

The Daily COVID-19 Literature Surveillance Summary

December 22, 2020



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COVID-19 Daily Literature Surveillance

COVID19LST



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

LEVEL OF EVIDENCE

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

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

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

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

How to cite the Levels of Evidence Table

OCEBM Levels of Evidence Working Group*. "The Oxford 2011 Levels of Evidence". Oxford Centre for Evidence-Based Medicine. <http://www.cebm.net/index.aspx?o=5653>

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EXECUTIVE SUMMARY

Climate

- Board members of the International Society of Vaccine (ISV) summarize their organization's recent efforts to [provide information and resources about COVID-19 vaccines](#) to members worldwide: they provide links to their recent virtual lecture series on COVID-19 vaccines and suggest their organization is a global leader on vaccine development that can provide balanced information to a variety of stakeholders. The authors encourage new researchers and developers to join the ISV at www.isv-online.org.

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CLIMATE

A TIMELY UPDATE OF GLOBAL COVID-19 VACCINE DEVELOPMENT

Klavinskis LS, Liu MA, Lu S.. Emerg Microbes Infect. 2020 Dec;9(1):2379-2380. doi: 10.1080/22221751.2020.1838246.
Level of Evidence: 5 - Opinion

BLUF

Board members of the International Society of Vaccine (ISV) summarize their organization's recent efforts to provide information and resources about COVID-19 vaccines to members worldwide. They provide links to their recent virtual lecture series on COVID-19 vaccines (Table 1) and suggest their organization is a global leader on vaccine development that can provide balanced information to a variety of stakeholders. The authors encourage new researchers and developers to join the ISV at www.isv-online.org.

SUMMARY

A detailed program for the ISV Congress in June and August 2020 can be found here: www.isvcongress.org

Recordings of presentations can be viewed at: https://www.youtube.com/channel/UC9_-f8tDAqOmVEZWqGeuFow

FIGURES

Table 1. List of congress speakers and titles of presentations.

Date	Name	Institute	Title of talk/panel discussion
Keynote Presentations			
June 22	Kwok-Yung Yuen	The University of Hong Kong	Overview of COVID-19; pathogenesis and epidemiology
	Nick Jackson	CEPI	Overview of COVID-19 Vaccine Development
July 21	Larry Corey	Fred Hutchinson Cancer Res. Center (COVID-19 Prevention Network)	COVID Vaccine Planning: The US Government Approach
	Marion Gruber	US FDA	Regulatory Considerations in the Development and Licensure of COVID-19 Vaccines
Aug 25	Myron Cohen	UNC-Chapel Hill	mAbs for COVID-19: Treatment and Prevention
	Lynda Stuart	Bill & Melinda Gates Foundation	COVID-19 Vaccine: How We Win the Race to Billions of Doses
Vaccine Product Updates			
June 22	Kate Broderick	Inovio Pharmaceuticals	Advantages of a DNA-based Approach to the Development of a COVID-19 Vaccine
	Barney Graham	VRC/NIAID/NIH	Rapid COVID-19 Vaccine Development Enabled by Prototype Pathogen Preparedness
	Sarah Gilbert	University of Oxford (Partner: AstraZeneca)	Rapid Progress with Development of ChAdOx1 nCoV-19
	Tao Zhu	CanSino Biological	Development of Adenovirus Vector Based COVID-19 Vaccine
July 21	Greg Glenn	Novavax	Progress with the Full Length Recombinant Spike Protein Nanoparticle Vaccine
	George Gao	China CDC	Development of Inactivated COVID-19 Vaccines
	Hanneke Schuitemaker	J& / Janssen	The Development of an Ad26-based SARS-CoV-2 Vaccine
	Kena Swanson	Pfizer (Partner: BioNTech)	COVID RNA Vaccine Candidate BNT162b1
Aug 25	Keith Chappell	The University of Queensland	Molecular Clamp Stabilized Recombinant Protein Subunit Vaccine for COVID-19
	John Shiver	Sanofi	Recombinant protein and mRNA Vaccine Candidates Against COVID-19
	Jacqueline Miller	Moderna	Moderna's Coronavirus Vaccine: Early Clinical Data and the COVE Phase III Efficacy and Safety Study
	Brian Ward	Medicago	Development of Plant-Derived SARS-CoV-2 Virus-Like Particle (CoVLP) Vaccine
Key Issue Panel Discussions			
June 22	Challenges for COVID-19 Vaccines Development: Are Human Challenge Studies Acceptable?		
	Peter Openshaw	Imperial College London	
	Stanley Perlman	University of Iowa	
	Stanley Plotkin	VaxConsult	
July 21	Challenges for COVID-19 Vaccines Development: The Roles of Animal Models		
	Bart Haagmans	Erasmus University	
	Vincent Munster	RML/NIH	
	Linda Saif	The Ohio State University	
Aug 25	The Role of T and B Cell Responses and Vaccine Assay Standards for Determining Efficacy		
	Alessandro Sette	La Jolla Institute of Immunology	
	Michel Nussenzweig	The Rockefeller University	
	Neil Almond	The National Institute for Biological Standards and Control (NIBSC), UK	

EPIDEMIOLOGY

SYMPTOMS AND CLINICAL PRESENTATION

ADULTS

COMPARISON OF COVID-19 INFECTIONS AMONG HEALTHCARE WORKERS AND NON-HEALTHCARE WORKERS

Kim R, Nachman S, Fernandes R, Meyers K, Taylor M, LeBlanc D, Singer AJ.. PLoS One. 2020 Dec 9;15(12):e0241956. doi: 10.1371/journal.pone.0241956. eCollection 2020.

Level of Evidence: 3 - Local non-random sample

BLUF

A retrospective cohort study conducted in an New York State emergency department between March 21, 2020 and June 2020 at Stony Brook University included 2,842 adult patients (193 healthcare workers (HCWs) and 2,649 non-healthcare workers) with positive SARS-CoV-2 RT-PCR test and found, upon presentation, lower frequency of tachypnea, hypoxemia, bilateral opacities on imaging, and lymphocytopenia among HCWs (Table 2). They also found that ICU admissions, need for invasive mechanical ventilation (IMV), and mortality were also lower among HCWs (Table 3). After controlling for confounding variables (Table 4), it was confirmed HCWs were less likely than non-HCWs to require hospital admission and there was no association of HCW having an increased risk of ICU admission, IMV, or mortality. These findings suggest HCWs with COVID-19 were more likely to have an identified COVID-19 exposure, present less-severely ill, and are less likely to require hospital admission. However, these results may be confounded by the fact that HCWs are generally younger and healthier at baseline, and previous literature has shown that HCWs may be at lower risk for comorbid chronic conditions.

