

The Daily COVID-19 Literature Surveillance Summary

December 17, 2020



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COVID-19 Daily Literature Surveillance

COVID19LST



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

LEVEL OF EVIDENCE

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

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

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

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

How to cite the Levels of Evidence Table

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

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

EXECUTIVE SUMMARY

Climate

- Operations officers from several international biomedical manufacturing companies discuss the ability of manufacturers to reduce distribution of counterfeit vaccines in light of counterfeit SARS-CoV-2 vaccines being found in Russia and Ecuador in 2020. Authors recommend [using various tracking methods](#) such as a GS1 2D DataMatrix barcode, QR code and matrix code, or Automatic Identification and Data Capture (AIDC) flow to scan and identify vaccines, trace them from the factory to delivery, and upload that data into an easily accessible system. They suggest such a tracing system is necessary to ensure the delivery of safe and authentic vaccines from factories to the public.

Epidemiology

- A team from Johns Hopkins University and Brown University conducted a [systematic review and meta-analysis of 77 studies](#) (38906 hospitalized patients) and found the overall prevalence of death from COVID-19 among hospitalized patients was 23% (19–27%) in the US and Europe versus 11% (7–16%) in China. Risk factors for death included age 60 or older ($sRR = 3.6$; 95% CI: 3.0–4.4; I² 77%), male gender ($sRR=1.3$; 1.2–1.4; I² 18%), smoking history ($sRR=1.3$; 1.1–1.6; I² 68%), COPD ($sRR=1.7$; 1.4–2.0; I² 66%), diabetes ($sRR=1.5$; 1.4–1.7; I² 58%), heart disease ($sRR=2.1$; 1.8– 2.4; I² 69%), CKD ($sRR = 2.5$; 2.1–3.0; I² 72%). They observed similar risk factors for severe disease (respiratory rate>30, oxygen saturation<93%, and $\text{PaO}_2/\text{FiO}_2 < 300$ and/or lung infiltrates>50% within 24–48 hours).
- Pediatricians from Arnold Palmer Hospital for Children in Orlando, Florida discuss the case of a [female infant born at 40 weeks gestation to a 15-year-old primigravida woman with asymptomatic COVID-19](#) who tested positive at 24 hours of life via rt-PCR. She developed a fever at 25 hours of life and later required supplemental oxygen, CPAP, and remdesivir to achieve an SpO_2 of 88% on day of life 4. On day of life 5, she developed acute respiratory failure requiring intubation and dexamethasone. The infant eventually developed superimposed bacterial pneumonia with *Staphylococcus lugdunensis* on sputum cultures, and after aggressive treatment was eventually weaned back to room air. The authors claim this case illustrates vertical transmission of COVID-19 is possible due to the rapid onset of symptoms after birth; however, neither the placenta nor the amniotic fluid were sampled. This case illustrates severe disease in a neonate with likely superimposed bacterial pneumonia and possible vertical transmission.

Transmission & Prevention

- Researchers from England studying COVID-19 transmission in the education system found that the [overall risk of SARS-CoV2 infection among children and school staff was low](#): there was minimal evidence of transmission from student to student or student to faculty member, and infected children most commonly acquired SARS-CoV-2 from family members at home. Data suggests that the rate of transmission in schools was directly correlated with regional COVID-19 prevalence, suggesting that re-opening schools may not significantly increase infection rates among children or school staff unless this is during a surge or in high prevalence areas.
- Members of the US Centers for Disease Control COVID-19 Response Team summarize their [recommended public health strategies for mitigation of community SARS-CoV-2 transmission](#): they recommend the use of face masks, maintaining physical distancing, prompt case investigation, avoiding crowded situations, increasing protection for persons at highest risk for severe COVID-19, adequately protecting healthcare workers, improved hygiene practices, avoiding unnecessary travel, and widespread use of safe vaccines. Authors suggest following such evidence-based measures will substantially contribute to combating transmission of COVID-19.

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CLIMATE

GLOBAL

EXPERTS DISCUSS COVID-19: VACCINE ALLOCATION, PLACEBO GROUPS, AND MORE

. JAMA. 2020 Dec 15;324(23):2354-2355. doi: 10.1001/jama.2020.24075.

Level of Evidence: 5 - Expert Opinion

BLUF

A group of experts including a former Centers for Disease Control director, an infectious disease physician, a lawyer, an expert in health equity, and a former Medicare/Medicaid administrator comment on SARS-CoV-2 vaccine access and the pandemic at large. Contributors discuss the groups at highest risk for COVID-19 infection (healthcare workers, elderly, and racial minorities), equity issues in vaccine prioritization, the pros (wider vaccination) and cons (failure to have an unvaccinated comparison group) of trial placebo groups receiving vaccines, and their thoughts on ending the pandemic, including the continued need to fill the gaps in knowledge of immunity and pathophysiology.

THE ROLE OF MANUFACTURERS IN THE IMPLEMENTATION OF GLOBAL TRACEABILITY STANDARDS IN THE SUPPLY CHAIN TO COMBAT VACCINE COUNTERFEITING AND ENHANCE SAFETY MONITORING

Jarrett S, Wilmansyah T, Bramanti Y, Alitamsar H, Alamsyah D, Krishnamurthy KR, Yang L, Pagliusi S.. Vaccine. 2020 Dec 14;38(52):8318-8325. doi: 10.1016/j.vaccine.2020.11.011. Epub 2020 Nov 13.

Level of Evidence: 5 - Expert Opinion

BLUF

Operations officers from several international biomedical manufacturing companies discuss the ability of manufacturers to reduce distribution of counterfeit vaccines in light of counterfeit SARS-CoV-2 vaccines being found in Russia and Ecuador in 2020. Authors recommend using various tracking methods such as a GS1 2D DataMatrix barcode (Figure 1), QR code and matrix code (Figure 2), or Automatic Identification and Data Capture (AIDC) flow (Figure 3) to scan and identify vaccines, trace them from the factory to delivery, and upload that data into an easily accessible system. They suggest such a tracing system is necessary to ensure the delivery of safe and authentic vaccines from factories to the public.

ABSTRACT

The counterfeiting of vaccines is an increasing problem globally with the safety of persons vaccinated, the trust in vaccines generally and the associated reputation of vaccine manufacturers and regulatory agencies at risk. This risk is especially critical with the on-going development of COVID-19 vaccines. The ability to track and trace vaccines through the vaccine supply chain down to persons vaccinated has to be enhanced. In this context of traceability, the global immunization community has recently set the barcoding of the primary packaging of vaccines, specifically vaccine vials and pre-filled syringes, as a top priority. Emerging vaccine manufacturers are already engaged in investigating ways to incorporate barcoding in their labelling and packaging using GS1 international standards. A specific pilot taking place in Indonesia by the national vaccine manufacturer, Bio Farma, shows the innovation of barcoding on primary packaging already underway with a relatively modest level of investment and success at this stage. This article highlights the efforts of industry and governments on the value of traceability and introduction to 2D barcodes. Access to financial resources and support from the international immunization community would accelerate such innovations leading to enhanced security of the vaccine supply chain.

