

# The Daily COVID-19 Literature Surveillance Summary

**October 28, 2020**



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# COVID-19 Daily Literature Surveillance

COVID19LST



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

# LEVEL OF EVIDENCE

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

Question	Step 1 (Level 1*)	Step 2 (Level 2*)	Step 3 (Level 3*)	Step 4 (Level 4*)	Step 5 (Level 5)
<b>How common is the problem?</b>	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
<b>Is this diagnostic or monitoring test accurate? (Diagnosis)</b>	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
<b>What will happen if we do not add a therapy? (Prognosis)</b>	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
<b>Does this intervention help? (Treatment Benefits)</b>	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
<b>What are the COMMON harms? (Treatment Harms)</b>	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
<b>What are the RARE harms? (Treatment Harms)</b>	Systematic review of randomized trials or n-of-1 trial	Randomized trial or (exceptionally) observational study with dramatic effect			
<b>Is this (early detection) test worthwhile? (Screening)</b>	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

- A review of data from the 2011-2016 National Health and Nutrition Examination Survey (NHANES; n=7744 participants) to estimate the proportion of the United States population with risk factors for severe COVID-19 found [73.7% had at least one risk factor](#) (most commonly obesity [41%] and hypertension [50.1%]), while low-income individuals and those with less education typically had more risk factors ( $p<0.01$ ).
- A comparative analysis by public health experts from Israel on crude case-fatality rates (CFR) within 7 countries found large differences in reported age distribution of COVID-19 cases and CFR variance, but minimal differences among pooled age-specific CFR, and CFR variance decreased significantly after age adjustment, suggesting that [utilization of age-specific and age-adjusted COVID-19 CFR data may be more accurate](#) than crude CFR when comparing between countries.
- Obstetricians from Shanxi Medical University in Taiyuan, China conducted a systematic review of studies (n=36) published between December 1, 2019 and June 10, 2020 on [outcomes of COVID-19 in pregnancy](#) and found less than 0.01% of samples from newborns born to women with COVID-19 were positive for SARS-CoV-2, however, 25.32% of infants were born prematurely ( $i^2=63.7\%$ ) and 35.87% of mothers were intubated ( $i^2=73.3\%$ ), with 4.95% admitted to the intensive care unit ( $i^2=68.3\%$ ).

## Transmission & Prevention

- A cohort study where the forehead temperature of 101 healthy male and female employees of a hospital in Tyrol, Austria was measured upon entrance to the hospital and after several subsequent time points found that forehead temperatures were the lowest upon entrance into the hospital due to the cold outdoor climate ( $-5.5^{\circ}\text{C}$  and  $0^{\circ}\text{C}$ ) and did not reach a steady-state until approximately 60 minutes after entrance, suggesting that [forehead temperatures may not be an effective screening tool for infectious disease such as COVID-19 in locations with a cold climate](#).

## Management

- A placebo-controlled, double-blind randomized clinical trial of [hospitalized COVID-19 positive patients not on mechanical ventilation](#) (n=242) found that patients who received tocilizumab (n=161) had similar rates of death or intubation (HR 0.83, 95%CI 0.38-1.81), worsened condition (HR 1.11, 95%CI 0.59-2.1), and supplemental oxygen requirement (HR 0.94, 95%CI 0.67-1.3) compared to the non-treatment control group (n=81).

## Adjusting Practice During COVID-19

- A letter to the editor proposes [implementation of "Chronic COVID Syndrome \(CCS\)"](#) as the appropriate nomenclature used in published work regarding the long term effects of COVID-19 infection, as well as a staging system based on the predominant organ involved in infection, so hospitals can anticipate complications and better clinically manage patients.
- A literature review conducted across various cardiovascular medical institutions throughout the United States aimed to refine previous American College of Cardiology's Sports and Exercise Cardiology [recommendations on a conservative return-to-play approach](#) with cardiac risk stratification for post-COVID-19 athletes, and to expand the approach to include the possibility of myocarditis and increased risk for sudden cardiac death during exercise despite a mild or asymptomatic infection.

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# EPIDEMIOLOGY

## THE PROPORTION OF ADULT AMERICANS AT RISK OF SEVERE COVID-19 ILLNESS

Li HL, Cheung BMY.. J Gen Intern Med. 2020 Oct 26. doi: 10.1007/s11606-020-06325-9. Online ahead of print.

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

### BLUF

A research group from the University of Hong Kong Division of Clinical Pharmacology and Therapeutics reviewed data from the 2011-2016 National Health and Nutrition Examination Survey (NHANES; n=7744 participants) to estimate the proportion of the United States population with risk factors for severe COVID-19. They found 73.7% had at least one risk factor (most commonly obesity [41%] and hypertension [50.1%]; Table 1), while low-income individuals and those with less education typically had more risk factors ( $p<0.01$ ; Table 2). Authors suggest a substantial proportion of the US population is at high risk, so individuals with risk factors should socially distance and consider lifestyle modifications (i.e. smoking and alcohol cessation, weight loss, diet) to mitigate overall risk.

### FIGURES

Table 1 Characteristics of the NHANES Participants Analyzed

	Overall	Age < 50 years	Age ≥ 50 years	P value
N	7744	3590	4154	
Age	49.5 ± 0.4	35.1 ± 0.3	63.5 ± 0.2	
Male	49.4 (48.2–51.0)	50.6 (49.0–52.0)	48.3 (46.5–50.0)	0.051
Ethnicity				
Non-Hispanic White	67.2 (62.8–71.0)	59.9 (54.8–65.0)	74.2 (70.0–78.0)	< 0.001
Non-Hispanic Black	10.3 (8.4–13.0)	11.2 (9.0–14.0)	9.5 (7.5–12.0)	
Mexican American	8.3 (6.3–11.0)	11.6 (9.0–15.0)	5.1 (3.5–7.0)	
Other Hispanics	6.0 (4.6–8.0)	7.5 (5.8–10.0)	4.5 (3.3–6.0)	
Non-Hispanic Asian	5.4 (4.4–7.0)	6.6 (5.4–8.0)	4.2 (3.3–5.0)	
Other ethnicities	2.9 (2.2–4.0)	3.2 (2.5–4.0)	2.6 (1.8–4.0)	
Prevalence of established risk factors				
≥ 1 established risk factor	58.9 (56.7–61.0)	47.9 (45.4–50.0)	69.5 (66.5–72.0)	< 0.001
Obesity	41.0 (38.9–43.0)	38.9 (36.3–41.0)	43.0 (40.1–46.0)	0.016
DM	24.0 (22.4–26.0)	11.7 (10.4–13.0)	35.8 (33.7–38.0)	< 0.001
CKD	18.4 (17.3–20.0)	9.0 (8.2–10.0)	27.6 (25.6–30.0)	< 0.001
Heart disease	8.0 (7.2–9.0)	1.8 (1.3–3.0)	14.0 (12.6–15.0)	< 0.001
COPD	7.6 (6.6–9.0)	4.5 (3.6–6.0)	10.6 (9.1–12.0)	< 0.001
Prevalence of probable risk factors				
≥ 1 probable risk factor	55.5 (53.2–58.0)	37.4 (34.7–40.0)	73.1 (70.3–76.0)	< 0.001
Asthma	8.9 (8.0–10.0)	7.6 (6.5–9.0)	10.2 (8.9–12.0)	0.011
Stroke	3.6 (3.2–4.0)	0.8 (0.5–1.0)	6.4 (5.6–7.0)	< 0.001
Liver disease	2.4 (2.1–3.0)	1.8 (1.3–2.0)	3.0 (2.4–4.0)	0.022
Hypertension	50.1 (47.9–52.0)	31.1 (28.8–34.0)	68.4 (65.3–71.0)	< 0.001
Taking immunosuppressive agents	2.5 (2.0–3.0)	1.2 (0.8–2.0)	3.6 (2.9–5.0)	< 0.001
Prevalence of any risk factors				
≥ 1 any risk factor	73.7 (71.6–76.0)	60.9 (58.2–63.0)	86.2 (83.7–88.0)	< 0.001
≥ 2 any risk factors	46.6 (44.5–49.0)	29.7 (27.5–32.0)	62.9 (60.2–66.0)	< 0.001
≥ 3 any risk factors	26.2 (24.3–28.0)	11.5 (10.0–13.0)	40.5 (37.8–43.0)	< 0.001

Data are presented as weighted mean ± standard error, or weighted percentage (95% confidence interval)

DM, diabetes mellitus; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease

P values for age group comparison were obtained by multivariate logistic regression, adjusted for sex and ethnicity, where appropriate, or by chi-square test, where appropriate

Obesity was defined as body mass index (BMI) ≥ 30 kg/m<sup>2</sup>

DM was defined as (1) answered "yes" to "Other than during pregnancy". Have you ever been told by a doctor or other health professional that you have diabetes or sugar diabetes?" or (2) glycosylated hemoglobin ≥ 6.5%, or (3) fasting glucose ≥ 126 mg/dL

Heart disease was defined as answering "yes" to any of the questions below: (1) "Has a doctor or other health professional ever told you that you had congestive heart failure?" or (2) "Has a doctor or other health professional ever told you that you had coronary heart disease?" or (3) "Has a doctor or other health professional ever told you that you had a heart attack (also called myocardial infarction)?"