ABSTRACT

OBJECTIVES: Healthcare workers face distinct occupational challenges that affect their personal health, especially during a pandemic. In this study we compare the characteristics and outcomes of Covid-19 patients who are and who are not healthcare workers (HCW). **METHODS:** We retrospectively analyzed a cohort of 2,842 adult patients with known HCW status and a positive SARS-CoV-2 RT-PCR test presenting to a large academic medical center emergency department (ED) in New York State from March 21 2020 through June 2020. Early in the pandemic we instituted a policy to collect data on patient occupation and exposures to suspected Covid-19. The primary outcome was hospital admission. Secondary outcomes were ICU admission, need for invasive mechanical ventilation (IMV), and mortality. We compared baseline characteristics and outcomes of Covid-19 adult patients based on whether they were or were not HCW using univariable and multivariable analyses. **RESULTS:** Of 2,842 adult patients (mean age 53+/-19 years, 53% male) 193 (6.8%) were HCWs and 2,649 (93.2%) were not HCWs. Compared with non-HCW, HCWs were younger (43 vs 53 years, $P<0.001$), more likely female (118/193 [61%] vs 1211/2649 [46%], $P<0.001$), and more likely to have a known Covid-19 exposure (161/193 [83%] vs 946/2649 [36%], $P<0.001$), but had fewer comorbidities. On presentation to the ED, HCW also had lower frequencies of tachypnea (12/193 [6%] vs 426/2649 [16%], $P<0.01$), hypoxemia (15/193 [8%] vs 564/2649 [21%], $P<0.01$), bilateral opacities on imaging (38/193 [20%] vs 1189/2649 [45%], $P<0.001$), and lymphocytopenia (6/193 [3%] vs 532/2649 [20%], $P<0.01$) compared to non-HCWs. Direct discharges home from the ED were more frequent in HCW 154/193 (80%) vs 1275/2649 (48%) $p<0.001$). Hospital admissions (38/193 [20%] vs 1264/2649 [47%], $P<0.001$), ICU admissions (7/193 [3%] vs 321/2649 [12%], $P<0.001$), need for IMV (6/193 [3%] vs 321/2649 [12%], $P<0.001$) and mortality (2/193 [1%] vs 219/2649 [8%], $P<0.01$) were lower than among non-HCW. After controlling for age, sex, comorbidities, presenting vital signs and radiographic imaging, HCW were less likely to be admitted (OR 0.6, 95%CI 0.3-0.9) than non HCW. **CONCLUSIONS:** Compared with non HCW, HCW with Covid-19 were younger, had less severe illness, and were less likely to be admitted.

FIGURES

Table 2. Signs, imaging and laboratory characteristics on presentation. Data are presented as numbers and percentages in parentheses unless otherwise specified.

	Non HCW	HCW	Difference in % unless otherwise specified (95% CI)
Fever>38° C	426 (16)	30 (16)	1 (-5-6)
Tachypnea (RR>24/min.)	335 (13)	12 (6)	7 (2-10)
Hypoxemia			
>94%	2065 (79)	176 (92)	-13 (-17 - -8)
89-93%	364 (14)	10 (5)	9 (4-12)
<88%	200 (8)	5 (3)	5 (1-7)
Bilateral opacities on imaging	1189 (45)	38 (20)	25 (18-31)
Leukopenia<4000/ml	157 (9)	9 (13)	-3 (-14-3)
Lymphocytopenia <1000/ml	532 (20)	12 (6)	14 (9-17)
Creatinine >1.5 mg/dL	272 (16)	5 (7)	9 (-1-14)
D-Dimer>750 mg/L	223 (23)	5 (10)	12 (-1-19)
CRP >8.2 mg/ml	650 (45)	21 (43)	2 (-13-16)
Procalcitonin>0.5 ng/ml	256 (18)	6 (13)	5 (-10-13)
AST>40 U/ml	721 (46)	30 (50)	-4 (-18-9)
Tropponin >0.06 ng/ml	130 (9)	2 (4)	5 (-6-9)
Mean (SD) length of symptoms prior to ED arrival, days	6 (7)	5 (5)	1.5 (0.5-2.5)

HCW: Healthcare worker; RR: Respiratory rate; SD: Standard deviation.

Table 2. Signs, imaging and laboratory characteristics on presentation. Data are presented as numbers and percentages in parentheses unless otherwise specified.

Table 3. Disposition. Data are presented as numbers and percentages in parentheses.

No. (%)	Non HCW	HCW	Difference in % unless otherwise specified (95% CI)
Discharged from ED	1275 (48)	154 (80)	-32 (-37 - -25)
Admitted to regular floor	1264 (48)	38 (20)	28 (21-34)
Direct admit to ICU	103 (4)	1 (0.5)	3 (1-4)
Died in ED	7 (0.3)	0 (0)	0.3 (-0.2-0.2)
Length of stay			
All	5.4 (10.1)	1.4 (4.0)	4.0 (3.3-4.7)
Discharged	0.05 (0.40)	0.02 (0.14)	0.03 (-0.04-0.09)
Admitted	10.5 (12.1)	6.9 (6.5)	3.6 (1.4-5.8)
Patients requiring IMV	255 (10)	6 (3)	7 (3-9)
Patients requiring ICU	321 (12)	7 (4)	8 (4-11)
Overall mortality	219 (8)	2 (1)	7 (4-9)

HCW: Healthcare worker; ED: Emergency department; CIU: Intensive care unit; IMV: Invasive mechanical ventilation.

Table 3. Disposition. Data are presented as numbers and percentages in parentheses.

	OR	95% CI
Hospital Admission		
Male sex	1.09	0.88–1.35
Age per year	1.05	1.04–1.06
Non-HCW	Reference	-
HCW	0.58	0.36–0.92
Temp > 38° C	2.10	1.57–2.81
Tachypnea >24/min.	6.00	3.56–10.11
Hypoxemia <94%	1.46	1.39–1.53
Any exposure	0.50	0.40–0.63
# comorbidities		
0	Reference	-
1	1.75	1.35–2.25
2+	4.06	3.01–5.47
Invasive Mechanical Ventilation		
Male	2.04	1.48–2.81
Age per year	0.99	0.98–1.00
Non-HCW	Reference	-
HCW	0.97	0.38–2.45
Temp > 38° C	1.30	0.92–1.83
Tachypnea > 24/min.	1.24	0.96–1.78
Hypoxemia <94%	1.09	1.06–1.12
Any exposure	1.22	0.88–1.68
# comorbidities		
0	Reference	-
1	1.36	0.91–2.04
2+	1.30	0.87–1.93
ICU Admission		
Male sex	1.73	1.30–2.29
Age per year	0.99	0.98–1.00
Non-HCW	Reference	-
HCW	0.80	0.33–1.91
Temp > 38° C	1.16	0.85–1.60
Tachypnea >24/min.	1.54	1.11–2.13
Hypoxemia	1.08	1.05–1.10
Any exposure	1.13	0.84–1.52
# comorbidities		
0	Reference	-
1	1.32	0.91–1.90
2+	1.40	0.97–2.00
Mortality		
Male	1.97	1.38–2.82
Age per year	1.05	1.04–1.07
Non-HCW	Reference	-
HCW	0.94	0.21–1.24
Temp > 38° C	0.77	0.48–1.22
Tachypnea >24/min.	1.45	0.97–2.16
Hypoxemia <94%	1.09	1.06–1.12
Any exposure	0.80	0.54–1.19
# comorbidities		
0	Reference	-
1	1.03	0.61–1.76
2+	1.50	0.94–2.41

<https://doi.org/10.1371/journal.pone.0241956.t004>

Table 4. Multivariable predictors of outcomes.

UNDERSTANDING THE PATHOLOGY

IN VITRO

COMPARATIVE MULTIPLEXED INTERACTOMICS OF SARS-COV-2 AND HOMOLOGOUS CORONAVIRUS NONSTRUCTURAL PROTEINS IDENTIFIES UNIQUE AND SHARED HOST-CELL DEPENDENCIES

Davies JP, Almasy KM, McDonald EF, Plate L.. ACS Infect Dis. 2020 Dec 2. doi: 10.1021/acsinfecdis.0c00500. Online ahead of print.

