (rigidity and bradykinesia)[a]	Diffuse slowing at 6–7 Hz, frontal sharp waves (+13)	Parietal white matter hyperintensity, cerebral atrophy (+13)	Cells: 1 WBC/μL Proteins: 32 mg/dL Qalb: 3.8 (+9)
4	Decreased level of consciousness, agitation, tonic muscle spasms	Diffuse slowing at 5–6 Hz, FIRDA (+0)	Cerebral small vessel disease (chronic) (+2)	Cells: 6 WBC/μL Proteins 35 mg/dL (+1)
5	Decreased level of consciousness, agitation, hemiparesis with pyramidal signs, extrapyramidal signs (rigidity and tremor), frontal release reflexes	Diffuse slowing at 5–6 Hz (+2)	Cerebral small vessel disease (chronic) (+45)	Cells: 1 WBC/μL Proteins: 29 mg/dL (+2)

D number of days after encephalopathy onset, *FIRDA* frontal intermittent rhythmic delta activity, *Qalb* CSF/serum albumin quotient, *WBC* white blood cell

[a]Extrapyramidal signs were already present before COVID-19 due to drug-induced parkinsonism

Table 2 Neurological clinical and investigative fndings

MEDICAL SUBSPECIALTIES

HEMATOLOGY AND ONCOLOGY

HIGH PREVALENCE OF ACQUIRED THROMBOPHILIA WITHOUT PROGNOSIS VALUE IN COVID-19 PATIENTS

Ferrari E, Sartre B, Squara F, Contenti J, Occelli C, Lemoel F, Levraut J, Doyen D, Dellamonica J, Mondain V, Chirio D, Risso K, Cua E, Orban JC, Ichai C, Labbaoui M, Mossaz B, Moceri P, Appert-Flory A, Fischer F, Toulon P.. J Am Heart Assoc. 2020 Sep 25:e017773. doi: 10.1161/JAHA.120.017773. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

A multidisciplinary team of French physicians from the University of Nice conducted a prospective cohort study of 89 patients with COVID-19 (Table 1) and found acquired thrombophilia was not significantly associated with increased risk of severe disease (p=0.89), DVT (p=0.71), or mortality (p=0.89) (Table 3). Most (71.9%) patients had antiphospholipid antibodies, and 20.2 % had protein S deficiency (Table 2), therefore authors suggest thrombophilia does not significantly influence disease course and its presence should not impact management of COVID-19 patients.

ABSTRACT

Background Recent literature reports a strong thrombotic tendency in patients hospitalized for a Covid-19 infection. This characteristic is quite unusual and seems specific to Covid-19 infections, especially in their severe form. Viral infections can trigger acquired thrombophilia which can then lead to thrombotic complications. We investigate for the presence of acquired thrombophilia, which could participate in this phenomenon and report their prevalence. We also wonder if these thrombophilias participate in the bad prognosis of severe Covid-19 infections. Methods and Results In 89 consecutive patients hospitalized for Covid-19 infection we found a 20% prevalence of protein S deficiency and a very high ie.: 72% prevalence of antiphospholipid antibodies: mainly lupus anticoagulant. The presence of PS deficiency or antiphospholipid antibodies was not linked with a prolonged aPTT nor with D-dimer, fibrinogen or C-reactive protein concentrations. These coagulation abnormalities are also not linked with thrombotic clinical events occurring during hospitalization nor with mortality. Conclusions We assess a high prevalence of positive tests detecting thrombophilia in Covid-19 infections. However, in our series, these acquired thrombophilias are not correlated with the severity of the disease nor with the occurrence of thrombotic events. Albeit the strong thrombotic tendency in Covid-19 infections, the presence of frequent acquired thrombophilia may be part of the inflammation storm of Covid-19 disease and should not systematically modify our strategy on prophylactic anticoagulant treatment which is already revised upwards in this pathology.

FIGURES

Table 1. Characteristics of patients hospitalized for Covid-19 infection.

Covid-19 patients characteristics (n=89)	
Age	68 [63-71]
Sex: Male	68.5%
CRP mg/l	105 [85-103]
D-dimer ng/ml	1799 [1441-2352]
Fibrinogen g/l	6.45 [5.96-6.75]
PT (%)	83 [81-85]
aPTT (sec)	29.7 [29.3-30.1]
Severe form	31/89 (35%)
DVT or PE	14/89 (15.7%)
Death	10/89 (11%)

CRP: C reactive protein, PT: Prothrombin Time, aPTT: activated partial thromboplastin time, DVT: Deep vein thrombosis, PE: pulmonary embolism

Table 2. Prevalence of coagulation abnormalities in Covid-19 population and comparison between severe and non-severe forms.