CKD was defined as (1) answering "yes" to "Have you ever been told by a doctor or other health professional that you had weak or failing kidney?" or (2) estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m<sup>2</sup> using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation, or (3) urine albumin – creatinine ratio ≥ 30 mg/g

COPD was defined as answering "yes" to either of the questions below: (1) "Has a doctor or other health professional ever told you that you had emphysema?" or (2) "Has a doctor or other health professional ever told you that you had chronic bronchitis?"

Asthma was defined as answering "yes" to both of the questions below: (1) "Has a doctor or other health professional ever told you that you have asthma?" and (2) "Do you still have asthma?"

Stroke was defined as answering "yes" to the question "Has a doctor or other health professional ever told you that you have asthma?"

Liver disease was defined as answering "yes" to both of the questions below: (1) "Has a doctor or other health professional ever told you that you had any kind of liver condition?" and (2) "Do you still have a liver condition?"

Hypertension was defined as (1) having at least three of the blood pressure measurements on the day of examination as ≥ 130 mmHg for systolic measurement or ≥ 80 mmHg for diastolic measurement, or (2) answering "yes" to "Have you ever been told by a doctor or other health professional that you had hypertension, also called high blood pressure?"

**Table 2** Prevalence of  $\geq 1$  Established and Any Risk Factor According to Ethnicity, Education Level, and Income level

	$\geq 1$ established risk factor	$\geq 1$ any risk factor	P value
Sex			
Male (referent)	56.8 (54.3–59.0)		
Female	60.8 (58.2–63.0)	0.055	0.019
Ethnicity			
Non-Hispanic White (referent)	58.0 (55.3–61.0)		
Non-Hispanic Black	68.7 (65.7–72.0)	< 0.001	< 0.001
Mexican American	64.9 (60.4–69.0)	< 0.001	0.355
Other Hispanics	57.9 (53.1–62.0)	0.412	0.534
Non-Hispanic Asian	39.5 (35.3–44.0)	< 0.001	< 0.001
Other ethnicities	64.5 (56.0–72.0)	0.087	0.036
Education level			
Low	67.1 (64.6–70.0)	0.324	0.977
Middle (referent)	63.2 (61.0–65.0)	< 0.001	< 0.001
High	46.9 (43.3–51.0)		
Income level			
Low	65.2 (62.6–68.0)	< 0.001	< 0.001
Low middle	64.3 (60.3–68.0)	< 0.001	0.002
High middle	62.9 (59.0–57.0)	0.002	0.144
High (referent)	52.9 (49.8–56.0)		

Data are presented as weighted percentage (95% confidence interval)

P values were obtained by multivariate logistic regression, adjusted for age, sex, ethnicity, education level, and income level, where appropriate  
Education level was classified as low (less than a high school degree), middle (high school graduate/GED or some college/AA degree), or high (college graduate or above)

Income level was classified as low (poverty income ratio (PIR) < 1.3), low middle (PIR  $\geq 1.3$  and < 1.85), high middle (PIR  $\geq 1.85$  and < 3), or high (PIR  $\geq 3$ )

## MODELING

### POTENTIAL OF SOLAR UV RADIATION FOR INACTIVATION OF CORONAVIRIDAE FAMILY ESTIMATED FROM SATELLITE DATA

Carvalho FRS, Henriques DV, Correia O, Schmalwieser AW.. Photochem Photobiol. 2020 Oct 19. doi: 10.1111/php.13345.

Online ahead of print.

Level of Evidence: 5 - Modeling

#### BLUF

Researchers mainly from Portuguese Institute for Sea and Atmosphere evaluated the effect of satellite retrieved solar ultraviolet radiation (UVR), as measured from the tropospheric emission monitoring service, on inactivating SARS-CoV2 in San Paulo, Vienna, Lisbon, and Reykjavik. They found that this method worked best in locations closer to the equator (daily survival fraction less than  $10^{-4}$ ; 99.99% inactivation rate throughout the year) as opposed to the northern latitudes where this type of result is only found in June and July (Figure 5, 6, 7). These findings suggest that UVR-based sterilization is most effective near the tropics and less effective in the northern hemisphere, possibly serving as a protective factor against COVID-19.

#### ABSTRACT

The pandemic Covid-19 disease affects people dramatically overall the globe by illness and death. Several strategies are applied to restrict the spread of this disease like lockdown, adequate social distance in different activities, hand disinfection and the use of masks. Potential hazard outdoors comes from released viruses, which may remain in the air for a while and settle down afterwards and contaminating surfaces. Solar ultraviolet radiation (UVR) is known to act as a natural environmental virucide. The virucidal effectiveness of UVR depends on a first order on the sensitivity of the virus against UVR as well as on the amount of incoming UVR. Here, we present estimates of the potential of solar UVR in inactivating SARS-CoV-2 in the environment. This is done by combining DNA-damaging surface solar UVR retrieved by satellites and the available information on fluence for inactivation of Coronaviridae. Our results show that solar UVR has a high potential to inactivate these viruses, but the degree depends strongly on location and season. In the sub-tropics (Sao Paulo, 23.5 S) the daily survival fraction is lower than  $10^{-4}$  during the whole year, while close at norther latitudes (Reykjavik, 64 N) such a reduction can be found in June and July only.

## FIGURES

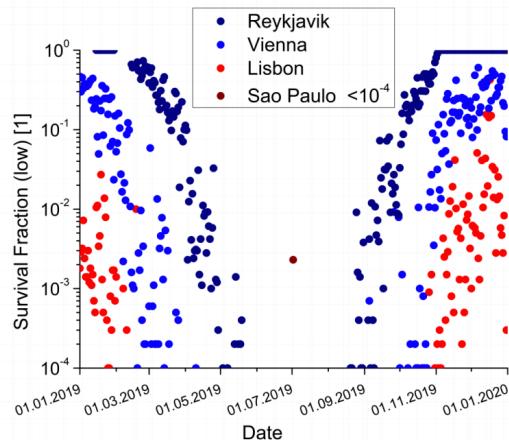


Figure 5. Daily survival fraction of Coronavirus after daily solar exposure estimated for Reykjavik, Vienna, Lisbon and Sao Paulo ( $<10^4$  during almost the whole year) for 2019.

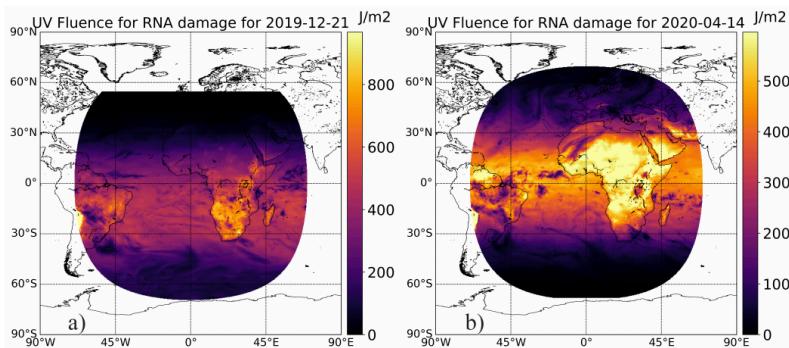


Figure 6. Daily cloud-modified fluence (J/m<sup>2</sup>) for RNA damage estimated for (a) Dec. 21st 2019 and (b) Apr.14th, 2020

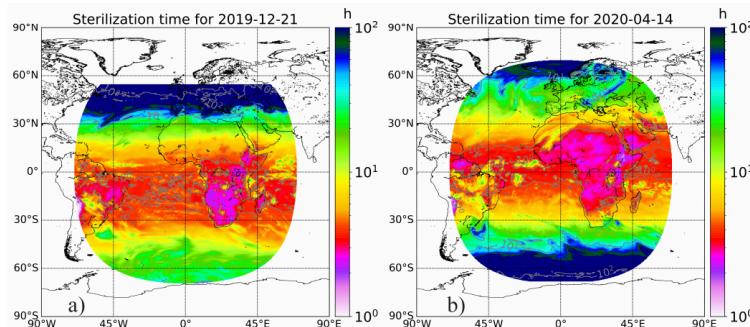


Figure 7. Daily exposure times (hour) for SARS-CoV-2 sterilization estimated for (a) Dec. 21st 2019 and (b) Apr.14th, 2020. Dashed colored areas correspond to high Ds and solid grey lines to low Ds

# THE CONFOUNDED CRUDE CASE-FATALITY RATES (CFR) FOR COVID-19 HIDE MORE THAN THEY REVEAL-A COMPARISON OF AGE-SPECIFIC AND AGE-ADJUSTED CFRS BETWEEN SEVEN COUNTRIES

Green MS, Peer V, Schwartz N, Nitzan D.. PLoS One. 2020 Oct 21;15(10):e0241031. doi: 10.1371/journal.pone.0241031. eCollection 2020.