Level of Evidence: 5 - Mechanism-based reasoning

BLUF

An in vitro study conducted by immunologists at Vanderbilt Institute for Infection in Nashville, Tennessee analyzed virus-host and protein-protein interactions of two non-structural coronavirus proteins (nsp2 and nsp4) that are critical for viral replication in 3 members of the beta coronavirus family to uncover how SARS-CoV-2 transmission mechanisms differ from other coronaviruses. They found SARS-CoV-2 homologs had unique interaction nodules compared to SARS-CoV-1 (Figures 3,4), including a lack of both nsp4 interactions with ubiquitin ligase complexes and the cholesterol biosynthesis pathway. Authors also highlight enrichment of interactions between mitochondria-associated membrane proteins and nsp2/nsp4 in SARS-CoV-2 (Figure 5). These findings outline potential molecular pathways for increased SARS-CoV-2 virulence, which may offer therapeutic targets to combat COVID-19.

ABSTRACT

Human coronaviruses (hCoVs) have become a threat to global health and society, as evident from the SARS outbreak in 2002 caused by SARS-CoV-1 and the most recent COVID-19 pandemic caused by SARS-CoV-2. Despite a high sequence similarity between SARS-CoV-1 and -2, each strain has a distinctive virulence. A better understanding of the basic molecular mechanisms mediating changes in virulence is needed. Here, we profile the virus-host protein-protein interactions of two hCoV nonstructural proteins (nsps) that are critical for virus replication. We use tandem mass tag-multiplexed quantitative proteomics to sensitively compare and contrast the interactomes of nsp2 and nsp4 from three betacoronavirus strains: SARS-CoV-1, SARS-CoV-2, and hCoV-OC43-an endemic strain associated with the common cold. This approach enables the identification of both unique and shared host cell protein binding partners and the ability to further compare the enrichment of common interactions across homologues from related strains. We identify common nsp2 interactors involved in endoplasmic reticulum (ER) Ca²⁺ signaling and mitochondria biogenesis. We also identify nsp4 interactors unique to each strain, such as E3 ubiquitin ligase complexes for SARS-CoV-1 and ER homeostasis factors for SARS-CoV-2. Common nsp4 interactors include N-linked glycosylation machinery, unfolded protein response associated proteins, and antiviral innate immune signaling factors. Both nsp2 and nsp4 interactors are strongly enriched in proteins localized at mitochondria-associated ER membranes suggesting a new functional role for modulating host processes, such as calcium homeostasis, at these organelle contact sites. Our results shed light on the role these hCoV proteins play in the infection cycle, as well as host factors that may mediate the divergent pathogenesis of OC43 from SARS strains. Our mass spectrometry workflow enables rapid and robust comparisons of multiple bait proteins, which can be applied to additional viral proteins. Furthermore, the identified common interactions may present new targets for exploration by host-directed antiviral therapeutics.

FIGURES

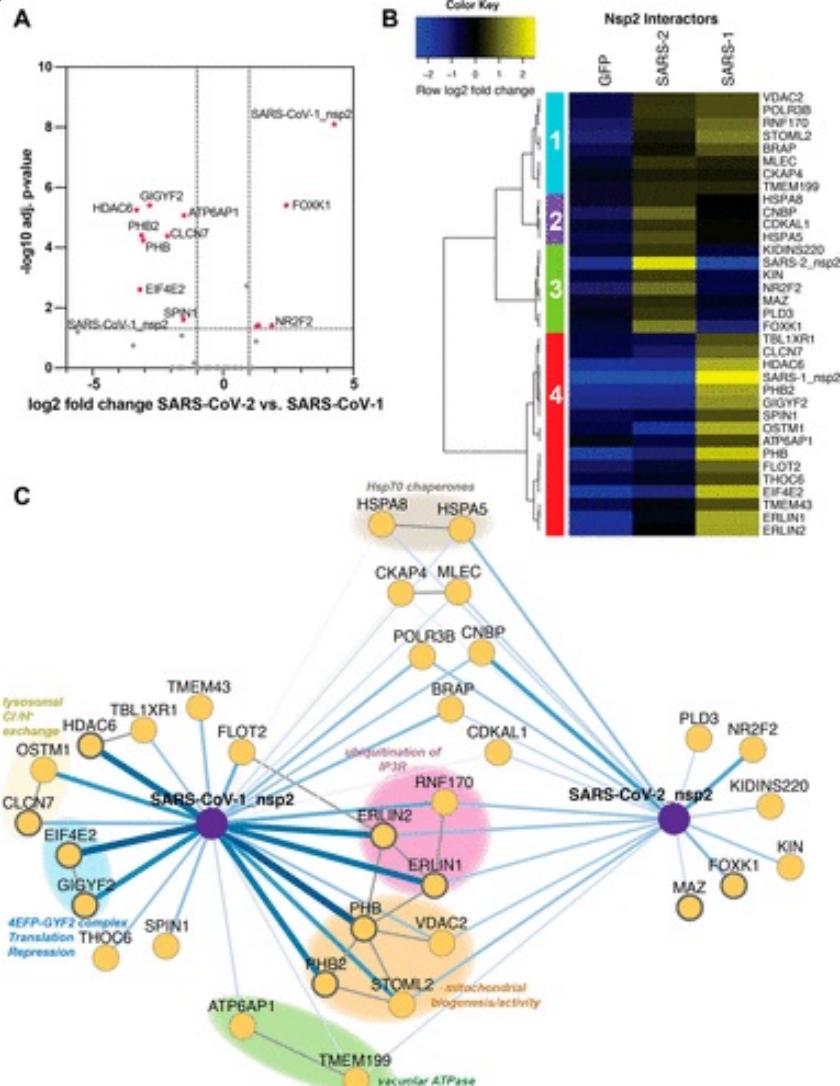


Figure 3. Quantitative comparison of SARS-CoV-1 and SARS-CoV-2 nsp2 interactors.

(A) Volcano plot comparing interactions between nsp2 homolog from SARS-CoV-1 and SARSCoV-2. Only high- and medium confidence interactors of nsp2 are shown. Highlighted proteins meet the filter criteria of adjusted p-value < 0.05 and $|\log_2 \text{fold change}| > 1$. (B) Heatmap comparing the enrichment of SARS-CoV-1 and SARS-CoV-2 nsp2 interactors compared to GFP control. $\log_2 \text{fold change}$ is color-coded and centered by row (blue low, yellow high enrichment). Hierarchical clustering using Ward's method shown on the left was carried out on euclidean distances of $\log_2 \text{fold changes}$ scaled by row. Clusters 1 and 2 corresponds to shared interactors of SARS-CoV-1 and -2 nsp2, while cluster 3 and 4 for are unique interactors for SARS-CoV-2 and SARS-CoV-1 nsp2, respectively. (C) Protein-protein interaction (PPI) network map of nsp2 homologs. Blue lines indicate viralhost PPIs, where line width corresponds to fold enrichment compared to the GFP control. Grey lines indicate annotated host-host PPIs in STRING (score > 0.75). Groups of interactors with a common functional role are highlighted.