	All patients n=89	Severe n=31	Non severe n=58	p
PT (%)	83 [81-85]	82 [76-87]	83 [81-87]	0.93
aPTT (sec)	29.7 [29.3-30.1]	30.1 [28.7-31.4]	29.7 [29.3-30.1]	0.6
D-dimers (ng/ml)	1799 [1441-2352]	4303 [2176-5993]	1435 [1010-1796]	0.001
Fibrinogen	6.45 [5.96-6.75]	7.05[5.9-8.0]	6.2[5.8-6.6]	0.1
PC deficiency prevalence % (n)	2.2% (2)	0	3.4% (2)	0.54
PC median activity %	58% [54-62]	/	58% [54-62]	/
PS deficiency prevalence % (n)	20.2% (18)	22.6% (7)	19% (11)	0.78
PS median activity %	31% [24-45]	32% [24-42]	31% [25-45]	0.91
AT deficiency prevalence % (n)	6.7% (6)	12.9% (4)	3.4% (2)	0.21
AT median activity %	64% [61-69]	63% [61-66]	64% [62-66]	0.95
aPL % (n)	71.9% (64)	71.0% (22)	72.4% (42)	0.90
LA % (n)	66.3% (59)	61.3% (19)	69% (40)	0.85
β2 GP1 % (n)	6.7% (6)	3.2% (1)	8.6% (5)	0.20
aCL % (n)	7.9% (7)	6.5% (2)	8.6% (5)	0.35
Double ⊕	2.2% (2)	0	3.4% (2)	0.45
Triple ⊕	3.4% (3)	0	5.2% (3)	0.40

PT: prothrombin time. aPTT: activated partial thromboplastin time. PC: protein C, PS: protein S, AT: antithrombin, aPL: antiphospholipid antibodies, LA ; lupus anticoagulant, aCL: anticardiolipin. Double positive were LA + aCL.

Table 3. Severity markers of Covid-19 infection and clinical events according to the presence of aPL.

	No aPL n = 25	aPL n = 64	P
Severe form	36%	34%	0.89
CRP mg/l	184 [122-258]	181 [146-218]	0.85
D-dimer ng/ml	1834 [989-4375]	1782 [1411-2743]	0.94
Fibrinogen	6.45 [4.56-7.25]	6.45[5.87-6.76]	0.61
aPTT (sec)	29.8 [29.2-30.2]	30.2 [28.6-32]	0.55
PT	82 [81-86]	83 [76-87]	0.92
PC deficiency prevalence % (n)	4% (1)	1.5% (1)	0.49
PC median activity %	61%	63%	0.83
PS deficiency prevalence % (n)	20% (5)	20% (13)	0.97
PS median activity %	32 [25-44]	34 [28-54]	0.83
AT deficiency prevalence % (n)	8% (2)	6.2% (4)	0.99
AT Median activity %	64% [61-66]	63% [61-67]	0.90
DVT	12%	9%	0.71
PE	4%	9%	0.40
Death	12%	11%	0.89

LA: Lupus anticoagulant. aPTT: activated prothrombin time. CRP: C reactive protein. DVT: Deep vein thrombosis. PE: pulmonary embolism. The same results are true considering LA instead of aPL.

ACUTE CARE

NEUROLOGY

NEUROLOGY AND COVID-19

Josephson SA, Kamel H.. JAMA. 2020 Sep 22;324(12):1139-1140. doi: 10.1001/jama.2020.14254.
Level of Evidence: Other - Expert Opinion

BLUF

Neurologists from the University of California San Francisco and Cornell University review the impact of the COVID-19 pandemic on the practice of neurology. They discuss pandemic-related adjustments in care such as telehealth for chronic condition follow-up, and the extent to which the pandemic has highlighted how socioeconomic disparities contribute to the development of neurological sequelae. Additionally, they review the limited existing literature on direct neurologic effects of SARS-CoV-2 (stroke, anosmia, myalgias, and post-infectious Guillain-Barré syndrome), and suggest that longitudinal studies to better define long-term neurological consequences of COVID-19 are necessary.