Level of Evidence: Other - Modeling

## BLUF

A comparative analysis conducted by public health experts from Israel on crude case-fatality rates (CFR) within 7 countries found large differences in reported age distribution of COVID-19 cases and CFR variance, but minimal differences among pooled age-specific CFR (Figures 1 & 2), and CFR variance decreased significantly after age adjustment (Figure 3). These results suggest utilization of age-specific and age-adjusted COVID-19 CFR data may be more accurate than crude CFR when comparing between countries.

## SUMMARY

Additional study details below:

- Crude CFR was defined as the number of deaths divided by the total number of cases, with age as a confounding variable.
- This research analyzed the effect of age-group on differences among 7 countries: Italy, Spain, Sweden, China, South Korea, Israel, and Canada.
- There were wide variations in age distribution pattern of COVID-19 cases between the 7 countries.
- Crude overall CFR showed wide variations (0.82% in Israel to 14.2% in Italy) but age-specific CFR had less variation (4.2% in China to 10.8% in Italy) (Figures 1 & 2).
- Pooled age-specific CFR by meta-analysis showed CFR was lowest among 20-29 year-olds (0.07%) and highest in the 80+ age group (26.92%).
- Age-group was considered to be the most important confounding variable in CFR differences as per meta-regression analysis ( $p<0.001$ ).

## ABSTRACT

**BACKGROUND:** Crude case-fatality rates (CFRs) for COVID-19 vary widely between countries. There are serious limitations in the CFRs when making comparisons. We examined how the age distribution of the cases is responsible for the COVID-19 CFR differences between countries. **METHODS:** COVID-19 cases and deaths, by ten-year age-groups, were available from the reports of seven countries. The overall and age-specific CFRs were computed for each country. The age-adjusted CFRs were computed by the direct method, using the combined number of cases in all seven countries in each age group as the standard population. A meta-analytic approach was used to obtain pooled age-specific CFRs. **FINDINGS:** The crude overall CFRs varied between 0.82% and 14.2% in the seven countries and the variation in the age-specific CFRs were much smaller. There was wide variation in the age distribution of the cases between countries. The ratio of the crude CFR for the country with the highest CFR to that with the lowest (6.28) was much lower for the age-adjusted CFRs rates (2.57). **CONCLUSIONS:** The age structure of the cases explains much of differences in the crude CFRs between countries and adjusting for age substantially reduces this variation. Other factors such as the definition of cases, coding of deaths and the standard of healthcare are likely to account for much of the residual variation. It is misleading to compare the crude COVID-19 CFRs between countries and should be avoided. At the very least, age-specific and age-adjusted CFRs should be used for comparisons.

## FIGURES

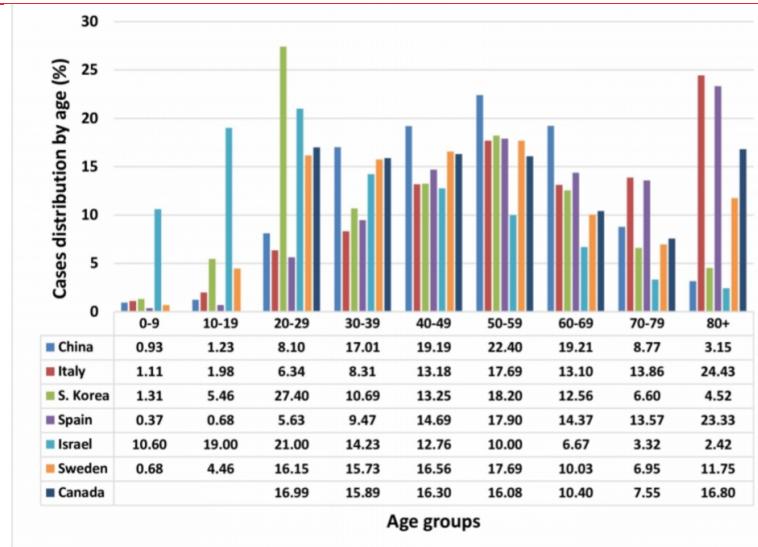


Figure 1: Distribution of cases (%) by age for seven countries—China, Italy, S Korea, Spain, Israel, Sweden, and Canada.

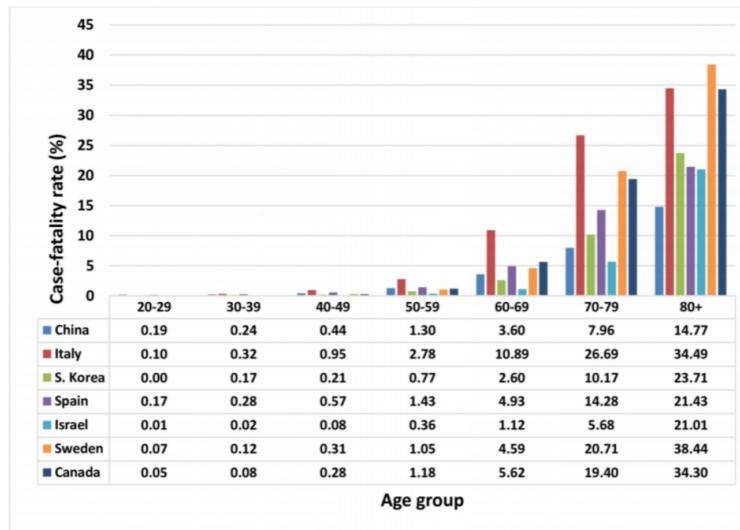


Figure 2: Age specific case-fatality rates (%) for seven countries—China, Italy, S Korea, Spain, Israel, Sweden, and Canada.

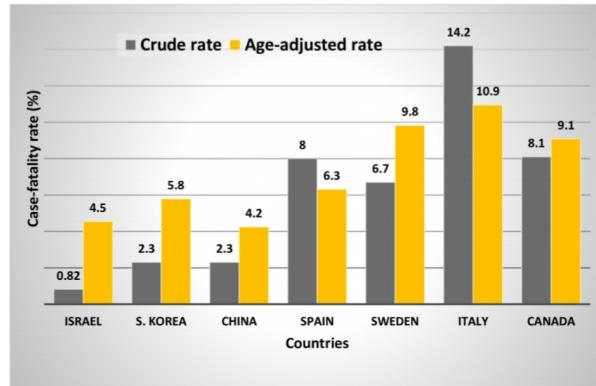


Figure 3: Crude (%) and age-adjusted case-fatality rates (%) by country for seven countries.

# SYMPTOMS AND CLINICAL PRESENTATION

## PREGNANT PERSONS

### CLINICAL MANIFESTATION, OUTCOMES IN PREGNANT WOMEN WITH COVID-19 AND THE POSSIBILITY OF VERTICAL TRANSMISSION: A SYSTEMATIC REVIEW OF THE CURRENT DATA

Han Y, Ma H, Suo M, Han F, Wang F, Ji J, Ji J, Yang H.. J Perinat Med. 2020 Oct 19:/j/jpme.ahead-of-print/jpm-2020-0431/jpm-2020-0431.xml. doi: 10.1515/jpm-2020-0431. Online ahead of print.

Level of Evidence: 2 - Systematic review of surveys that allow matching to local circumstances

#### BLUF

Obstetricians from Shanxi Medical University in Taiyuan, China conducted a systematic review of studies (n=36) published between December 1, 2019 and June 10, 2020 on outcomes of COVID-19 in pregnancy. They found less than 0.01% of samples from newborns born to women with COVID-19 were positive for SARS-CoV-2 (Table 4). However, 25.32% of infants were born prematurely ( $i^2=63.7\%$ , Figure 4) and 35.87% of mothers were intubated ( $i^2=73.3\%$ ), with 4.95% admitted to the intensive care unit ( $i^2=68.3\%$ )(Table 3). The results suggest vertical transmission of SARS-CoV-2 is unlikely, but risk of other serious outcomes may be relatively high.