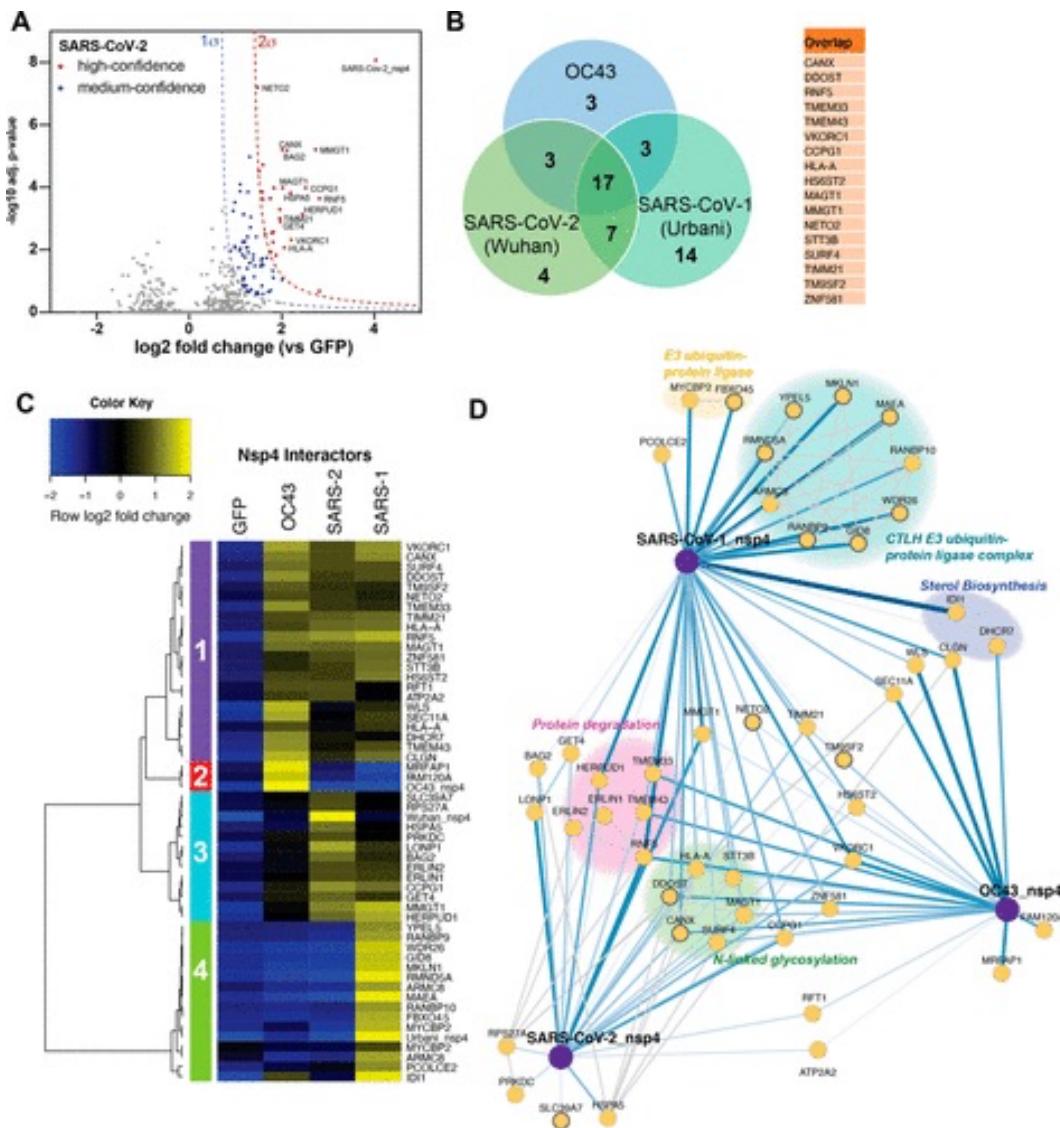


Figure 4. Comparative profiling of nsp4 interactions.

(A) Volcano plot of the SARS-CoV-2 nsp4 datasets to identify medium- and high-confidence interactors. Plotted are log2 TMT intensity differences for proteins between nsp4 bait channels and GFP mock transfections versus -log10 adjusted p-values. Curves for the variable cutoffs used to define high-confidence (red) or medium confidence (blue) interactors are shown. 1s = 0.66. Equivalent volcano plot for SARS-CoV-1 and OC43 nsp4 are shown in Figure S5B-C. (B) Venn diagram of interactors from nsp4 homologs. Overlapping nsp4 interactors between all strains are listed in the adjacent table. (C) Heatmap comparing the enrichment of interactors for the different nsp4 homologs. log2 fold change is color-coded and centered by row (blue low, yellow high enrichment). Hierarchical clustering using Ward's method shown on the left was carried out on euclidean distances of log2 fold changes scaled by row. Clusters 1 corresponds to shared interactors of SARS-CoV-1, -2, and OC43 nsp4. Cluster 2, and 4 contain unique interactors for OC43 and SARS-CoV-1 nsp4, respectively, while cluster 3 contains shared interactors of SARS-CoV-1 and SARS-CoV2. (D) Protein-protein interaction (PPI) network map of interactors of nsp4 homolog. Blue lines indicate measured viral-host PPIs, where line width corresponds to fold enrichment compared to the GFP control. Grey lines indicate annotated host-host PPIs in STRING (score > 0.75). Groups of interactors with a common functional role are highlighted.

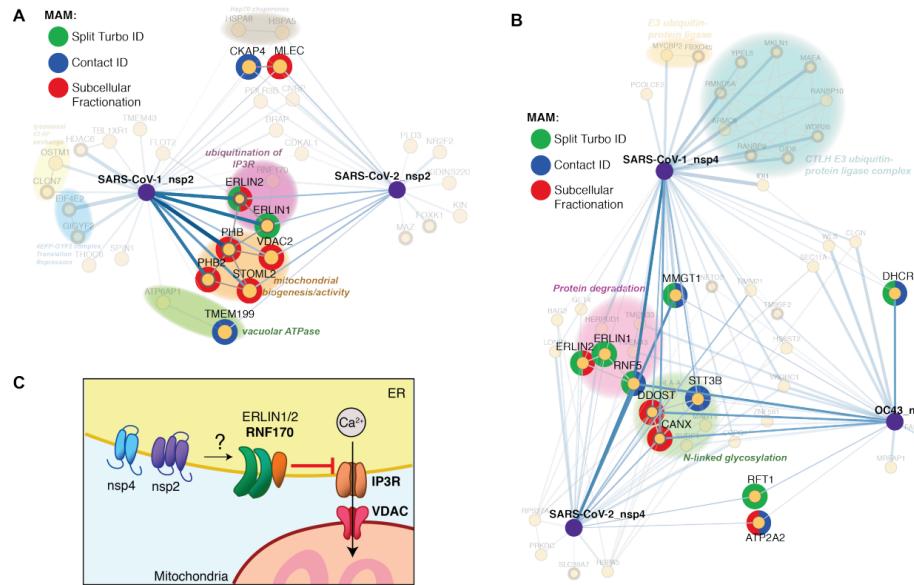


Figure 5. Enrichment of mitochondria-associated membrane (MAM) proteins as nsp2 and nsp4 interactors.

(A–B) Interactors of nsp2 (A) and nsp4 (B) homolog annotated for MAM proteins. The lists of interactors were cross-referenced with previous publications profiling the MAM proteome (SplitTurbo ID, Contact-ID, and subcellular fractionation). (C) Proposed model for how SARS-CoV nsp2 and nsp4 utilize ERLIN1/2 and interacting protein factors to regulate ER Ca²⁺ signaling at MAMs.

TRANSMISSION & PREVENTION

PREVENTION IN THE COMMUNITY

IMPLEMENTING MITIGATION STRATEGIES IN EARLY CARE AND EDUCATION SETTINGS FOR PREVENTION OF SARS-COV-2 TRANSMISSION - EIGHT STATES, SEPTEMBER-OCTOBER 2020

Coronado F, Blough S, Bergeron D, Proia K, Sauber-Schatz E, Beltran M, Rau KT, McMichael A, Fortin T, Lackey M, Rohs J, Sparrow T, Baldwin G.. MMWR Morb Mortal Wkly Rep. 2020 Dec 11;69(49):1868-1872. doi: 10.15585/mmwr.mm6949e3.