OPHTHALMOLOGY

PROOF-OF-CONCEPT CALCULATIONS TO DETERMINE THE HEALTH-ADJUSTED LIFE-YEAR TRADE-OFF BETWEEN INTRAVITREAL ANTI-VEGF INJECTIONS AND TRANSMISSION OF COVID-19

Boyd MJ, Scott DAR, Squirrell DM, Wilson GA.. Clin Exp Ophthalmol. 2020 Sep 9. doi: 10.1111/ceo.13855. Online ahead of print.
Level of Evidence: 5 - Modeling

BLUF

Ophthalmologists in New Zealand constructed a statistical model to weigh risks and benefits of performing anti-VEGF intraocular injections in patients with neovascular age-related macular degeneration (nAMD) during the COVID-19 pandemic. Using health-adjusted life years (HALYs) lost to compare expected disease burden from COVID-19 to visual impairment secondary to nAMD in a variety of theoretical scenarios, authors found expected burden from visual impairment outweighed that from COVID-19 unless the latter's prevalence was very high (Table 2, 4) and suggest continuing anti-VEGF injections during the pandemic minimizes overall HALYs lost.

ABSTRACT

BACKGROUND: Clinical ophthalmological guidelines encourage the assessment of potential benefits and harms when deciding whether to perform elective ophthalmology procedures during the COVID-19 pandemic, in order to minimize the risk of disease transmission. METHOD: We performed probability calculations to estimate COVID-19 infection status and likelihood of disease transmission among neovascular age-related macular degeneration patients and health-care workers during anti-VEGF procedures, at various community prevalence levels of COVID-19. We then applied the expected burden of COVID-19 illness and death expressed through health-adjusted life-years (HALYs) lost. We compared these results to the expected disease burden of severe visual impairment if sight protecting anti-VEGF injections were not performed. RESULTS: Our calculations suggest a wide range of contexts where the benefits of treatment to prevent progression to severe visual impairment or blindness are greater than the expected harms to the patient and immediate health care team due to COVID-19. For example, with appropriate protective equipment the benefits of treatment outweigh harms when the chance of progression to severe visual impairment is >0.044% for all scenarios where COVID-19 prevalence was 1/1000, even when the attack rate in the clinical setting is very high (5-43%). CONCLUSION: Unless COVID-19 prevalence is very high, the reduced disease burden from avoiding visual impairment outweighs the expected HALYs lost from COVID-19 transmission. This finding is driven by the fact that HALYs lost when someone suffers severe visual impairment for 5 years are equivalent to nearly 400 moderate cases of infectious disease lasting 2 weeks each.

Active community COVID-19 case prevalence	65-year-old, monthly anti-VEGF injections		75-year-old, monthly anti-VEGF injections		75-year-old, monthly anti-VEGF injections		One-time anti-VEGF injection: 75-year-old
	optimistic assumptions	pessimistic assumptions	optimistic assumptions	pessimistic assumptions	optimistic assumptions	pessimistic assumptions	pessimistic assumptions
1/10,000	<0.001%	0.001%	<0.001%	0.002%	<0.001%	0.004%	<0.001%
1/1,000	0.001%	0.011%	0.003%	0.022%	0.005%	0.044%	0.004%
1/100	0.013%	0.111%	0.025%	0.217%	0.051%	0.436%	0.036%
1/10	0.127%	1.11%	0.252%	2.17%	0.506%	4.36%	0.362%

Table 2: Threshold risk of untreated disease progression necessary for the risk of withholding treatment to be greater than the risk of giving it: personal protective equipment is available and provides 96% reduction in transmission

Active community COVID-19 case prevalence	65-year-old, monthly anti-VEGF injections (optimistic assumptions)	No PPE: 65-year-old, monthly anti-VEGF injections, (optimistic assumptions)	85-year-old, monthly anti-VEGF injections (pessimistic assumptions)	No PPE: 85-year-old, monthly anti-VEGF injections, (pessimistic assumptions)
1/10,000	0.122	0.122	0.032	0.032
1/1,000	0.122	0.121	0.032	0.029
1/100	0.122	0.118	0.031	0.002
1/10	0.120	0.090	0.020	-0.273

Table 4: Expected net HALY benefit to patient assuming a 5% probability of progression from moderate to severe vision loss

SENSITIVITY OF NASOPHARYNGEAL, OROPHARYNGEAL, AND NASAL WASH SPECIMENS FOR SARS-COV-2 DETECTION IN THE SETTING OF SAMPLING DEVICE SHORTAGE

Calame A, Mazza L, Renzoni A, Kaiser L, Schibler M.. Eur J Clin Microbiol Infect Dis. 2020 Sep 17. doi: 10.1007/s10096-020-04039-8. Online ahead of print.