FIGURES

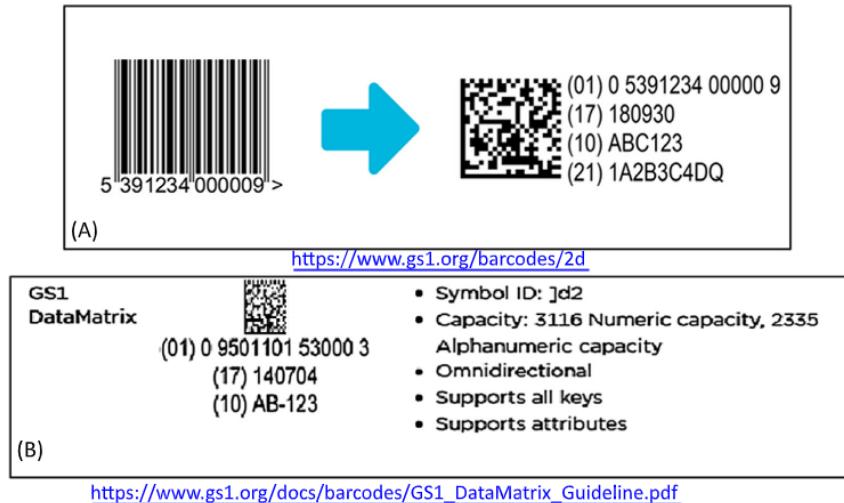


Fig. 1. Illustration of the GS1 2D DataMatrix barcode. (A) This is an illustration of GS1 barcode and corresponding DataMatrix, which is a 2D matrix (or two-dimensional) barcode which may be printed as a square or rectangular symbol made up of individual dots or squares [16]. The 2D representation is an ordered grid of dark and light dots bordered by a finder pattern. The finder pattern is partly used to specify the orientation and structure of the symbol. The data is encoded using a series of dark or light dots based upon a pre-determined size. The size of these dots is known as the X-dimension. (B) A single 2D barcode can hold a significant amount of information and may remain legible even when printed at a small size or etched onto a product. 2D barcodes are used in a wide range of industries, from manufacturing and warehousing to logistics and healthcare.

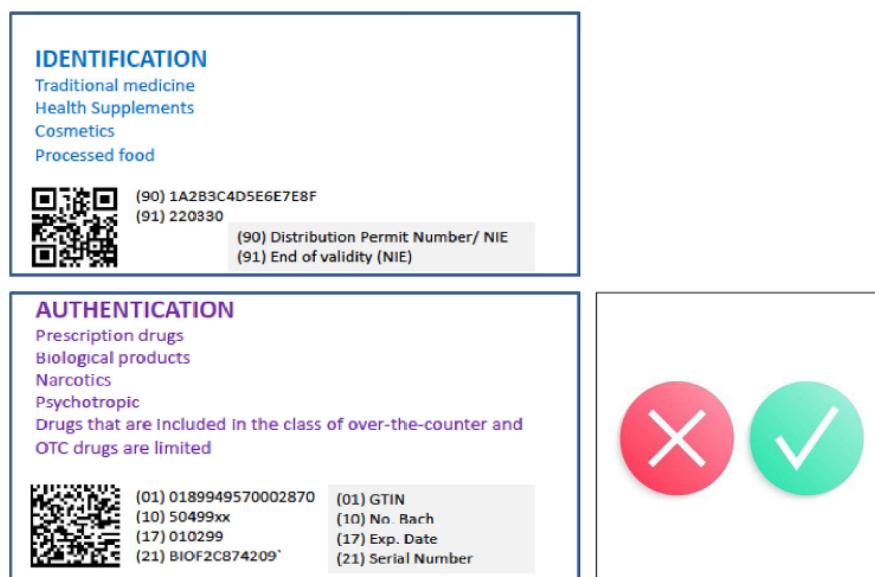


Fig. 2. Differential Use of QR code and Matrix code in the Indonesian track and trace system Traceability demands that codes be readable from the beginning until the end of their lifecycle. Both data matrix codes and QR codes are scalable, but small components such as electronic devices are typically marked with data matrix codes since they can encode more characters within the same space. Some markings have cells that are as small as $300 \mu\text{m}^2$, whereas other markings are as large as 1 m^2 . QR codes are less compact in size and are therefore not typically used for small items. In Indonesia the regulatory authority defined that 2D data Matrix is to be used for biologicals including vaccines, and other prescription drugs, instead of QR. Upon scanning with a smartphone the screen will show specific information and whether the product could be used or not, based on recognition from the integrated data system.

SERIALIZATION & AGGREGATION CONCEPT

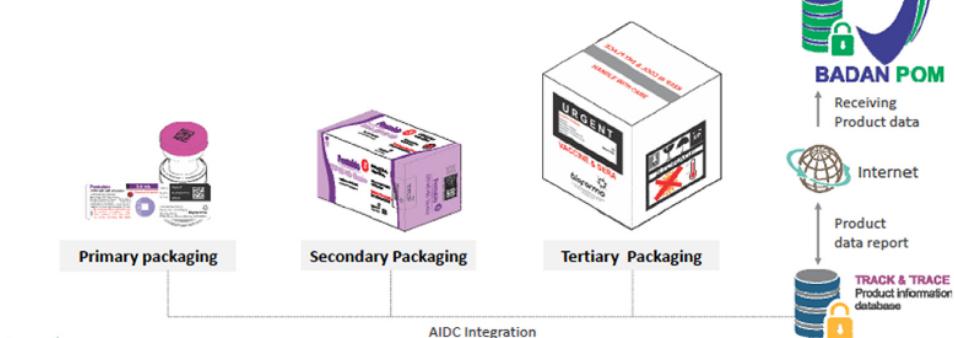


Fig. 3. Automatic Identification and Data Capture (AIDC) flow from primary to tertiary packaging level. Automatic Identification and Data Capture (AIDC) refers to the methods of automatically identifying objects, collecting data about them, and entering that data directly into computer systems, without human involvement, i.e. barcodes or standards on secondary and tertiary packaging levels for vaccines. They facilitate product and data flow between supply chain partners.