#### ABSTRACT

Objectives To assess perinatal outcomes of COVID-19 infections during pregnancy and the possibility of vertical transmission.

Methods An analysis was performed using Stata 15.0, and Q-test was used to evaluate the heterogeneity of the included studies. Results The most common symptoms were found to be fever (64.78%), cough (59.81%) and shortness of breath or dyspnea (23.86%). Of this 88.73% patients demonstrated typical COVID-19 signs on chest CT or X-ray. Intubation was carried out in 35.87% of patients, and 4.95% of mothers were admitted to the intensive care unit, where the rate of maternal death was <0.01% and that of premature delivery was 25.32%. The rate of the birth weight being <2,500 g was 30.65% and that of Neonatal intensive care unit (NICU) admission was 24.41%. Positive nasopharynx swabs or sputum from newborns was <0.01%. Conclusions Pregnant patients with COVID-19 most commonly presented with fever, cough, shortness of breath and dyspnea, most of which possessed imaging manifestations. The risk of intubation and admission to intensive care unit were high. The risk of premature delivery was higher, leading to a high risk of NICU admission and low neonatal birthweight. Vertical transmission of SARS-CoV-2 from mother to child was found to be unlikely.

#### FIGURES

Table 3: Complications, maternal outcomes, and mode of delivery.

Types		n (studies)	Event	Total	Proportion, %	95% CI, %	Heterogeneity			
							X <sup>2</sup>	I <sup>2</sup>	Variance	p-Value
Complications	Gestational hypertension or preeclampsia	27	24	381	<0.01	0.00–0.00	11.36	<0.01	<0.01	0.99
	Premature rupture of membranes	27	32	176	4.03	0.16–11.22	22.14	<0.01	<0.01	0.68
Main outcome measures	Intubation	26	36	221	35.87	10.29–65.04	93.74	73.33	0.44	<0.01
	ICU	31	81	895	4.95	0.01–15.15	94.53	68.26	0.10	<0.01
Pregnancy outcomes	Death	33	13	1005	<0.01	0.00–0.00	53.19	39.84	0.03	0.01
	Full term delivery	35	543	743	68.53	55.87–80.29	91.75	62.94	0.09	<0.01
Mode of delivery	Premature delivery	35	188	743	25.32	14.19–37.74	93.66	63.70	0.09	<0.01
	Spontaneous abortion or artificial abortion	35	20	743	<0.01	0.00–0.00	43.40	21.67	0.01	0.13
	Stillbirth	34	8	663	<0.01	0.00–0.00	33.22	0.66	0.04	0.46
	Caesarean delivery for SARS-CoV-2	29	135	586	28.59	13.11–46.14	82.57	66.09	0.12	<0.01
	Caesarean delivery for other indications	29	254	586	34.63	22.69–47.28	44.63	37.26	0.04	0.02
	Vaginal delivery	35	283	733	26.83	13.04–42.45	149.77	77.30	0.19	<0.01

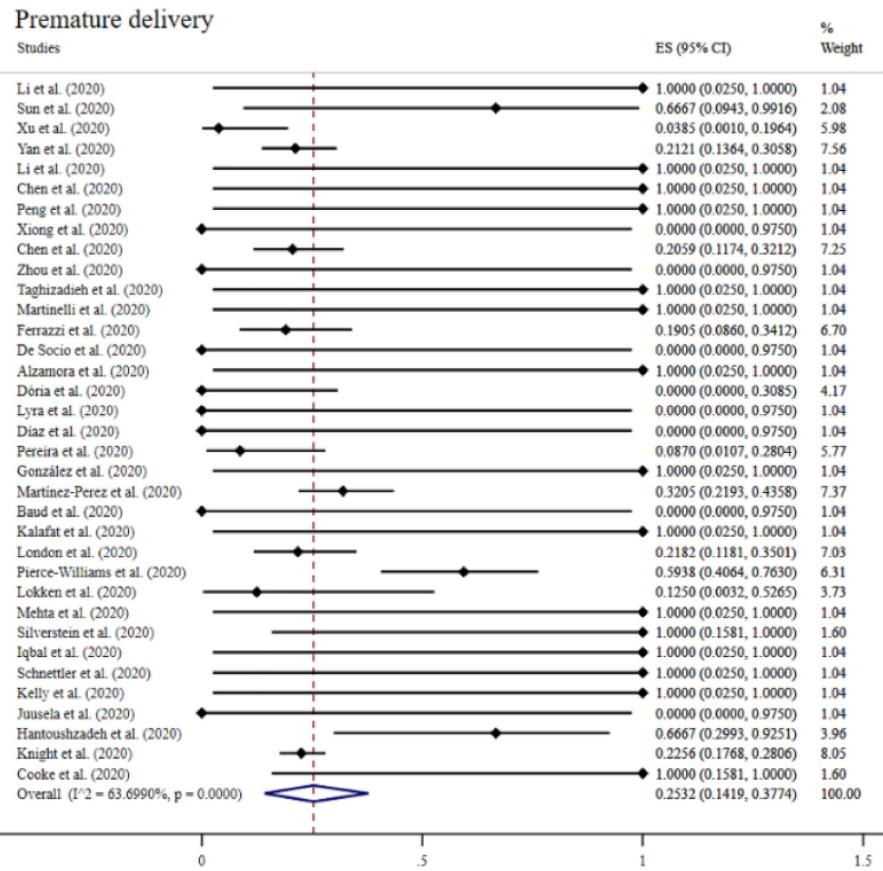


Figure 4: Forest plots of pooled prevalence of premature delivery.

Table 4: Neonatal outcomes and samples PCR results.

Types	n (studies)	Event	Total	Proportion, %	95% CI, %	Heterogeneity			
						$\chi^2$	$I^2$	Variance	p-Value
Neonatal outcomes	1 min Apgar score $\leq 7$	21	12	160	18.76 0.32–48.46	69.96	71.41	0.46	<0.01
	5 min Apgar score $\leq 7$	22	9	202	0.65 0.00–12.30	43.76	52.02	0.15	0.00
	Birth weight <2,500 g	15	12	33	30.65 9.84–54.98	14.39	2.72	0.01	0.42
	Asphyxia	22	4	223	<0.01 0.00–0.00	23.95	12.32	0.02	0.30
	Intubation	18	7	54	11.13 0.00–39.99	33.59	49.40	0.32	<0.01
	NICU	26	108	341	24.41 7.44–45.09	104.62	76.10	0.27	<0.01
	Neonatal death	32	5	599	0.00 0.00–0.00	21.16	<0.01	<0.01	0.91
Samples test	Nasopharynx swabs or sputum from newborns positive for SARS-CoV-2	30	21 <sup>a</sup>	559	<0.01 0.00–0.00	32.42	10.54	0.01	0.30
SARS-CoV-2	Cord blood	7	0	16	0.00 0.00–6.40	1.11	<0.01	<0.01	1.00
	Amniotic fluid	8	0	17	0.00 0.00–6.34	1.21	<0.01	<0.01	1.00
	Placenta	8	1	13	0.04 0.00–23.87	4.73	<0.01	<0.01	0.69
	Cervical or vaginal secretions	3	0	3	0.00 0.00–61.92	<0.01	<0.01	<0.01	<0.01
	Breast milk	6	0	10	0.00 0.00–20.72	0.22	<0.01	<0.01	1.00

<sup>a</sup>Six of the 21 newborns tested positive for SARS-CoV-2 RNA within the first 12 h after birth, two of which were from unassisted vaginal births and four were born by caesarean. No viral analyses were performed on umbilical cord blood, placenta, or vaginal secretions.

# TRANSMISSION & PREVENTION

## DEVELOPMENTS IN TRANSMISSION & PREVENTION

### DAYLIGHT-INDUCED ANTIBACTERIAL AND ANTIVIRAL COTTON CLOTH FOR OFFENSIVE PERSONAL PROTECTION

Tang P, Zhang Z, El-Moghazy AY, Wisuthiphaet N, Nitin N, Sun G.. ACS Appl Mater Interfaces. 2020 Oct 22. doi: 10.1021/acsami.0c15540. Online ahead of print.

Level of Evidence: Other - Mechanism-based reasoning

#### BLUF

Biologic engineers from the Department of Biological and Agricultural Engineering at University of California, Davis subjected cationic cotton fabrics to chemisorption with photosensitizers Rose Bengal (Rb) and anthraquinone-2-sulfonic acid sodium salt monohydrate (2-AQS) to synthesize antibacterial/antiviral cotton fabrics (PIFs) for use in face masks (Figure 1). The study found that the PIFs reduced bacterial counts of *E. Coli* and *L. Innocua* by 99.999% (Table 1) even after three washes and seven days of light exposure (Table 3). Though they did not investigate PIF's antiviral capabilities specifically, authors suggest this method could potentially be used to create bactericidal masks that may reduce transmission of SARS-CoV-2.