Level of Evidence: 3 - Local non-random sample

BLUF

Members of the US Centers for Disease Control (CDC) COVID-19 Response Team conducted a mixed-methods study involving an online survey, in-depth interviews, and one virtual site visit to evaluate implementation of CDC recommended COVID-19 mitigation strategies at seven federally funded Head Start programs providing care for children aged 0-5 in eight states (55 centers). All programs reported implementing CDC recommended standard operating procedures and had policies for responding to a positive SARS-CoV-2 test in staff or children (Box). Authors conclude Head Start programs successfully implemented CDC-recommended mitigation strategies, allowing them to limit SARS-CoV-2 transmission while providing an important community resource.

ABSTRACT

The Head Start program, including Head Start for children aged 3-5 years and Early Head Start for infants, toddlers, and pregnant women, promotes early learning and healthy development among children aged 0-5 years whose families meet the annually adjusted Federal Poverty Guidelines* throughout the United States. These programs are funded by grants administered by the U.S. Department of Health and Human Services' Administration for Children and Families (ACF). In March 2020, Congress passed the Coronavirus Aid, Relief, and Economic Security (CARES) Act, which appropriated \$750 million for Head Start, equating to approximately \$875 in CARES Act funds per enrolled child. In response to the coronavirus disease 2019 (COVID-19) pandemic, most states required all schools (K-12) to close or transition to virtual learning. The Office of Head Start gave its local programs that remained open the flexibility to use CARES Act funds to implement CDC-recommended guidance (1) and other ancillary measures to provide in-person services in the early phases of community transmission of SARS-CoV-2, the virus that causes COVID-19, in April and May 2020, when many similar programs remained closed. Guidance included information on masks, other personal protective equipment, physical setup, supplies necessary for maintaining healthy environments and operations, and the need for additional staff members to ensure small class sizes. Head Start programs successfully implemented CDC-recommended mitigation strategies and supported other practices that helped to prevent SARS-CoV-2 transmission among children and staff members. CDC conducted a mixed-methods analysis to document these approaches and inform implementation of mitigation strategies in other child care settings. Implementing and monitoring adherence to recommended mitigation strategies reduces risk for COVID-19 transmission in child care settings. These approaches could be applied to other early care and education settings that remain open for in-person learning and potentially reduce SARS-CoV-2 transmission.

FIGURES

BOX. COVID-19 mitigation strategies implemented by Head Start and Early Head Start child care programs — eight states,* September–October 2020

Everyday prevention actions

- Reinforcement of hand hygiene behavior and respiratory etiquette
- Supervised handwashing and hand-sanitizing for children
- Intensified cleaning and disinfection efforts (e.g., with toys, frequently touched surfaces, and bedding)
- Required use of masks for staff members, visitors, and children aged >2 years
- Social distancing to the extent possible
- Daily health screening procedures on arrival for children and staff members
- Drop-off and pick-up procedures
- Monitoring for absenteeism
- Ability to monitor and restock supplies
- Steps to increase ventilation including installation of ion air purifiers
- Steps to decrease occupancy in areas without increased ventilation
- Use of outdoor space as much as possible
- Cohorting by classroom to minimize exposure between groups

Actions when someone is ill

- COVID-19 point of contact identified
- Staff members trained in COVID-19 safety protocols
- Requiring ill children and staff members to stay at home
- Vigilance for symptoms
- Daily screening of staff members and children for signs and symptoms before facility entry
- Standard operating procedures for when a child or staff member experiences symptoms
- Identification of isolation room
- Plan to notify local health official of COVID-19 cases
- Plan to distribute instructions for primary care referral, testing, or both
- Plan to distribute instructions or guidance for home isolation
- Plan to require close contacts to wait 14 days before returning
- Flexible COVID-19 medical leave policies for staff members

Communications and support

- Training and ongoing reinforcing of standard operating procedures and mitigation measures with caregivers, teachers, and other staff members
- Vigilance and training for the identification of COVID-19 related symptoms
- Masks and other personal protective equipment (e.g., face shields and gowns) provided to teachers and other staff members
- Incentives to adhere to mitigation strategies
- Flexible medical leave policies for staff members with emphasis on persons at higher risk for severe illness and those with caregiving responsibilities
- Flexible work hours and staggered shifts
- Telework options for staff members at higher risk for severe illness

Abbreviation: COVID-19 = coronavirus disease 2019.

*Alaska, Georgia, Idaho, Maine, Missouri, Texas, Washington, and Wisconsin.

SUMMARY OF GUIDANCE FOR PUBLIC HEALTH STRATEGIES TO ADDRESS HIGH LEVELS OF COMMUNITY TRANSMISSION OF SARS-COV-2 AND RELATED DEATHS, DECEMBER 2020

Honein MA, Christie A, Rose DA, Brooks JT, Meaney-Delman D, Cohn A, Sauber-Schatz EK, Walker A, McDonald LC, Liburd LC, Hall JE, Fry AM, Hall AJ, Gupta N, Kuhnert WL, Yoon PW, Gundlapalli AV, Beach MJ, Walke HT; CDC COVID-19 Response Team.. MMWR Morb Mortal Wkly Rep. 2020 Dec 11;69(49):1860-1867. doi: 10.15585/mmwr.mm6949e2.

Level of Evidence: 5 - Guidelines and Recommendations

BLUF

Authors from the CDC COVID-19 Emergency Response team outline 10 practical and sustainable recommendations to reduce the spread of SARS-CoV-2 transmission, especially during upcoming holidays. These are consistent with previous COVID-19 precautions and include face mask usage, physical distancing, limiting of contacts, avoidance of large crowds and travel, protection of essential workers and high-risk individuals, increased testing and isolation of infected people, and widespread vaccine distribution. By abiding to these evidence-based strategies, we can mitigate the pandemic's detrimental health, social, and economic sequelae.

ABSTRACT

In the 10 months since the first confirmed case of coronavirus disease 2019 (COVID-19) was reported in the United States on January 20, 2020 (1), approximately 13.8 million cases and 272,525 deaths have been reported in the United States. On October 30, the number of new cases reported in the United States in a single day exceeded 100,000 for the first time, and by December 2 had reached a daily high of 196,227.* With colder weather, more time spent indoors, the ongoing U.S. holiday season, and silent spread of disease, with approximately 50% of transmission from asymptomatic persons (2), the United States has entered a phase of high-level transmission where a multipronged approach to implementing all evidence-based public health strategies at both the individual and community levels is essential. This summary guidance highlights critical evidence-based CDC recommendations and sustainable strategies to reduce COVID-19 transmission. These strategies include 1) universal face mask use, 2) maintaining physical distance from other persons and limiting in-person contacts, 3) avoiding nonessential indoor spaces and crowded outdoor spaces, 4) increasing testing to rapidly identify and isolate infected persons, 5) promptly identifying, quarantining, and testing close contacts of persons with known COVID-19, 6) safeguarding persons most at risk for severe illness or death from infection with SARS-CoV-2, the virus that causes COVID-19, 7) protecting essential workers with provision of adequate personal protective equipment and safe work practices, 8) postponing travel, 9) increasing room air ventilation and enhancing hand hygiene and environmental disinfection, and 10) achieving widespread availability and high community coverage with effective COVID-19 vaccines. In combination, these strategies can reduce SARS-CoV-2 transmission, long-term sequelae or disability, and death, and mitigate the pandemic's economic impact. Consistent implementation of these strategies improves health equity, preserves health care capacity, maintains the function of essential businesses, and supports the availability of in-person instruction for kindergarten through grade 12 schools and preschool. Individual persons, households, and communities should take these actions now to reduce SARS-CoV-2 transmission from its current high level. These actions will provide a bridge to a future with wide availability and high community coverage of effective vaccines, when safe return to more everyday activities in a range of settings will be possible.