THE GRANTING OF EMERGENCY USE DESIGNATION TO COVID-19 CANDIDATE VACCINES: IMPLICATIONS FOR COVID-19 VACCINE TRIALS

Singh JA, Upshur REG.. Lancet Infect Dis. 2020 Dec 8:S1473-3099(20)30923-3. doi: 10.1016/S1473-3099(20)30923-3. Online ahead of print.

Level of Evidence: 5 - Expert Opinion

BLUF

Public health research professionals from the University of Toronto (Canada) and Howard College School of Law (South Africa) discuss the implications of granting emergency use authorization for COVID-19 vaccines before the conclusion of their phase 3 trials. While the benefits of authorizing a vaccine early are obvious, some important considerations include:

- Demographics of participants in the studies differ from the populations prioritized to receive the vaccine first and populations found to be at higher risk for severe COVID-19.
- Lack of evidence that the vaccine decreases transmission as well as incidence of ICU admission or death.
- Effects on ongoing trials, including unblinding and loss of trial volunteers.
- Lack of evidence on long-term efficacy and potential side effects.
- Lack of vaccine confidence from the public.

ABSTRACT

An efficacious COVID-19 vaccine is currently the world's leading research priority. Several nations have indicated that if there is a compelling case for use of a vaccine before it is licensed, they would be prepared to authorise its emergency use or conditional approval on public health grounds. As of Dec 1, 2020, several developers of leading COVID-19 candidate vaccines have indicated that they have applied, or intend to apply, for emergency authorisation for their vaccines. Should candidate vaccines attain emergency use designation and be programmatically deployed before their phase 3 trials conclude, such a strategy could have far reaching consequences for COVID-19 vaccine research and the effective control of the COVID-19 pandemic. These issues merit careful consideration.

EPIDEMIOLOGY

EVIDENCE OF EXPOSURE TO SARS-COV-2 IN CATS AND DOGS FROM HOUSEHOLDS IN ITALY

Patterson EI, Elia G, Grassi A, Giordano A, Desario C, Medardo M, Smith SL, Anderson ER, Prince T, Patterson GT, Lorusso E, Lucente MS, Lanave G, Lauzi S, Bonfanti U, Stranieri A, Martella V, Solari Basano F, Barrs VR, Radford AD, Agrimi U, Hughes GL, Paltrinieri S, Decaro N.. Nat Commun. 2020 Dec 4;11(1):6231. doi: 10.1038/s41467-020-20097-0.

Level of Evidence: 3 - Local non-random sample

BLUF

A team of virologists and veterinarians from Italy and the UK tested samples (either oral, nasal, or rectal) from 494 cats and dogs from Italian households between March and May 2020 for evidence of SARS-CoV-2 infection. They found that all samples tested negative for SARS-CoV-2 via rt-PCR, including 38 cats and 38 dogs with ongoing respiratory symptoms. However, 15/451 (3.3%) of dogs and 11/191 (5.8%) of cats had measurable neutralizing antibody titers, with dogs more likely to have positive serologies if they were from COVID-19 positive households ($p=0.004$) (Table 2). Authors suggests that further research is needed into animal susceptibility to SARS-CoV-2 and the possibility of human-animal transmission.

ABSTRACT

SARS-CoV-2 emerged from animals and is now easily transmitted between people. Sporadic detection of natural cases in animals alongside successful experimental infections of pets, such as cats, ferrets and dogs, raises questions about the susceptibility of animals under natural conditions of pet ownership. Here, we report a large-scale study to assess SARS-CoV-2 infection in 919 companion animals living in northern Italy, sampled at a time of frequent human infection. No animals tested PCR positive. However, 3.3% of dogs and 5.8% of cats had measurable SARS-CoV-2 neutralizing antibody titers, with dogs from COVID-19 positive households being significantly more likely to test positive than those from COVID-19 negative households. Understanding risk factors associated with this and their potential to infect other species requires urgent investigation.

FIGURES

Table 2

Seropositivity among dogs and cats, split into risk factor groupings where data were available^a.

Risk factor	Dogs			Cats		
	No. + (total)	%	<i>p</i>	No. + (total)	%	<i>p</i>
Household						
Covid+	6 (47)	12.8%	0.004	1 (22)	4.5%	
Covid-	2 (133)	1.5%		1 (38)	2.6%	
Suspected Covid+	1 (7)	14.3%		0 (3)	0.0%	
Sex						
Male	7 (83)	8.4%	0.045	2 (31)	6.5%	
Female	2 (105)	1.9%		0 (30)	0.0%	
Age (years)						
<1	0 (20)	0.0%	na	0 (9)	0.0%	na
1–3	5 (70)	7.1%		1 (22)	4.5%	
4–7	2 (83)	2.4%		1 (19)	5.3%	
8+	4 (137)	2.9%		2 (62)	3.2%	
Unknown	4 (141)	2.8%		7 (78)	9.0%	

^aFor household and sex, *p*-value determined by two-sided Fisher's exact test. Household COVID+ defined as one or more members of a household with a confirmed positive COVID-19 test. All the information was not available for all the animals. Both household ($p = 0.004$) and sex ($p = 0.045$) were associated with COVID seropositivity among dogs, whereas neither household ($p = 1.000$) nor sex ($p = 0.492$) were associated with COVID seropositivity among cats.

SYMPTOMS AND CLINICAL PRESENTATION

PREVALENCE AND PREDICTORS OF DEATH AND SEVERE DISEASE IN PATIENTS HOSPITALIZED DUE TO COVID-19: A COMPREHENSIVE SYSTEMATIC REVIEW AND META-ANALYSIS OF 77 STUDIES AND 38,000 PATIENTS

Dorjee K, Kim H, Bonomo E, Dolma R.. PLoS One. 2020 Dec 7;15(12):e0243191. doi: 10.1371/journal.pone.0243191. eCollection 2020.

Level of Evidence: 2 - Systematic review of inception cohort studies

BLUF

A team from Johns Hopkins University and Brown University conducted a systematic review and meta-analysis of 77 studies (38906 hospitalized patients)(Figure 1) and found the overall prevalence of death from COVID-19 among hospitalized patients was 23% (19–27%) in the US and Europe versus 11% (7–16%) in China. Risk factors for death included age 60 or older [sRR = 3.6; 95% CI: 3.0–4.4; I² 77%], male gender [sRR=1.3; 1.2–1.4; I² 18%], smoking history [sRR=1.3; 1.1–1.6; I² 68%], COPD [sRR=1.7; 1.4–2.0; I² 66%], diabetes [sRR=1.5; 1.4–1.7; I² 58%], heart disease [sRR=2.1; 1.8– 2.4; I² 69%], CKD [sRR =2.5; 2.1–3.0; I² 72%] (Table 2). They observed similar risk factors for severe disease (respiratory rate>30, oxygen saturation<93%, and PaO₂/FiO₂<300 and/or lung infiltrates>50% within 24–48 hours)(Table 3). Authors suggest identifying modifiable risk factors including smoking, diabetes, and hypertension offers an opportunity to lower COVID-19 mortality if addressed.