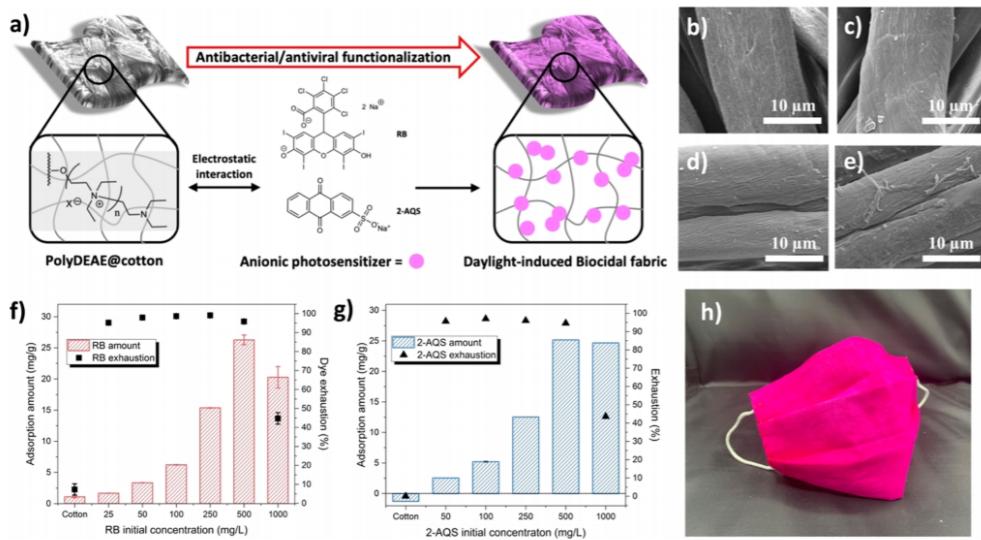
#### ABSTRACT

Cotton fabrics with durable and reusable daylight-induced antibacterial/antiviral functions were developed by using a novel fabrication process, which employs strong electrostatic interaction between cationic cotton fibers and anionic photosensitizers. The cationic cotton contains polycationic short chains produced by a self-propagation of 2-diehtylaminoethyl chloride (DEAE-Cl) on the surface of cotton fibers. Then, the fabric (i.e., polyDEAE@cotton) can be readily functionalized with anionic photosensitizers like rose Bengal and sodium 2-anthraquinone sulfate to produce biocidal reactive oxygen species (ROS) under light exposure and consequently provide the photo-induced biocidal functions. The biocidal properties of the photo-induced fabrics (PIFs) were demonstrated by ROS production measurements, bactericidal performance against bacteria (e.g., *E. coli* and *L. innocua*), and antiviral results against T7 bacteriophage. The PIFs achieved 99.9999% (6 log) reductions against bacteria and the bacteriophage within 60 min of daylight exposure. Moreover, the PIFs showcase excellent washability and photostability, making them ideal materials for reusable face masks and protective suits with improved biological protections compared with traditional PPE. This work demonstrated that the cationized cotton could serve as a platform for different functionalization applications, and the resulting fiber materials could inspire the development of reusable and sustainable PPE with significant bioprotective properties to fight the COVID-19 pandemic as well as the spread of other contagious diseases.

#### FIGURES

Table 1. Surface Hydrophobicity and Daylight-Induced Antibacterial Function of PS-Adsorbed polyDEAE@Cotton Fabrics

samples	WCA (°) (1 s/20 s)	the reduction rate of bacterial count (%)			
		30 min	60 min	30 min	60 min
Pristine cotton	0/0	0.00%	0.00%	0.00%	0.00%
polyDEAE@cotton	0/0	98.50%	99.25%	85.75%	96.19%
50 mg/L RB	108.2/0	99.99%	99.9999%	99.999%	99.999%
100 mg/L RB	114.2/0	77.50%	99.99%	99.999%	99.999%
250 mg/L RB	122.0/120.0	6.07%	99.29%	99.98%	99.999%
250 mg/L AQS	85.0/0	99.97%	99.9999%	99.98%	99.98%
500 mg/L AQS	110.0/0	99.9999%	99.9999%	99.999%	99.999%



**Figure 1.** (a) Schematic illustration of the fabrication of daylight-induced antibacterial and antiviral textiles. SEM images of (b) cotton, (c) polyDEAE@cotton, and (d) RB-dyed polyDEAE@cotton. (e) 2-AQS-dyed polyDEAE@cotton. Adsorption amount and dye exhaustion of (f) RB and (g) 2-AQS on polyDEAE@cotton with different initial concentrations. The “cotton” in the x axis means pristine cotton dyed with 250 mg/L RB or 2-AQS. (h) Design of a face mask based on PIFs.

**Table 3. Washability and Photostability of PS-Dyed polyDEAE@Cotton Fabrics in Terms of Antibacterial Functions (60 min Daylight Irradiation)**

samples	the reduction rate of bacterial count (%)									
	E. coli ( $10^5$ CFU/mL)			L. innocua ( $10^5$ CFU/mL)						
	before wash	1st wash	2nd wash <sup>a</sup>	3rd wash <sup>a</sup>	after 7 days of light exposure	Before wash	1st wash	2nd wash <sup>a</sup>	3rd wash <sup>a</sup>	after 7 days of light exposure
50 mg/L RB	99.9999%	99.9997%	99.9999%	99.9999%	99.9999%	99.9999%	99.99%	99.9999%	99.9999%	99.999%
100 mg/L RB	99.99%	99.9995%	99.99%	99.98%	99.9999%	99.999%	99.999%	99.999%	99.999%	99.999%
250 mg/L AQS	99.9999%	65.71%			99.74%	99.999%	99.94%			98.10%

<sup>a</sup>The wash was performed with Lander-O-Meter and each washing equals to 5 times of household hand washes.

## PREVENTION IN THE HOSPITAL

### COVID-19 SCREENING: ARE FOREHEAD TEMPERATURE MEASUREMENTS DURING COLD OUTDOOR TEMPERATURES REALLY HELPFUL?

Dzien C, Halder W, Winner H, Lechleitner M.. Wien Klin Wochenschr. 2020 Oct 23:1-5. doi: 10.1007/s00508-020-01754-2. Online ahead of print.

Level of Evidence: 3 - Non-randomized controlled cohort/follow-up study

#### BLUF

Investigators within Internal medicine at Landeskrankenhaus Hochzirl-Natters (Australialia) performed a cohort study where the forehead temperature of 101 healthy male and female employees of a hospital in Tyrol, Austria was measured upon entrance to the hospital and after several subsequent time points. They found that forehead temperatures were the lowest upon entrance into the hospital due to the cold outdoor climate (-5.5 °C and 0 °C) and did not reach a steady-state until approximately 60 minutes after entrance (Figure 1). This study suggests that forehead temperatures may not be an effective screening tool for infectious disease such as COVID-19 in locations with a cold climate and that further screening measures are necessary.

## ABSTRACT

**BACKGROUND:** Body temperature control is a frequently used screening test for infectious diseases, such as Covid-19 (Sars-CoV-2). We used this procedure to test the body temperature of staff members in a hospital in Tyrol (Austria), where the Covid-19 disease occurred in March 2020. The hospital is located in a mountain area at 995 m above sea level with low outdoor temperatures during early spring season. Under these conditions, we analyzed whether forehead temperature control offers a sufficient screening tool for infectious diseases. **METHODS:** Forehead temperature of 101 healthy male and female employees was measured with an infrared thermometer directly after entering the hospital (0 min), followed by further controls after 1 min, 3 min, 5 min and 60 min. We also tracked the outside temperature and the temperature at the entrance hall of the hospital. **RESULTS:** Complete data of body temperature were available for 46 female and 46 male study participants. The average forehead temperature measured directly after entrance to the hospital was the lowest (0 min)  $33.17 \pm 1.45$  C, and increased constantly to  $34.90 \pm 1.49$  C after 1 min,  $35.77 \pm 1.10$  C after 3 min,  $36.08 \pm 0.79$  C after 5 min, and  $36.6 \pm 0.24$  C after 60 min. The outside temperature ranged between -5.5 C and 0 C, the indoor temperature had a constant value of 20.5 C. **CONCLUSION:** Our results indicate that forehead infrared temperature control is not an appropriate tool to screen for infectious disease directly at the entrance of a building, at least during early spring season with cold outdoor temperatures.