PLACEBO-CONTROLLED TRIALS OF COVID-19 VACCINES - WHY WE STILL NEED THEM

WHO Ad Hoc Expert Group on the Next Steps for Covid-19 Vaccine Evaluation, Krause PR, Fleming TR, Longini IM, Peto R, Beral V, Bhargava B, Cravioto A, Cramer J, Ellenberg SS, Figueroa JP, Halloran E, Henao-Restrepo AM, Ryan MJ, Levine MM, Nason M, Nohynek HM, Plotkin S, Rees H, Singh JA, Swaminathan S.. N Engl J Med. 2020 Dec 2. doi: 10.1056/NEJMmp2033538. Online ahead of print.

Level of Evidence: 5 - Expert Opinion

BLUF

This discussion by the WHO Ad Hoc Expert Group on the Next Steps for Covid-19 Vaccine describes a need for blinded, randomized placebo-controlled trials in order to collect high quality data regarding the new COVID-19 vaccines. They caution against unblinding and vaccination of participants in the placebo arms of current studies and urge for continuation of Phase 3 trials comprised of 20,000 vaccine recipients with 20,000 controls. They emphasize the ethical dilemma between ongoing collection of valuable data on long-term vaccine efficacy versus protecting the volunteers enrolled in vaccine studies, but suggest a global effort to collect such data could increase likelihood of identifying vaccines with favorable benefit-risk profiles.

PREVENTION IN THE HOSPITAL

COVID-19 AND RESPIRATORY PROTECTION FOR HEALTHCARE PROVIDERS

Sozkes S, Sozkes S.. Int J Occup Med Environ Health. 2020 Nov 24;128171. doi: 10.13075/ijomeh.1896.01666. Online ahead of print.

Level of Evidence: 5 - Review / Literature Review

BLUF

This review of 32 papers conducted by biomedical engineering and ICU specialists in Turkey searched respirator data via scientific databases (including Web of Science, PubMed, and Medline) on May 5, 2020 and found reusable elastomeric respirator devices (RERs) to consistently provide higher levels of protection (Figures 5,6) up to 15 times more compared to disposable options (surgical or N95 masks), indicating a significant correlation between mask fit-to-face characteristic and amount of protection provided (Table 2). Multiple studies also confirmed no significant difference of infection transmission between surgical and N95 masks. Authors suggest reusable respirators may offer improved protection, decreased incidence of leakages, better fit, and increased stability, while also mitigating supply/demand concerns due to shortages of personal protective equipment.

ABSTRACT

This article has investigated the considerations of healthcare facilities to utilize reusable respirators as an alternative to disposable respirators during the COVID-19 pandemic. The decision to choose specific equipment should be based on the protection factors and also on the overall analysis of given conditions. International scientific databases, such as Web of Science, PubMed and MedLine, were searched on May 5, 2020, with the following key words: COVID-19, respiratory protection, surgical masks, filtering facepiece respirators (FFRs) and disposable respirators. The differences between various respiratory protective equipment, i.e., surgical masks, respirators such as FFRs, elastomeric half-facepiece respirators, elastomeric full-facepiece respirators and powered air-purifying respirators (PAPRs), were compared. Reusable elastomeric respirators (RERs) may provide a better adaptation to the face and may be more stable when used by healthcare providers (HCPs). Protection factors were found to be higher in FFRs compared to surgical masks. While FFRs provide a one-tenth decrease in the inhaled aerosol concentration, PAPRs diminish the inhaled aerosol up to one-twenty-fifth. Even with some full-face PAPRs and helmets, the protection factor assigned by the Occupational Safety and Health Administration can reach a value up to 1000. For HCPs, the evidence shown in this article provides an additional support for the utilization of RERs. Such equipment might be less prone to leakages, can provide a better fit, and indicates a better stability compared to disposable FFRs (N95 and similar). By providing higher protection factors, reusable elastomeric respirators are recommended to be used by HCPs under controlled cleaning and disinfection protocols.

FIGURES



Figure 5. A reusable elastomeric half-facepiece respirator P3 Filters 6035 (3M™ 7502, USA): a) front view, b) lateral view



Figure 6. A reusable elastomeric full-facepiece respirator P3
Filters 6035 (3M™ 6800, USA): a) front view, b) lateral view

Table 2. Filtration efficiency requirements and standards with assigned or nominal protection factors for respiratory protective equipment [2-4,13,25,26,28,29,32]

Equipment	Origin	Standard	Filter classification	Efficiency	APFs*/NPFs*
FFR	USA	NIOSH 42 CFR 84	N95	≥95%	4 APFs
			N99	≥99%	10 APFs
			N100	≥99.97%	20 APFs
	Europe	EN 149:2001	FFP1	≥80%	4 NPFs
			FFP2	≥94%	12 NPFs
			FFP3	≥99%	50 NPFs
	China	GB 2626-2006	KN/KP90	≥90%	n.a.
			KN/KP95	≥95%	n.a.
			KN/KP100	≥99.97%	n.a.
Reusable elastomeric half-facepiece respirator	Europe	EN 143:2000/ EN 140:1999/ EN 136:1998	P1	≥80%	4 NPFs
			P2	≥94%	12 NPFs
			P3	≥99.95%	48 NPFs
Reusable elastomeric full-facepiece respirator	Europe	EN 143:2000/ EN 140:1999/ EN 136:1998	P1	≥80%	5 NPFs
			P2	≥94%	16 NPFs
			P3	≥99.95%	1000 NPFs
PAPR with a hood or a helmet	Europe	EN 12941 (TH1: inward leakage max 10%; TH2: inward leakage max 2%; TH3: inward leakage max 0.2%) HEPA	TH1	≥99.97%	10 NPFs
			TH2	≥99.97%	50 NPFs
			TH3	≥99.97%	500 NPFs
PAPR with a tight-fitting mask	Europe	EN 12942, HEPA	TM1	≥99.97%	20 NPFs
			TM2	≥99.97%	200 NPFs
			TM3	≥99.97%	2000 NPFs

APFs – assigned protection factors; FFR – filtering facepiece respirator; HEPA – high-efficiency particulate air; NPFs – nominal protection factors;

PAPR – powered air-purifying respirator.

* Europe uses NPFs, while USA uses APFs.

n.a. – not available.

ADJUSTING PRACTICE DURING COVID-19

PEDIATRICS

INJURIES IN THE TIME OF COVID-19

Keays G, Friedman D, Gagnon I.. Health Promot Chronic Dis Prev Can. 2020 Dec 9;40(11-12):336-341. doi: 10.24095/hpcdp.40.11/12.02. Epub 2020 Sep 11.

Level of Evidence: 4 - Case-series, case-control, or historically controlled studies

BLUF

Based on a previously reported decrease in hospital ED visits for acute conditions such as strokes and heart attacks, researchers from McGill University, Montréal, Quebec, Canada analyzed data from the Canadian Hospitals Injury Reporting and Prevention Program (CHIRPP) to compare the number of pediatric injury-related ED visits to Montreal Children's Hospital during the COVID-19 pandemic (specifically from March 16 to May 15, 2020) to the average number of visits during the same two months from the years 1993-2019. There was a significant decrease in pediatric injury-related ED visits in all pediatric age groups during COVID-19 (Figure 1), suggesting parents were less likely to bring their child to a hospital after an injury during the pandemic than pre-pandemic.