Level of Evidence: 3 - Non-consecutive studies, or studies without consistently applied reference standards

BLUF

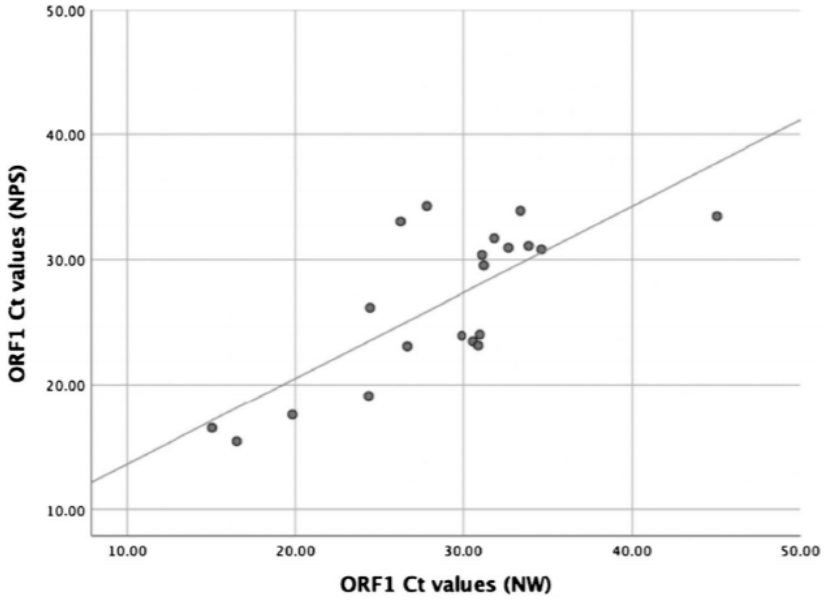
Lab medicine faculty from Geneva University Hospitals in Switzerland performed a cross-sectional study comparing sensitivities of different samples for detection of ORF1 and E-protein genes via RT-PCR in 29 SARS-CoV-2 positive patients. They found oropharyngeal washes (mean rRT-PCR delta cycle threshold[Ct]:1.24 for ORF1, 1.32 for E-protein; Pearson r: 0.88) and nasal washes (mean delta Ct: 1.77 ORF1,1.73 E-protein; Pearson r: 0.75) demonstrated similar levels of sensitivity compared to nasopharyngeal swabs (current standard of care)(Figure 1, 2). They also validated a cell culture medium (Dulbecco's modified Eagle medium) for sample transport (mean delta Ct of 0.67 for E-gene and 0.53 for ORF-1), suggesting that these alternative methods for sample collection can be reliably used in the setting of testing supply shortages.

ABSTRACT

In the context of an unprecedented shortage of nasopharyngeal swabs (NPS) or sample transport media during the coronavirus disease 2019 (COVID-19) crisis, alternative methods for sample collection are needed. To address this need, we validated a cell culture medium as a viral transport medium, and compared the analytical sensitivity of SARS-CoV-2 RT-PCR in nasal wash (NW), oropharyngeal swab (OPS), and NPS specimens. Both the clinical and analytical sensitivity were comparable in these three sample types. OPS and NW specimens may therefore represent suitable alternatives to NPS for SARS-CoV-2 detection.

FIGURES

Fig. 1 Correlation between rRT-PCR cycle threshold (Ct) values obtained with nasal washes (NW) and with nasopharyngeal swabs (NPS). Each dot represents one of the 20 patients who had a NW and a NPS. One negative specimen by NW was arbitrary fixed at a Ct value of 45. The trend line is estimated by a simple linear regression