## FIGURES

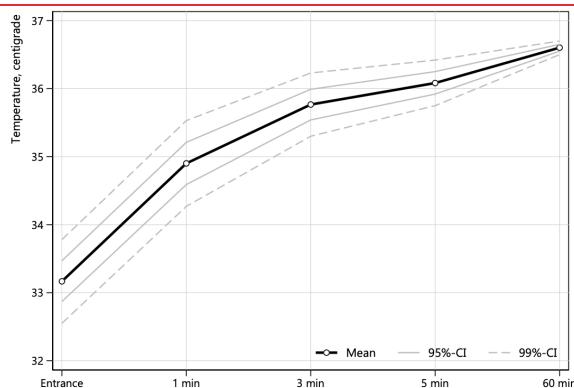


Figure. 1 Temperature profiles at different measuring times along with 5% CI and 0.01% CI

## MANAGEMENT

### ACUTE CARE

#### EFFICACY OF TOCILIZUMAB IN PATIENTS HOSPITALIZED WITH COVID-19

Stone JH, Frigault MJ, Serling-Boyd NJ, Fernandes AD, Harvey L, Foulkes AS, Horick NK, Healy BC, Shah R, Bensaci AM, Woolley AE, Nikiforow S, Lin N, Sagar M, Schrager H, Huckins DS, Axelrod M, Pincus MD, Fleisher J, Sacks CA, Dougan M, North CM, Halvorsen YD, Thurber TK, Dagher Z, Scherer A, Wallwork RS, Kim AY, Schoenfeld S, Sen P, Neilan TG, Perugino CA, Unizony SH, Collier DS, Matza MA, Yinh JM, Bowman KA, Meyerowitz E, Zafar A, Drobni ZD, Bolster MB, Kohler M, D'Silva KM, Dau J, Lockwood MM, Cubbinson C, Weber BN, Mansour MK; BACC Bay Tocilizumab Trial Investigators.. N Engl J Med. 2020 Oct 21. doi: 10.1056/NEJMoa2028836. Online ahead of print.

Level of Evidence: 2 - Randomized trial or observational study with dramatic effect

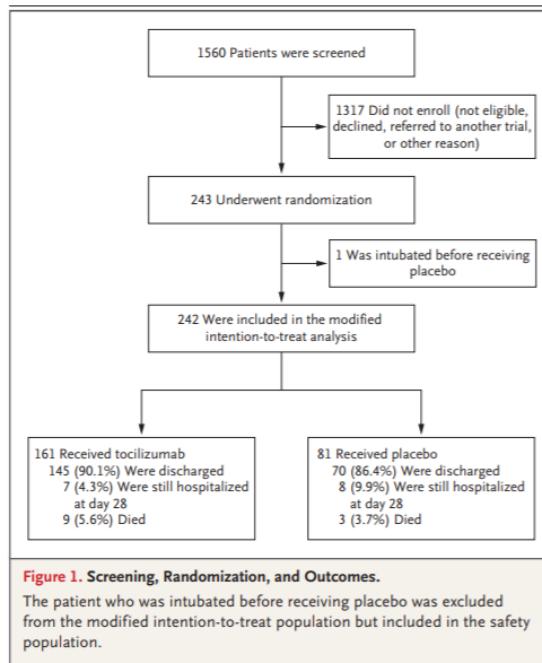
#### BLUF

A multidisciplinary team of physicians from various hospitals in Massachusetts described a placebo-controlled, double-blind randomized clinical trial of COVID-19 positive patients not on mechanical ventilation (n=242; Figure 1) hospitalized between April 20 and June 15, 2020. They used intention-to-treat analysis (Table 2, Figure 2) and found that patients who received tocilizumab (an interleukin-6 antagonist; n=161) had similar rates of death or intubation (HR 0.83, 95%CI 0.38-1.81), worsened condition (HR 1.11, 95%CI 0.59-2.1), and supplemental oxygen requirement (HR 0.94, 95%CI 0.67-1.3) compared to the non-treatment control group (n=81). Authors suggest tocilizumab may not be an effective treatment in reducing risk of intubation or death for non-ventilated (moderately ill) COVID-19 patients but recommend further studies to confirm these findings.

#### ABSTRACT

**BACKGROUND:** The efficacy of interleukin-6 receptor blockade in hospitalized patients with coronavirus disease 2019 (Covid-19) who are not receiving mechanical ventilation is unclear. **METHODS:** We performed a randomized, double-blind, placebo-controlled trial involving patients with confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, hyperinflammatory states, and at least two of the following signs: fever (body temperature >38 C), pulmonary infiltrates, or the need for supplemental oxygen in order to maintain an oxygen saturation greater than 92%. Patients were randomly assigned in a 2:1 ratio to receive standard care plus a single dose of either tocilizumab (8 mg per kilogram of body weight) or placebo. The primary outcome was intubation or death, assessed in a time-to-event analysis. The secondary efficacy outcomes were clinical worsening and discontinuation of supplemental oxygen among patients who had been receiving it at baseline, both assessed in time-to-event analyses. **RESULTS:** We enrolled 243 patients; 141 (58%) were men, and 102 (42%) were women. The median age was 59.8 years (range, 21.7 to 85.4), and 45% of the patients were Hispanic or Latino. The hazard ratio for intubation or death in the tocilizumab group as compared with the placebo group was 0.83 (95% confidence interval [CI], 0.38 to 1.81; P = 0.64), and the hazard ratio for disease worsening was 1.11 (95% CI, 0.59 to 2.10; P = 0.73). At 14 days, 18.0% of the patients in the tocilizumab group and 14.9% of the patients in the placebo group had had worsening of disease. The median time to discontinuation of supplemental oxygen was 5.0 days (95% CI, 3.8 to 7.6) in the tocilizumab group and 4.9 days (95% CI, 3.8 to 7.8) in the placebo group (P = 0.69). At 14 days, 24.6% of the patients in the tocilizumab group and 21.2% of the patients in the placebo group were still receiving supplemental oxygen. Patients who received tocilizumab had fewer serious infections than patients who received placebo. **CONCLUSIONS:** Tocilizumab was not effective for preventing intubation or death in moderately ill hospitalized patients with Covid-19. Some benefit or harm cannot be ruled out, however, because the confidence intervals for efficacy comparisons were wide. (Funded by Genentech; ClinicalTrials.gov number, NCT04356937.).

## FIGURES



**Table 4.** Adverse Events in the Safety Population.\*

Event	Tocilizumab (N=161)	Placebo (N=82)	P Value
	no. of patients (%)		
Death	9 (5.6)	4 (4.9)†	0.81
Hypersensitivity reaction to infusion	2 (1.2)	2 (2.4)	0.52
Infection of grade ≥3	13 (8.1)	14 (17.1)	0.03
Grade 3	12 (7.5)	14 (17.1)	
Grade 4	1 (0.6)	0	
Myocardial infarction	0	1 (1.2)	0.15
Deep venous thrombosis	2 (1.2)	3 (3.7)	0.18
Pulmonary embolism	2 (1.2)	2 (2.4)	0.47
Stroke	2 (1.2)	0	0.31
Seizure	0	1 (1.2)	0.13
Arterial ischemia	1 (0.6)	0	0.49
Gastrointestinal perforation	0	0	—
Demyelinating disorder	0	0	—
Elevated liver-function values			
ALT, grade ≥3	8 (5.0)	4 (4.9)	0.99
Grade 3	8 (5.0)	4 (4.9)	
Grade 4	0	0	
AST, grade ≥3	6 (3.7)	3 (3.7)	0.99
Grade 3	6 (3.7)	2 (2.4)	
Grade 4	0	1 (1.2)	
Neutropenia, grade ≥3	22 (13.7)	1 (1.2)	0.002
Grade 3	21 (13.0)	1 (1.2)	
Grade 4	1 (0.6)	0	
Thrombocytopenia, grade ≥3	1 (0.6)	0	0.51
Grade 3	1 (0.6)	0	
Grade 4	0	0	
Bleeding	0	1 (1.2)	0.15
Other‡	21 (13.0)	14 (17.1)	0.15

\* The percentage of patients who had at least one occurrence of each type of adverse event is reported. Grade was calculated as the maximum grade reported across occurrences within a patient. The percentages of patients with adverse events were compared with the use of a Mantel-Haenszel test stratified according to enrolling site without adjustment for multiple comparisons. ALT denotes alanine aminotransferase, and AST aspartate aminotransferase.

† One patient who died was intubated before receiving placebo and was excluded from the modified intention-to-treat population but included in the safety population.

‡ Other events are listed in detail in Table S6.