ABSTRACT

INTRODUCTION: Progression of COVID-19 to severe disease and death is insufficiently understood. **OBJECTIVE:** Summarize the prevalence of risk factors and adverse outcomes and determine their associations in COVID-19 patients who were hospitalized. **METHODS:** We searched Medline, Embase and Web of Science for case-series and observational studies of hospitalized COVID-19 patients through August 31, 2020. Data were analyzed by fixed-effects meta-analysis using Shore's adjusted confidence intervals to address heterogeneity. **RESULTS:** Seventy-seven studies comprising 38906 hospitalized patients met inclusion criteria; 21468 from the US-Europe and 9740 from China. Overall prevalence of death [% (95% CI)] from COVID-19 was 20% (18-23%); 23% (19-27%) in the US and Europe and 11% (7-16%) for China. Of those that died, 85% were aged>=60 years, 66% were males, and 66%, 44%, 39%, 37%, and 27% had hypertension, smoking history, diabetes, heart disease, and chronic kidney disease (CKD), respectively. The case fatality risk [% (95% CI)] were 52% (46-60) for heart disease, 51% (43-59) for COPD, 48% (37-63) for chronic kidney disease (CKD), 39% for chronic liver disease (CLD), 28% (23-36%) for hypertension, and 24% (17-33%) for diabetes. Summary relative risk (sRR) of death were higher for age>=60 years [sRR = 3.6; 95% CI: 3.0-4.4], males [1.3; 1.2-1.4], smoking history [1.3; 1.1-1.6], COPD [1.7; 1.4-2.0], hypertension [1.8; 1.6-2.0], diabetes [1.5; 1.4-1.7], heart disease [2.1; 1.8-2.4], CKD [2.5; 2.1-3.0]. The prevalence of hypertension (55%), diabetes (33%), smoking history (23%) and heart disease (17%) among the COVID-19 hospitalized patients in the US were substantially higher than that of the general US population, suggesting increased susceptibility to infection or disease progression for the individuals with comorbidities. **CONCLUSIONS:** Public health screening for COVID-19 can be prioritized based on risk-groups. Appropriately addressing the modifiable risk factors such as smoking, hypertension, and diabetes could reduce morbidity and mortality due to COVID-19; public messaging can be accordingly adapted.

FIGURES

Table 3. Pooled prevalence of severe disease stratified by epidemiological risk factors in COVID-19 patients.

Risk group or outcome	Prevalence of Severe Disease (Case Severity Risk) and Risk Factors			Summary Relative Risk of Severe Disease			
	No. of studies	Prevalence of severe disease and case severity risk*, % (95% CI)	Prevalence of risk factor in people with severe disease, % (95% CI)	No. of studies	Fixed Effects sRR; 95% CI (Shore adjusted)	Random Effects ^a sRR; (95% CI)	Heterogeneity I^2 ; c^2 ; p value
Severe disease	25	20 (16–25)	N/A	N/A	N/A	N/A	N/A
Age ≥ 60 years	26	48 (39–59)	56 (52–61)	29	1.57 (1.36–1.80)	1.76 (1.50–2.07)	85%; 184; p<0.01
Male	45	40 (34–47)	63 (61–66)	47	1.26 (1.18–1.35)	1.33 (1.22–1.44)	38%; 75; p<0.01
Smoking history	27	39 (34–46)	26 (21–32)	27	1.29 (1.18–1.42)	1.32 (1.18–1.47)	33%; 39; p = 0.05
Current smoker	13	38 (28–53)	13 (9–20)	15	1.52 (1.21–1.91)	1.25 (94–1.66)	75%; 56; p<0.01
COPD	24	43 (35–52)	14 (12–17)	29	1.71 (1.49–1.97)	1.83 (1.54–2.18)	84%; 179; p<0.01
Hypertension	39	44 (37–53)	55 (50–61)	40	1.46 (1.28,1.65)	1.54 (1.33,1.78)	77%; 168; p<0.01
Diabetes	43	43 (38–49)	33 (30–38)	44	1.48 (1.35–1.63)	1.64 (1.47–1.82)	59%; 104; p<0.01
Cardiovascular disease	37	56 (48–65)	28 (24–33)	38	1.54 (1.39–1.72)	1.74 (1.52–1.98)	77%; 164; p<0.01
Chronic kidney disease	22	36 (33–40)	26 (19–37)	27	1.56 (1.31–1.86)	1.42 (1.15–1.76)	85%; 176; p<0.01
Chronic Liver Disease	12	43(32–57)	5 (3–7)	15	1.63 (1.23–2.15)	1.66 (1.16–2.36)	82%; 76; p<0.01

*Case severity risk represent total number of people developing severe disease in the specific risk group divided by total population in that risk group.

^a Prevalence of risk factor in severe disease represent total number of people with the risk factor divided by total population with severe disease.

Table 2. Pooled prevalence of death stratified by epidemiological risk factors in COVID-19 patients hospitalized between December 2019–August 2020.

Risk factor or Outcome	Overall prevalence of risk across studies		Pooled Prevalence of Death (Case Fatality Risk) and Risk Factor			Summary Relative Risk of Death			
	No. of studies	Pooled prevalence of risk factor and death, % (95% CI)	No. of studies	*Case fatality risk (Prevalence of death in risk group), % (95% CI)	*Prevalence of risk factor in persons who died, % (95% CI)	No. of studies	Fixed Effects sRR; (95% CI) Shore adjusted	Random Effects ^a sRR; (95% CI)	Heterogeneity I^2 ; c^2 ; p value
Death	60	20 (18–23)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Age ≥ 60 years	41	48 (44–53)	18	35 (28–43)	85 (80–89)	24	3.61 (2.96–4.39)	1.29 (1.03–1.62)	77%; 99; p<0.01
Male	75	59 (57–60)	31	26 (21–32)	66 (64–69)	36	1.31 (1.22–1.40)	1.34 (1.24–1.45)	18%; 43; p = 0.17
Smoking history	41	26 (22–31)	11	27 (24–32)	44 (38–50)	13	1.28 (1.06–1.55)	1.41 (1.12–1.78)	68%; 37; p<0.01
Current smoker	21	10 (7–13)	7	21 (14–29)	13 (7–24)	8	1.43 (91–2.26)	1.53 (95–2.45)	78%; 32; p<0.01
COPD	52	9 (8–11)	20	51 (36–71)	12 (7–19)	22	1.70 (1.42–2.04)	1.74 (1.43–2.13)	66%; 61; p<0.01
Hypertension	64	50 (46–54)	29	28 (23–36)	66 (61–70)	32	1.76 (1.58–1.96)	1.88 (1.66–2.13)	56%; 70; p<0.01
Diabetes	67	28 (25–31)	29	24 (17–33)	39 (35–44)	33	1.50 (1.35–1.66)	1.60 (1.42–1.79)	58%; 77; p<0.01
Cardiovascular disease	65	17 (15–20)	29	52 (46–60)	37 (32–43)	34	2.08 (1.81–2.39)	2.25 (1.92–2.64)	69%; 106; p<0.01
Chronic kidney disease	47	13 (11–16)	18	48 (37–63)	27 (21–34)	23	2.52 (2.11–3.00)	2.39 (1.91–2.99)	72%; 79; p<0.01
Chronic Liver Disease	31	2(2–3)	8	39(31–50)	6 (4–8)	9	2.65 (1.88–3.75)	1.99 (1.26–3.16)	77%; 35; p<0.01