ABSTRACT

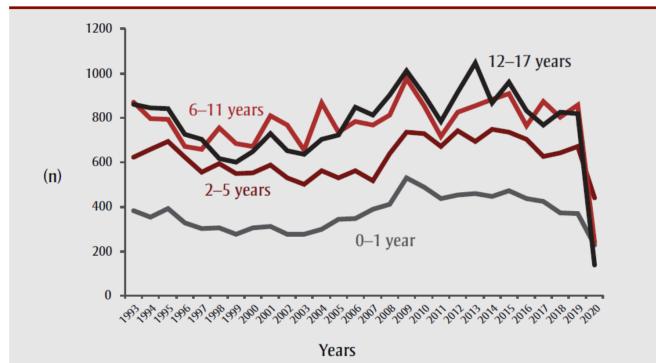
INTRODUCTION: Research has shown that during the 2003 SARS pandemic, emergency department (ED) visits among the pediatric population decreased. We set out to investigate if this was also true for injury-related ED visits during the COVID-19 pandemic. **METHODS:** Using data from the Canadian Hospitals Injury Reporting and Prevention Program (CHIRPP), we looked at 28 years of injury-related ED visits at the Montreal Children's Hospital, a provincially designated Pediatric Trauma Centre.

We compared data from a two-month period during the COVID-19 lockdown (16 March to 15 May) to the same period in previous years (1993-2019) to determine whether the 2020 decrease in ED visit numbers was unprecedented (i.e. a similar decrease had never occurred) for different age groups, nature of injuries, mechanisms and severity. **RESULTS:** The 2020 decrease was unprecedented across all age groups between 1993 and 2019. When compared with the 2015 to 2019 average, the decrease was smallest in children aged 2 to 5 years (a 35% decrease), and greatest in the group aged 12 to 17 years (83%). Motor vehicle collisions and sports-related injuries practically vanished during the COVID-19 lockdown. Surprisingly, more children aged 6 to 17 years presented with less urgent injuries during the COVID-19 lockdown than in previous years.

CONCLUSION: As was the case with SARS in 2003, COVID-19 acted as a deterrent for pediatric ED visits. The lockdown in particular had a profound impact on injury-related visits. The de-confinement period will be monitored to determine the impact in both the short and the long term.

FIGURES

Figure 1. Number of injury-related visits to Montreal Children's Hospital emergency department, per age group, from 16 March to 15 May, 1993 to 2020



R&D: DIAGNOSIS & TREATMENTS

DEVELOPMENTS IN TREATMENTS

BARICITINIB PLUS REMDESIVIR FOR HOSPITALIZED ADULTS WITH COVID-19

Kalil AC, Patterson TF, Mehta AK, Tomashek KM, Wolfe CR, Ghazaryan V, Marconi VC, Ruiz-Palacios GM, Hsieh L, Kline S, Tapson V, Iovine NM, Jain MK, Sweeney DA, El Sahly HM, Branche AR, Regalado Pineda J, Lye DC, Sandkovsky U, Luetkemeyer AF, Cohen SH, Finberg RW, Jackson PEH, Taiwo B, Paules CI, Arquinchona H, Goepfert P, Ahuja N, Frank M, Oh MD, Kim ES, Tan SY, Mularski RA, Nielsen H, Ponce PO, Taylor BS, Larson L, Roushanel NG, Saklawi Y, Cantos VD, Ko ER, Engemann JJ, Amin AN, Watanabe M, Billings J, Elie MC, Davey RT, Burgess TH, Ferreira J, Green M, Makowski M, Cardoso A, de Bono S, Bonnett T, Proschan M, Deye GA, Dempsey W, Nayak SU, Dodd LE, Beigel JH.. N Engl J Med. 2020 Dec 11. doi: 10.1056/NEJMoa2031994. Online ahead of print.

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

BLUF

Physicians across the United States conducted a double-blind, randomized, placebo-controlled trial evaluating baricitinib (Janus kinase inhibitor) with remdesivir in 1033 hospitalized adults with COVID-19, and found that the combination of baricitinib plus remdesivir was superior to remdesivir alone in serious adverse events (16.0% vs. 21.0%, p=0.03), 28-day mortality rate (5.1% vs. 7.8%, hazard ratio=0.65, Figure 2), and recovery time (7 days vs. 8 days, p=0.03, Figure 3), especially among those already being treated with high-flow oxygen or noninvasive ventilation such as CPAP or BiPAP (10 days vs. 18 days). This study demonstrates the safety and efficacy of this drug combination, which may have advantages over other treatment options currently being utilized.

ABSTRACT

BACKGROUND: Severe coronavirus disease 2019 (Covid-19) is associated with dysregulated inflammation. The effects of combination treatment with baricitinib, a Janus kinase inhibitor, plus remdesivir are not known. **METHODS:** We conducted a double-blind, randomized, placebo-controlled trial evaluating baricitinib plus remdesivir in hospitalized adults with Covid-19. All the patients received remdesivir (<=10 days) and either baricitinib (<=14 days) or placebo (control). The primary outcome was the time to recovery. The key secondary outcome was clinical status at day 15. **RESULTS:** A total of 1033 patients underwent randomization (with 515 assigned to combination treatment and 518 to control). Patients receiving baricitinib had a median time to recovery of 7 days (95% confidence interval [CI], 6 to 8), as compared with 8 days (95% CI, 7 to 9) with control (rate ratio for recovery, 1.16; 95% CI, 1.01 to 1.32; P = 0.03), and a 30% higher odds of improvement in clinical status at day 15 (odds ratio, 1.3; 95% CI, 1.0 to 1.6). Patients receiving high-flow oxygen or noninvasive ventilation at enrollment had a time to recovery of 10 days with combination treatment and 18 days with control (rate ratio for recovery, 1.51; 95% CI, 1.10 to 2.08). The 28-day mortality was 5.1% in the combination group and 7.8% in the control group (hazard ratio for death, 0.65; 95% CI, 0.39 to 1.09). Serious adverse events were less frequent in the combination group than in the control group (16.0% vs. 21.0%; difference, -5.0 percentage points; 95% CI, -9.8 to -0.3; P = 0.03), as were new infections (5.9% vs. 11.2%; difference, -5.3 percentage points; 95% CI, -8.7 to -1.9; P = 0.003). **CONCLUSIONS:** Baricitinib plus remdesivir was superior to remdesivir alone in reducing recovery time and accelerating improvement in clinical status among patients with Covid-19, notably among those receiving high-flow oxygen or noninvasive ventilation. The combination was associated with fewer serious adverse events. (Funded by the National Institute of Allergy and Infectious Diseases; ClinicalTrials.gov number, NCT04401579.).