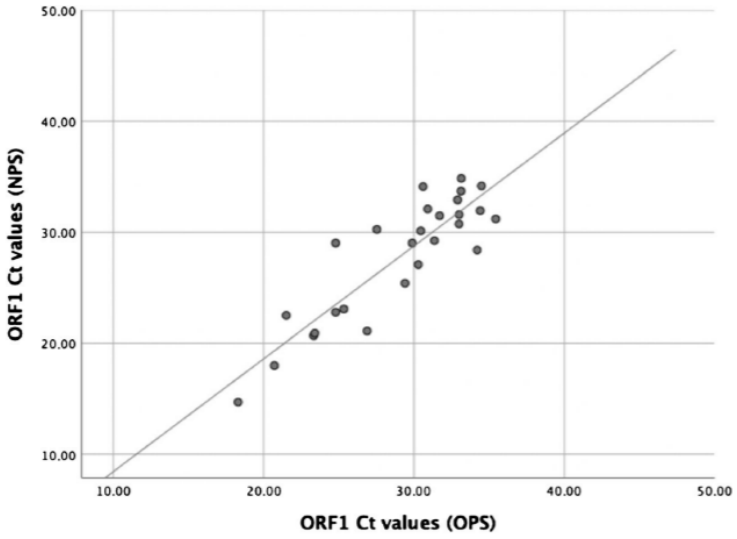


Fig. 2 Correlation between rRT-PCR cycle threshold (Ct) values obtained with oropharyngeal swabs (OPS) and with nasopharyngeal swabs (NPS). Each dot represents one of the 27 patients who had positive OPS and NPS. The trend line is estimated by a simple linear regression

DEVELOPMENTS IN TREATMENTS

CONVALESCENT PLASMA FOR PATIENTS WITH SEVERE COVID-19: A MATCHED COHORT STUDY

Rogers R, Shehadeh F, Mylona EK, Rich J, Neill M, Touzard-Romo F, Geffert S, Larkin J, Bailey JA, Lu S, Sweeney J, Mylonakis E.. Clin Infect Dis. 2020 Oct 10:ciaa1548. doi: 10.1093/cid/ciaa1548. Online ahead of print.
Level of Evidence: 3 - Non-randomized controlled cohort/follow-up study

BLUF

Researchers at Brown University Warren Alpert Medical School who conducted a matched cohort study of 241 COVID-19-positive patients found that convalescent plasma treatment did not significantly reduce mortality rate (Table 3). However, patients 65 years old and above who received convalescent plasma were discharged more frequently than those in the control group. The authors recommend further study with randomization into the efficacy of convalescent plasma therapy in older patients.

ABSTRACT

BACKGROUND: The efficacy of convalescent plasma (CP) for the treatment of COVID-19 remains unclear. METHODS: In a matched cohort analysis of hospitalized patients with severe COVID-19, the impact of CP treatment on in-hospital mortality was evaluated using univariate and multivariate Cox proportional-hazards models, and the impact of CP treatment on time to hospital discharge was assessed using a stratified log-rank analysis. RESULTS: 64 patients who received CP a median of 7 days after symptom onset were compared to a matched control group of 177 patients. The incidence of in-hospital mortality was 12.5% and 15.8% in the CP and control groups, respectively (p = 0.52). There was no significant difference in the risk of in-hospital mortality between the two groups (adjusted hazard ratio [aHR] 0.93, 95% confidence interval [CI] 0.39 - 2.20). The overall rate of hospital discharge was not significantly different between the two groups (rate ratio [RR] 1.28, 95% CI 0.91 - 1.81), although there was a significantly increased rate of hospital discharge among patients 65-years-old or greater who received CP (RR 1.86, 95% CI 1.03 - 3.36). There was a greater than expected frequency of transfusion reactions in the CP group (2.8% reaction rate observed per unit transfused). CONCLUSIONS: We did not demonstrate a significant difference in risk of mortality or rate of hospital discharge between the CP and control groups. There was a signal for improved outcomes among the elderly, and further adequately powered randomized studies should target this subgroup when assessing the efficacy of CP treatment.

All cause in-hospital mortality	Unadjusted HR (95% CI)	Adjusted HR (95% CI)	
		Model 1[a]	Model 2[b]
Overall (n = 64)	0.73 (0.32 – 1.69)	0.91 (0.39 – 2.15)	0.93 (0.39 – 2.20)
AI ≥ 1.4[c] (n = 32)	1.08 (0.41 – 2.80)	1.09 (0.41 – 2.86)	1.17 (0.43 – 3.19)
AI ≥ 5[d] (n = 18)	0.35 (0.05 – 2.62)	0.38 (0.05 – 2.98)	0.39 (0.05 – 3.08)

Abbreviations: HR, hazard ratio; CI, confidence interval; AI, SARS-CoV-2 IgG antibody index

[a]Adjusted for age, gender, race, and baseline oxygen requirements.

[b]Adjusted for age, gender, race, baseline oxygen requirements, remdesivir use, and corticosteroid use.

[c]At least 1 unit with AI ≥ 1.4, but not 2 units both with AI ≥ 5

[d]Two units both with AI ≥ 5

Table 3. Multivariate analysis of the impact of convalescent plasma treatment on all cause in-hospital mortality as compared to the control group.

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