*Case fatality risk of represent total number of people that died in the specific risk group divided by total population in the risk group.

^a Prevalence of risk group in dead represent total number of people having the risk group divided by total population that died.

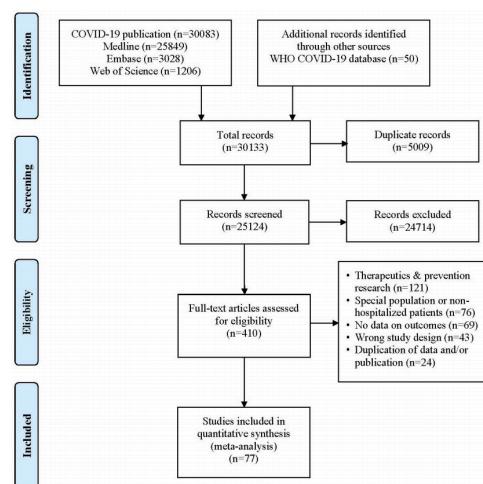


Fig 1. PRISMA flow diagram for selection of studies.

SARS-COV-2 PNEUMONIA IN A NEWBORN TREATED WITH REMDESIVIR AND COVID-19 CONVALESCENT PLASMA

Hopwood AJ, Jordan-Villegas A, Gutierrez LD, Cowart MC, Vega-Montalvo W, Cheung WL, McMahan MJ, Gomez MR, Laham FR.. J Pediatric Infect Dis Soc. 2020 Dec 11:piaa165. doi: 10.1093/jpids/piaa165. Online ahead of print.

Level of Evidence: 5 - Case report

BLUF

Pediatricians from Arnold Palmer Hospital for Children in Orlando, Florida discuss the case of a female infant born at 40 weeks gestation to a 15-year-old primigravida woman with asymptomatic COVID-19 who tested positive at 24 hours of life via rt-PCR. She developed a fever at 25 hours of life and later required supplemental oxygen, CPAP, and remdesivir to achieve an SpO₂ of 88% on day of life 4. On day of life 5, she developed acute respiratory failure requiring intubation and dexamethasone (Figure 1). The infant eventually developed superimposed bacterial pneumonia with *Staphylococcus lugdunensis* on sputum cultures, and after aggressive treatment was eventually weaned back to room air. The authors claim this case illustrates vertical transmission of COVID-19 is possible due to the rapid onset of symptoms after birth; however, neither the placenta nor the amniotic fluid were sampled. This case illustrates severe disease in a neonate with likely superimposed bacterial pneumonia and possible vertical transmission.

FIGURES

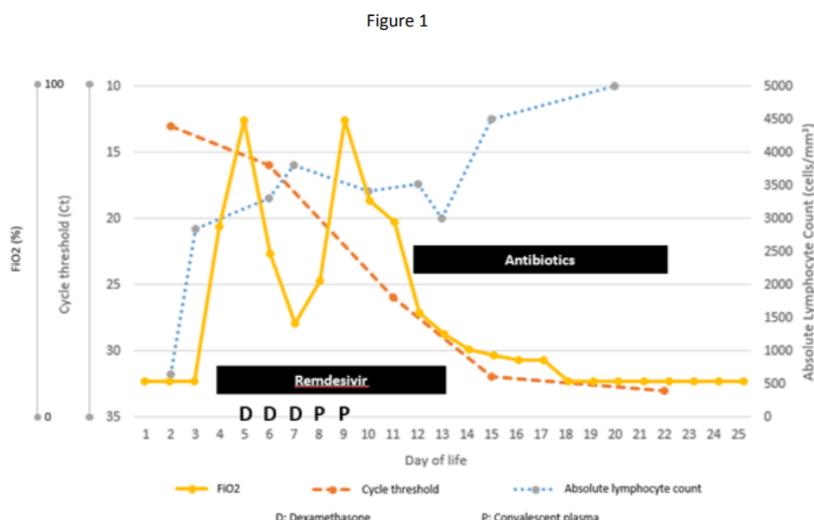


Figure 1. Clinical Course of an Infant with SARS-CoV-2 Pneumonia Treated with Remdesivir and COVID-19 Convalescent Plasma: Convalescent plasma was administered in two separate infusions to assess for tolerability and dose escalation. Nafcillin and vancomycin were given for ten days to treat *Staphylococcus lugdunensis* pneumonia.

UNDERSTANDING THE PATHOLOGY

HOW SARS-COV-2 (COVID-19) SPREADS WITHIN INFECTED HOSTS - WHAT WE KNOW SO FAR

Sanyal S.. Emerg Top Life Sci. 2020 Dec 11;4(4):371-378. doi: 10.1042/ETLS20200165.

Level of Evidence: 5 - Review / Literature Review

BLUF

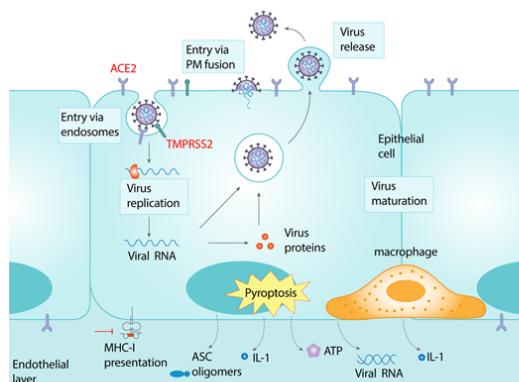
An expert in virus-host interaction from the University of Oxford reviews the current knowledge of how SARS-CoV-2 spreads within infected hosts. They review entry mechanisms, namely how Neuropilin 1 and ACE II facilitate SARS-CoV-2 entry into host cells and that cells expressing ACE II and TMPRSS2 (a mucosa-specific serine protease) are susceptible to infection (Figure 1). She also reviews viral replication, assembly, release, and cell-cell spread and concludes with a discussion of host immunity invasion via MHC-I antigen presentation downregulation in concert with upregulation of cytokine secretion. The author suggests COVID-19 progression is a "combined effect of virus spread and aberrant immune responses," and that understanding the underlying mechanisms will allow the creation of appropriate therapies.