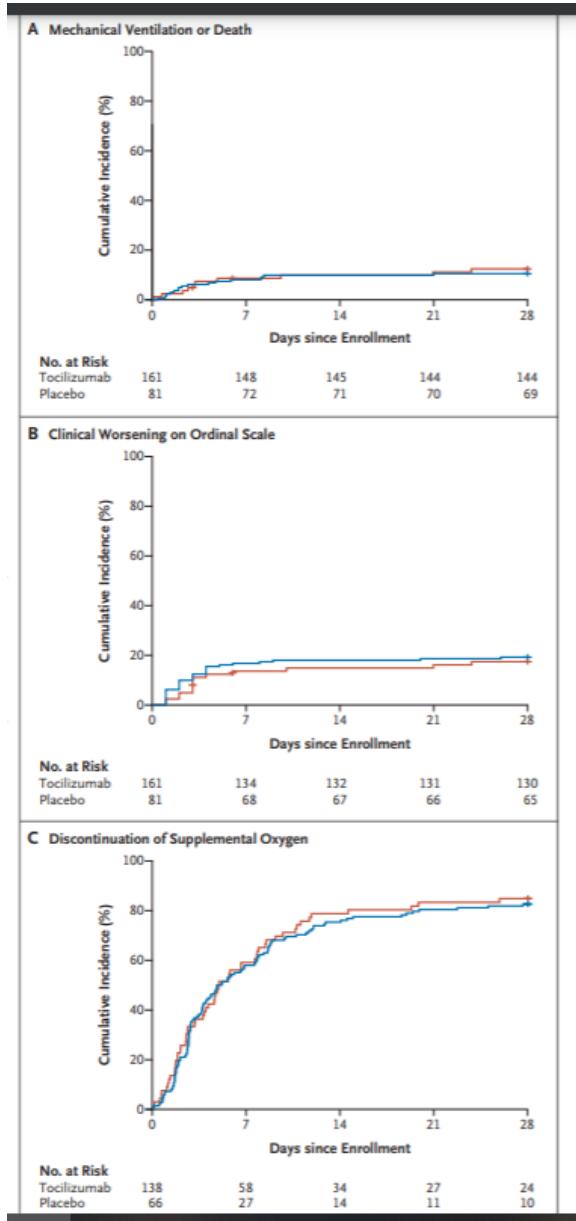


Figure 2. Kaplan-Meier Analyses of Efficacy Outcomes. Tocilizumab Placebo Shown are Kaplan-Meier curves for the time-to-event analyses of mechanical ventilation or death (Panel A); clinical worsening, defined as an increase in score on an ordinal clinical improvement scale (scores range from 1 to 7, with higher scores indicating worse clinical condition) by at least 1 point among patients who had been receiving supplemental oxygen at baseline or at least 2 points among those who had not been receiving supplemental oxygen at baseline (Table S2) (Panel B); and discontinuation of supplemental oxygen among patients who had been receiving it at baseline (Panel C).

# ADJUSTING PRACTICE DURING COVID-19

## CHRONIC COVID SYNDROME: NEED FOR AN APPROPRIATE MEDICAL TERMINOLOGY FOR LONG-COVID AND COVID LONG-HAULERS

Baig AM.. J Med Virol. 2020 Oct 23. doi: 10.1002/jmv.26624. Online ahead of print.

Level of Evidence: Other - Expert Opinion

### BLUF

A letter to the editor by Dr. Abdul Mannan Baig from Aga Khan University in Pakistan proposes implementation of "Chronic COVID Syndrome (CCS)" as the appropriate nomenclature used in published work regarding the long term effects of COVID-19 infection, as well as a staging system based on the predominant organ involved in infection, so hospitals can anticipate complications and better clinically manage patients (Figure 1). Authors suggest use of CCS is more proper than "long-COVID" or "long-haulers" that have been utilized in other recently published articles to represent chronic COVID-19 infection.

### ABSTRACT

With the ongoing pandemic of coronavirus diseases (COVID-19) caused by SARS-CoV-2, there has been a surge in research and publications related to its pathogenesis and the clinical presentation of the affected patients. Many aspects of this novel virus have raised confusion including the naming of the virus and the disease it causes, the staging of its clinical presentation to highlight a few such occurrences. An emerging aspect of the clinical presentation related to COVID-19 is the long-term effects, which in the absence of any consensus has been termed as long-covid and long-haulers in recent publications. As the COVID-19 is a zoonotic infection and comes under a medically related disease, the term chronic covid syndrome (CCS) would be a more traditional way of symbolizing the so-called long-covid and long-haulers in COVID-19. Though the renaming of this chronic state of now well-recognized chronicity seen in COVID-19 would not affect its prognosis, this is much needed to recognize this entity with a more appropriate nomenclature as published work is making its way into databases like Google Scholar and PubMed. This article is protected by copyright. All rights reserved.

### FIGURES

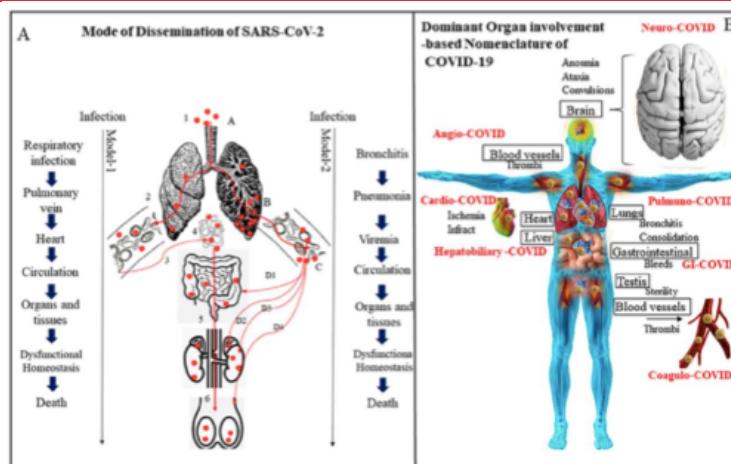


Figure 1. Spread of SARS-CoV-2 in the human body. (A) Entry into the respiratory tract can lead to dissemination (Model-1) via vascular spread sequence (arrows-left panel) and/or pneumonic consolidation (Model-2) (arrows-right panel) resulting in the fatal outcome (B) An ACE2 expression dependent dominant organ involvement pattern may emerge (red-text) after three weeks at present called long-COVID that needs better terminology like chronic COVID syndrome (CCS).

## MEDICAL SUBSPECIALTIES

### CARDIOLOGY

#### **CORONAVIRUS DISEASE 2019 AND THE ATHLETIC HEART: EMERGING PERSPECTIVES ON PATHOLOGY, RISKS, AND RETURN TO PLAY**

Kim JH, Levine BD, Phelan D, Emery MS, Martinez MW, Chung EH, Thompson PD, Baggish AL.. JAMA Cardiol. 2020 Oct 26. doi: 10.1001/jamacardio.2020.5890. Online ahead of print.

Level of Evidence: Other - Guidelines and Recommendations

#### **BLUF**

A literature review conducted across various cardiovascular medical institutions throughout the United States aimed to refine previous American College of Cardiology's Sports and Exercise Cardiology recommendations on a conservative return-to-play approach with cardiac risk stratification for post-COVID-19 athletes, and to expand the approach to include the possibility of myocarditis and increased risk for sudden cardiac death during exercise despite a mild or asymptomatic infection. As we await the arrival of critical data regarding potential cardiac dangers in athletes, authors recommend return-to-play protocols for various levels and ages of athletes (Figures 1, 2, 3).

#### **ABSTRACT**

**Importance:** Cardiac injury with attendant negative prognostic implications is common among patients hospitalized with coronavirus disease 2019 (COVID-19) infection. Whether cardiac injury, including myocarditis, also occurs with asymptomatic or mild-severity COVID-19 infection is uncertain. There is an ongoing concern about COVID-19-associated cardiac pathology among athletes because myocarditis is an important cause of sudden cardiac death during exercise. **Observations:** Prior to relaxation of stay-at-home orders in the US, the American College of Cardiology's Sports and Exercise Cardiology Section endorsed empirical consensus recommendations advising a conservative return-to-play approach, including cardiac risk stratification, for athletes in competitive sports who have recovered from COVID-19. Emerging observational data coupled with widely publicized reports of athletes in competitive sports with reported COVID-19-associated cardiac pathology suggest that myocardial injury may occur in cases of COVID-19 that are asymptomatic and of mild severity. In the absence of definitive data, there is ongoing uncertainty about the optimal approach to cardiovascular risk stratification of athletes in competitive sports following COVID-19 infection. **Conclusions and Relevance:** This report was designed to address the most common questions regarding COVID-19 and cardiac pathology in athletes in competitive sports, including the extension of return-to-play considerations to discrete populations of athletes not addressed in prior recommendations. Multicenter registry data documenting cardiovascular outcomes among athletes in competitive sports who have recovered from COVID-19 are currently being collected to determine the prevalence, severity, and clinical relevance of COVID-19-associated cardiac pathology and efficacy of targeted cardiovascular risk stratification. While we await these critical data, early experiences in the clinical oversight of athletes following COVID-19 infection provide an opportunity to address key areas of uncertainty relevant to cardiology and sports medicine practitioners.