FIGURES

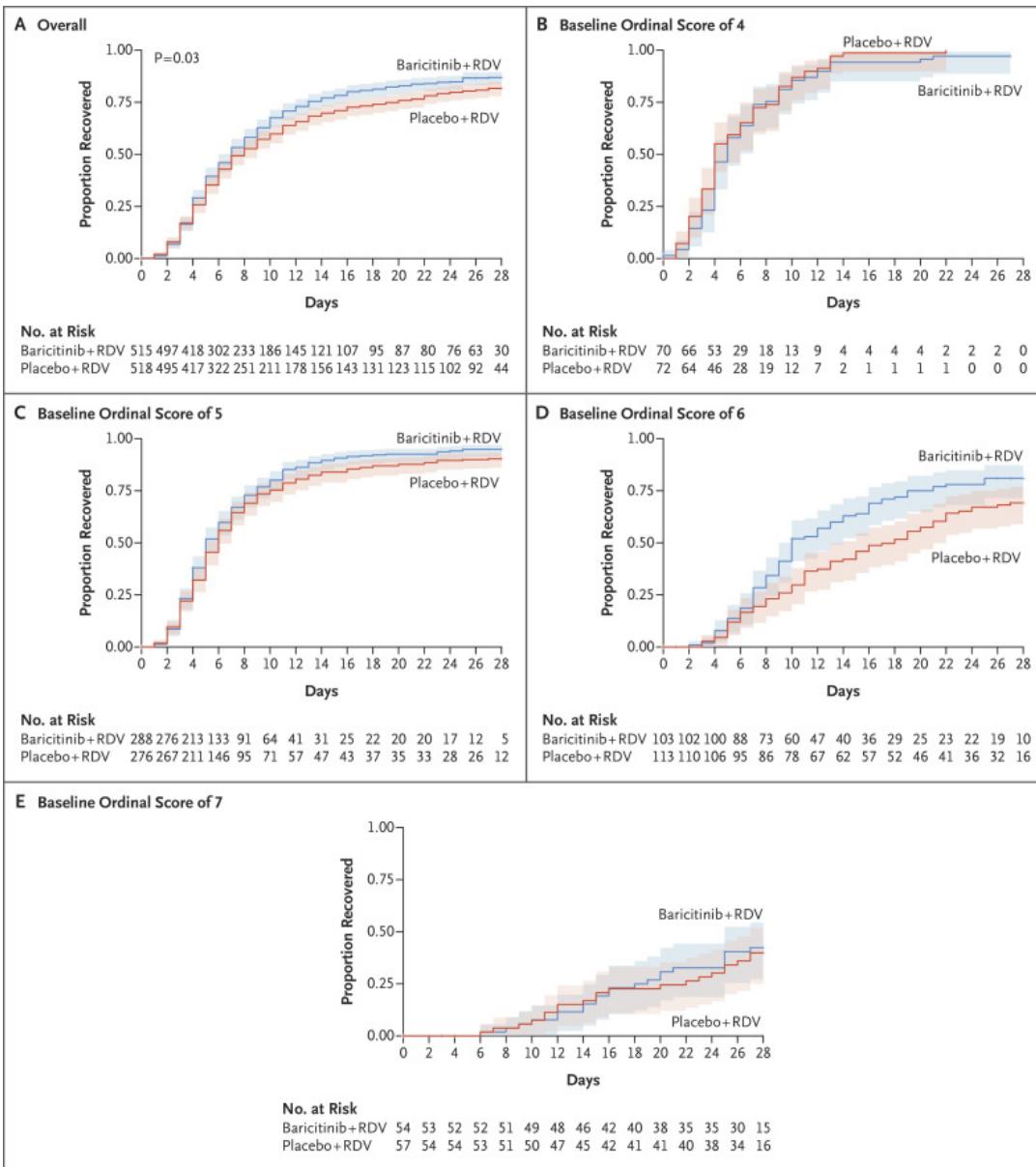


Figure 2. Kaplan-Meier Estimates of Cumulative Recoveries. Cumulative recovery estimates are shown in the overall population (Panel A), in patients with a baseline score of 4 on the ordinal scale (not requiring oxygen; Panel B), in those with a baseline score of 5 (requiring oxygen; Panel C), in those with a baseline score of 6 (receiving high-flow oxygen or noninvasive mechanical ventilation; Panel D), and in those with a baseline score of 7 (receiving mechanical ventilation or extracorporeal membrane oxygenation [ECMO]; Panel E). Shaded areas indicate 95% confidence intervals.

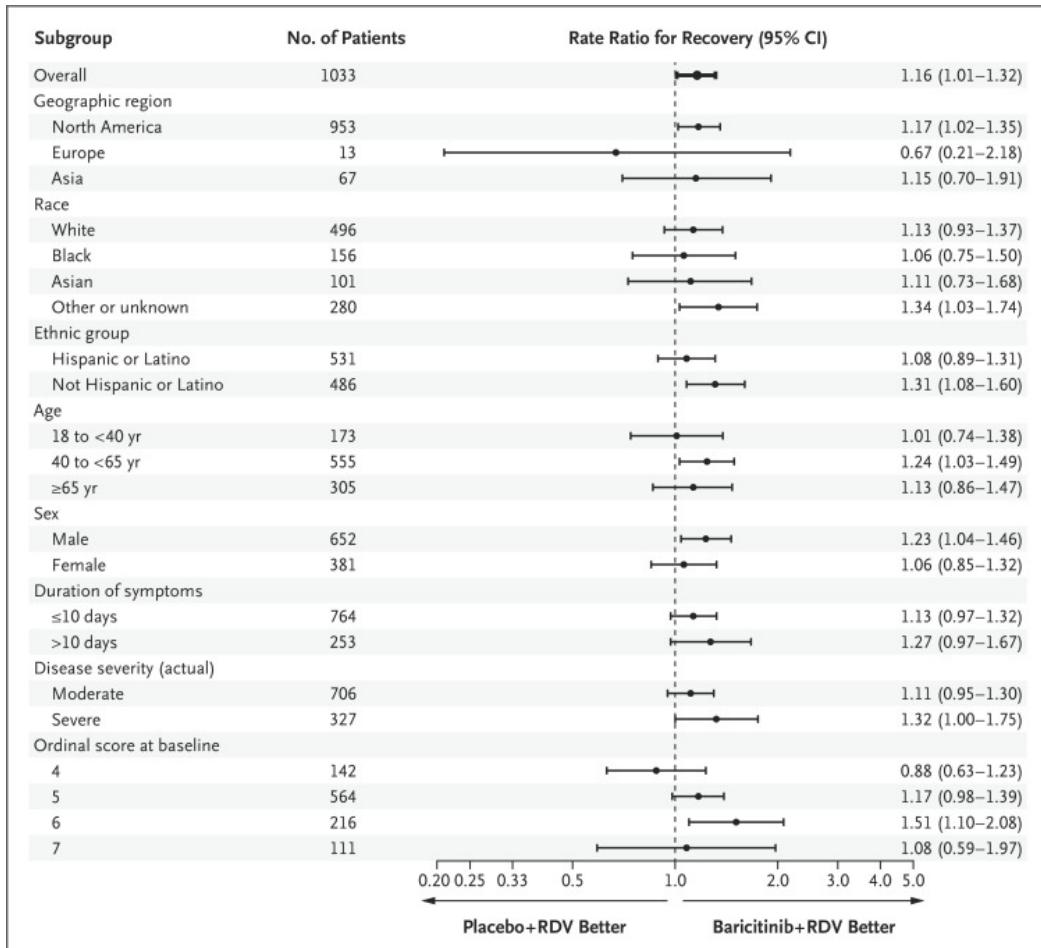


Figure 3. Time to Recovery According to Subgroup. The widths of the confidence intervals have not been adjusted for multiplicity and therefore cannot be used to infer treatment effects. Race and ethnic group were reported by the patients. With respect to “other” race, the categories that were used when data on race were reported included American Indian or Alaska Native and Native Hawaiian or other Pacific Islander.

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