ABSTRACT

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of the ongoing pandemic of coronavirus disease 2019 (COVID-19), belongs to the betacoronavirus genus and shares high homology to the severe acute respiratory syndrome coronavirus (SARS-CoV) that emerged in 2003. These are highly transmissible and pathogenic viruses which very likely originated in bats. SARS-CoV-2 uses the same receptor, angiotensin-converting enzyme 2 (ACE2) as SARS-CoV, and spreads primarily through the respiratory tract. Although several trials for vaccine development are currently underway, investigations into the virology of SARS-CoV-2 to understand the fundamental biology of the infectious cycle and the associated immunopathology underlying the clinical manifestations of COVID-19 are crucial for identification and rational design of effective therapies. This review provides an overview of how SARS-CoV-2 infects and spreads within human hosts with specific emphasis on key aspects of its lifecycle, tropism and immunopathological features.

FIGURES

Figure 1.



[VIEW LARGE](#)

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Schematic of the intracellular lifecycle of SARS-CoV-2 and associated immunopathology.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infects cells expressing the surface receptors angiotensin-converting enzyme 2 (ACE2) and TMPRSS2, resulting in entry of the virus via the endocytic machinery or upon fusion at the plasma membrane. The viral genome is released into the cytosol upon fusion of the viral and host membranes and undergoes replication, transcription, translation and assembly to form viral progenies that are released into the extracellular space via unknown mechanisms. Amplification and release of the virus leads to host cell pyroptosis and release of damage-associated molecular patterns, including ATP, nucleic acids and ASC oligomers. This is accompanied by secretion of pro-inflammatory cytokines and chemokines culminating in a cytokine storm. On the other hand MHC-I restricted antigen presentation is downregulated most likely by binding of the viral Orf8 protein, resulting in attenuated T-cell activation, thereby contributing to the common clinical feature of lymphopenia.

TRANSMISSION & PREVENTION

PREVENTION IN THE COMMUNITY

SARS-COV-2 INFECTION AND TRANSMISSION IN EDUCATIONAL SETTINGS: A PROSPECTIVE, CROSS-SECTIONAL ANALYSIS OF INFECTION CLUSTERS AND OUTBREAKS IN ENGLAND

Ismail SA, Saliba V, Lopez Bernal J, Ramsay ME, Ladhani SN.. Lancet Infect Dis. 2020 Dec 8:S1473-3099(20)30882-3. doi: 10.1016/S1473-3099(20)30882-3. Online ahead of print.

Level of Evidence: 3 - Local non-random sample

BLUF

Researchers from England studying COVID-19 transmission in the education system found that the overall risk of SARS-CoV2 infection among children and school staff was low. There was minimal evidence of transmission from student to student or student to faculty member, and infected children most commonly acquired SARS-CoV-2 from family members at home. Data suggests that the rate of transmission in schools was directly correlated with regional COVID-19 prevalence, suggesting that re-opening schools may not significantly increase infection rates among children or school staff unless this is during a surge or in high prevalence areas.

ABSTRACT

BACKGROUND: Understanding severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and transmission in educational settings is crucial for ensuring the safety of staff and children during the COVID-19 pandemic. We estimated the rate of SARS-CoV-2 infection and outbreaks among staff and students in educational settings during the summer half-term (June-July, 2020) in England. **METHODS:** In this prospective, cross-sectional analysis, Public Health England initiated enhanced national surveillance in educational settings in England that had reopened after the first national lockdown, from June 1 to July 17, 2020. Educational settings were categorised as early years settings (<5-year-olds), primary schools (5-11-year-olds; only years 1 and 6 allowed to return), secondary schools (11-18-year-olds; only years 10 and 12), or mixed-age settings (spanning a combination of the above). Further education colleges were excluded. Data were recorded in HPZone, an online national database for events that require public health management. RT-PCR-confirmed SARS-CoV-2 event rates and case rates were calculated for staff and students, and direction of transmission was inferred on the basis of symptom onset and testing dates. Events were classified as single cases, coprimary cases (at least two confirmed cases within 48 h, typically within the same household), and outbreaks (at least two epidemiologically linked cases, with sequential cases diagnosed within 14 days in the same educational setting). All events were followed up for 28 days after educational settings closed for the summer holidays. Negative binomial regression was used to correlate educational setting events with regional population, population density, and community incidence. **FINDINGS:** A median of 38 000 early years settings (IQR 35 500-41 500), 15 600 primary schools (13 450-17 300), and 4000 secondary schools (3700-4200) were open each day, with a median daily attendance of 928 000 students (630 000-1 230 000) overall. There were 113 single cases of SARS-CoV-2 infection, nine coprimary cases, and 55 outbreaks. The risk of an outbreak increased by 72% (95% CI 28-130) for every five cases per 100 000 population increase in community incidence ($p<0.0001$). Staff had higher incidence than students (27 cases [95% CI 23-32] per 100 000 per day among staff compared with 18 cases [14-24] in early years students, 6 0 cases [4 3-8 2] in primary schools students, and 6 8 cases [2 7-14] in secondary school students]), and most cases linked to outbreaks were in staff members (154 [73%] staff vs 56 [27%] children of 210 total cases). Probable direction of transmission was staff to staff in 26 outbreaks, staff to student in eight outbreaks, student to staff in 16 outbreaks, and student to student in five outbreaks. The median number of secondary cases in outbreaks was one (IQR 1-2) for student index cases and one (1-5) for staff index cases. **INTERPRETATION:** SARS-CoV-2 infections and outbreaks were uncommon in educational settings during the summer half-term in England. The strong association with regional COVID-19 incidence emphasises the importance of controlling community transmission to protect educational settings. Interventions should focus on reducing transmission in and among staff. **FUNDING:** Public Health England.