## FIGURES

**Figure 1. Proposed Coronavirus Disease 2019 (COVID-19) Return-to-Play Algorithm for Athletes in Competitive High School Sports**

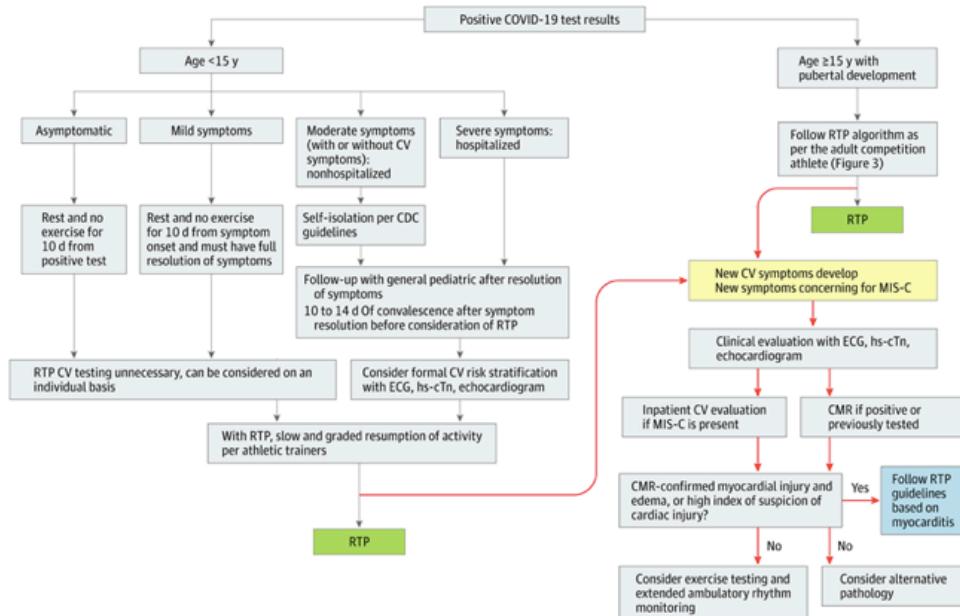


Figure 1. Proposed Coronavirus Disease 2019 (COVID-19) Return-to-Play Algorithm for Athletes in Competitive High School Sports

**Figure 2. Proposed Coronavirus Disease 2019 (COVID-19) Return-to-Play Algorithm for Recreational Masters Athletes**

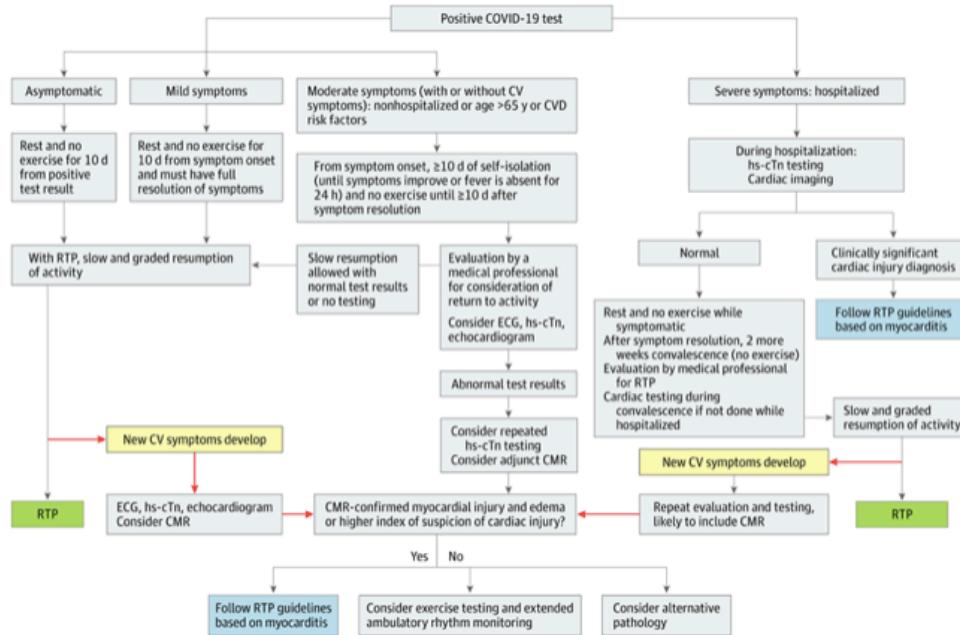


Figure 2: Proposed Coronavirus Disease 2019 (COVID-19) Return-to-Play Algorithm for Recreational Masters Athletes

**Figure 3. Proposed Coronavirus Disease 2019 (COVID-19) Return-to-Play Algorithm for Adult Athletes in Competitive Sports**

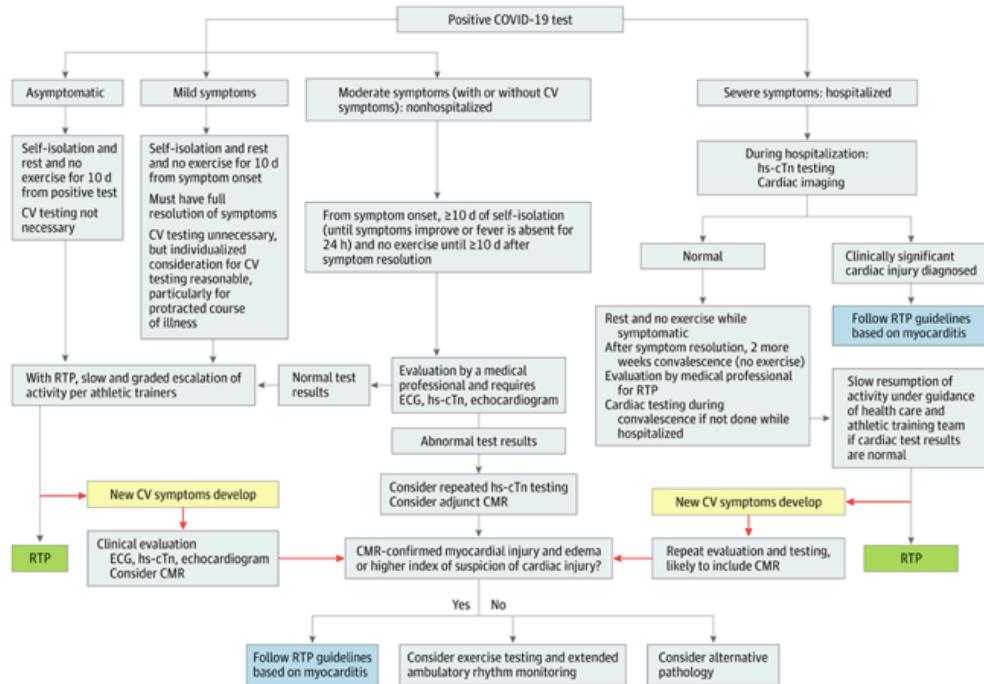


Figure 3. Proposed Coronavirus Disease 2019 (COVID-19) Return-to-Play Algorithm for Adult Athletes in Competitive Sports

## R&D: DIAGNOSIS & TREATMENTS

### DEVELOPMENTS IN TREATMENTS

#### **COVID-19, HYPERCOAGULABILITY AND CAUTIOUSNESS WITH CONVALESCENT PLASMA**

Sanfilippo F, La Rosa V, Oliveri F, Astuto M.. Am J Respir Crit Care Med. 2020 Oct 21. doi: 10.1164/rccm.202008-3139LE.  
Online ahead of print.

Level of Evidence: Other - Expert Opinion

#### **BLUF**

Physicians from Azienda Ospedaliero Universitaria Policlinico Vittorio Emanuele Catania believe that the results of Patel et al.'s (2020) cohort study, which highlighted the large role of hypercoagulability in COVID-19-associated respiratory failure, may be used to critique Joyner et al.'s (2020) results on the safety of convalescent plasma (CP) therapy. Specifically, they argue that Joyner et al.'s study was limited by a short time of observation (4 hours) for side effects of CP and a lack of investigation into potential adverse events of CP administration in the setting of underlying hypercoagulability. For this reason, future studies on CP should include longer periods of observation for side effects of CP therapy and consider the potential adverse outcomes of using CP therapy in hypercoagulable, COVID-19 patients.

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