FIGURES

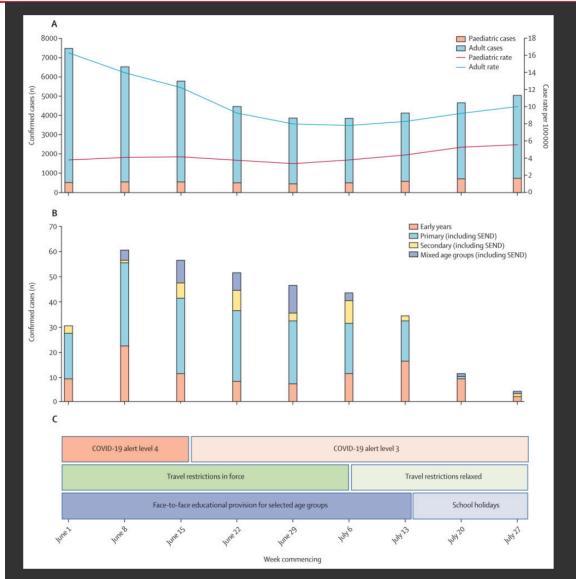


Figure 1. Trends of confirmed adult and pediatric cases in the general population compared to the educational setting

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

Members of the US Centers for Disease Control COVID-19 Response Team summarize their recommended public health strategies for mitigation of community SARS-CoV-2 transmission. They recommend the use of face masks, maintaining physical distancing, prompt case investigation, avoiding crowded situations, increasing protection for persons at highest risk for severe COVID-19, adequately protecting healthcare workers, improved hygiene practices, avoiding unnecessary travel, and widespread use of safe vaccines (Table 1). Authors suggest following such evidence-based measures will substantially contribute to combating transmission of COVID-19.

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.

FIGURES

Recommended public health strategies	Individual- and household-level strategies	Community-level strategies (at state or local level)	Links to guidance
Universal use of face masks	Consistent and correct use of face masks, including within the household if there is a COVID-19 case or a person with a known or possible exposure in the household	Issue policies or directives mandating universal use of face masks in indoor (nonhousehold) settings Plan for provision of face masks for specific populations if needed	Considerations for wearing masks: https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/cloth-face-cover-guidance.html Caring for someone sick at home, when to wear a mask or gloves: https://www.cdc.gov/coronavirus/2019-ncov/if-you-are-sick/care-for-someone.html#face-covering Protect your home: https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/protect-your-home.html
Physical distancing and limiting contacts	Maintain physical distance (≥ 6 feet) from other persons when possible, and limit number of contacts with persons outside the immediate household	Physical barriers and visual reminders might promote adherence to maintaining physical distance	Social distancing: https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/social-distancing.html Personal and social activities: https://www.cdc.gov/coronavirus/2019-ncov/daily-life-coping/personal-social-activities.html
Avoid nonessential indoor spaces and crowded outdoor settings	Avoid nonessential indoor spaces and crowded outdoor settings	Issue policies or directives restricting some nonessential indoor spaces that pose the highest risk for transmission Promoting flexible worksites (e.g., telework); apply limits to occupancy of indoor spaces and to the size of social gatherings	Daily activities and going out: https://www.cdc.gov/coronavirus/2019-ncov/daily-life-coping/going-out.html Considerations for events and gatherings: https://www.cdc.gov/coronavirus/2019-ncov/community/large-events/considerations-for-events-gatherings.html
Increased testing, diagnosis, and isolation	Persons with a known exposure to someone with COVID-19, with possible exposure, or who experience symptoms should promptly seek testing; symptomatic or infected persons should isolate promptly; exposed persons should quarantine	Increase access to testing, including expanded screening testing of prioritized persons/groups, prioritizing those with many interactions (or interactions with persons at high risk) based on their occupational or residential setting Promptly report test results to the person tested and to public health authorities	Testing: https://www.cdc.gov/coronavirus/2019-ncov/testing/index.html Expanded screening testing: https://www.cdc.gov/coronavirus/2019-ncov/php/open-america/expanded-screening-testing.html Isolate if you are sick: https://www.cdc.gov/coronavirus/2019-ncov/if-you-are-sick/isolation.html Guidance for health departments about COVID-19 testing in the community: https://www.cdc.gov/coronavirus/2019-ncov/php/open-america/testing.html
Prompt case investigation and contact tracing to identify, quarantine, and test close contacts	Persons with diagnosed COVID-19 should provide names of known contacts; close contacts should anticipate a call from the health department, answer the call, adhere to quarantine, seek testing, and encourage their household members to quarantine	When incidence is high and overwhelms capacity, prioritize case investigation and contact tracing to promptly quarantine and test close contacts, based on time since sample collection and risk for spread to others (e.g., those working in high-density settings)	When to quarantine: https://www.cdc.gov/coronavirus/2019-ncov/if-you-are-sick/quarantine.html Contact tracing (your health): https://www.cdc.gov/coronavirus/2019-ncov/daily-life-coping/contact-tracing.html Contact tracing (health departments): https://www.cdc.gov/coronavirus/2019-ncov/php/open-america/contact-tracing/index.html Prioritizing case investigation and contact tracing: https://www.cdc.gov/coronavirus/2019-ncov/php/contact-tracing/contact-tracing-plan/prioritization.html Quarantine: https://www.cdc.gov/coronavirus/2019-ncov/more/scientific-brief-options-to-reduce-quarantine.html
Safeguarding persons most at risk for severe illness or death	Persons with underlying medical conditions or risk factors that place them at increased risk for severe illness or death should minimize contact with nonhousehold members and nonessential indoor spaces	Protect persons most at risk for severe illness or death through 1) identifying populations at high risk in the community and 2) expanding access to testing, provision of support services, and messaging	People at increased risk: https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/index.html

See table footnotes on the next page.

Table 1. Individual- and community-level public health strategies to reduce SARS-CoV-2 transmission.

Recommended public health strategies	Individual- and household-level strategies	Community-level strategies (at state or local level)	Links to guidance
Protecting essential workers	Essential workers should employ all available public health strategies to reduce their risk (e.g., wear face masks and keep physical distance)	Protect essential workers through policies directing administrative and structural prevention as well as expanded testing	<p>Essential services and critical infrastructure: https://www.cdc.gov/coronavirus/2019-ncov/community/workplaces-businesses/essential-services.html</p> <p>COVID-19 critical infrastructure sector response planning: https://www.cdc.gov/coronavirus/2019-ncov/community/critical-infrastructure-sectors.html</p> <p>CISA guidance on the essential critical infrastructure workforce: https://www.cisa.gov/publication/guidance-essential-critical-infrastructure-workforce</p>
Postponing travel	<p>Travel should be postponed. Those who choose to travel internationally should be tested with a viral test 1–3 days before departure and retested 3–5 days after arrival; domestic travelers should also consider getting tested</p> <p>Travelers should stay home or reduce nonessential activities before and after travel and be diligent about mask wearing, physical distancing, hand hygiene, and symptom monitoring</p>	<p>Issue policies or directives mandating universal use of face masks on all modes of public transportation</p>	<p>Travel: https://www.cdc.gov/coronavirus/2019-ncov/travelers/index.html</p> <p>When not to travel: https://www.cdc.gov/coronavirus/2019-ncov/travelers/when-to-delay-travel.html</p> <p>Wear face masks on public transportation conveyances and at transportation hubs: https://www.cdc.gov/coronavirus/2019-ncov/travelers/face-masks-public-transportation.html</p> <p>Mask and travel guidance: https://www.cdc.gov/quarantine/masks/mask-travel-guidance.html</p> <p>Domestic travel: https://www.cdc.gov/coronavirus/2019-ncov/travelers/travel-during-covid19.html</p> <p>Testing and international air travel: https://www.cdc.gov/coronavirus/2019-ncov/travelers/testing-air-travel.html</p>
Increased room air ventilation, enhanced hand hygiene, and cleaning and disinfection	Increase room air ventilation	Enhance ventilation and cleaning and disinfection, particularly of essential indoor spaces	SARS-CoV-2 and potential airborne transmission: https://www.cdc.gov/coronavirus/2019-ncov/more/scientific-brief-sars-cov-2.html
Frequent handwashing		Ensure provision of adequate hand sanitation supplies	<p>Ventilation: https://www.cdc.gov/coronavirus/2019-ncov/community/general-business-faq.html#Ventilation</p> <p>When and how to wash your hands: https://www.cdc.gov/handwashing/when-how-handwashing.html</p> <p>Cleaning and disinfecting: https://www.cdc.gov/coronavirus/2019-ncov/community/clean-disinfect/index.html</p>
Widespread availability and coverage with effective vaccines	<p>Seek vaccine when appropriate following ACIP recommendations</p> <p>Continue to follow all mitigation measures until community vaccination coverage is adequate</p>	<p>Plan for distribution and administration of vaccines to achieve high community coverage</p> <p>Communicate that mitigation measures still need to be followed until community vaccination coverage is determined to be adequate</p>	<p>Vaccines: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/index.html</p> <p>Vaccination planning: https://www.cdc.gov/vaccines/covid-19/planning/index.html</p>

Abbreviations: ACIP = Advisory Committee on Immunization Practices; COVID-19 = coronavirus disease 2019.
 * <https://www.cdc.gov/coronavirus/2019-ncov/communication/guidance-list.html>.

Table 1 (continued): Individual- and community-level public health strategies to reduce SARS-CoV-2 transmission.

THERMAL INACTIVATION OF COVID-19 SPECIMENS IMPROVES RNA QUALITY AND QUANTITY

Hemati M, Soosanabadi M, Ghorashi T, Ghaffari H, Vahedi A, Sabbaghian E, Rasouli Nejad Z, Salati A, Danaei N, Kokhaei P.. J Cell Physiol. 2020 Dec 11. doi: 10.1002/jcp.30206. Online ahead of print.

Level of Evidence: 5 - Modeling

BLUF

A multidisciplinary team from Semnan University of Medical Sciences in Iran investigated the effect of thermal inactivation on accuracy of SARS-CoV-2 RT-PCR results using oropharyngeal and nasopharyngeal samples from 36 patients hospitalized with suspected COVID-19. They found that thermally inactivated specimens (incubation at 60°C for 30 min) had increased quantity of RNA ($p=0.028$)(Figure 1) and RNA copy number for both N ($p=0.009$) and ORF1ab genes, ($p=0.032$)(Figure 2) compared to the active samples that did not undergo inactivation. The authors conclude that thermal inactivation of SARS-CoV-2 testing samples protects lab workers from the risk of viral contamination while simultaneously increasing the quality and quantity of extracted RNA.

ABSTRACT

The rapid spread of coronavirus disease 2019 (COVID-19), a disease caused by severe acute respiratory syndrome coronavirus 2, poses a huge demand for immediate diagnosis. Real-time reverse transcriptase-polymerase chain reaction (rRT-PCR) of nasopharyngeal (NP) and oropharyngeal (OP) swabs have been used to confirm the clinical diagnosis. To avoid the risk of viral-exposure of laboratory workers, thermal inactivation is currently recommended but has unknown effects on the accuracy of the rRT-PCR results. Thirty-six NP/OP specimens were collected from COVID-19 patients and subjected to thermal inactivation (60 C for 30 min) or the RNA extraction processes to activate the form. Here, our data showed that the concentration of extracted-RNA increases upon thermal inactivation compared to the active form ($p = .028$). Significantly higher levels of RNA copy number were obtained in inactivated compared to the active samples for both N and ORF1ab genes ($p = .009$, $p = .032$, respectively). Thermal inactivation elevated concentration and copy number of extracted-RNA, possibly through viral-capsid degradation and/or nucleoprotein denaturation.

FIGURES

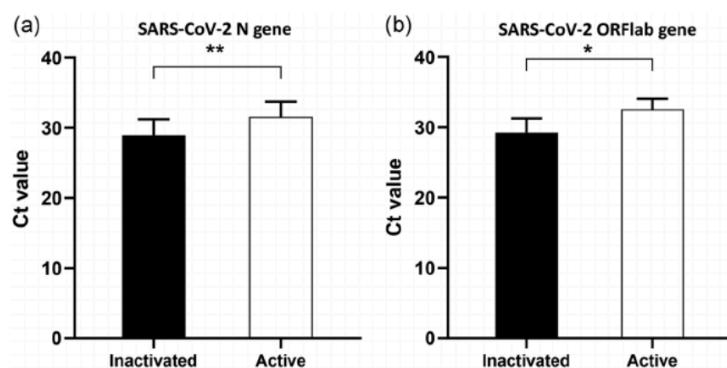


FIGURE 2 Impact of thermal inactivation on real-time PCR results of extracted-RNA. To determine the effect of thermal inactivation protocol (60°C, 30 min) on SARS-CoV-2 quantity, the N- and ORF1ab-gene expression was assessed in both inactivated and active samples using real-time PCR assay ($n = 7$). (a) Results showed that the expression of N-gene with C_t value mean 28.97 in inactivated samples is lower than its expression in active samples with C_t value mean 31.57 ($p = .009$). (b) Similarly, the expression of ORF1ab-gene in inactivated samples had a lower C_t value with a mean of 29.26 than its expression in active samples with a mean of C_t value 32.54 ($p = .032$). Significant p values were calculated using the paired t -test after passing the normality test (Kolmogorov-Smirnov). Values are the mean \pm SEM (error bars). PCR, polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2. * $p < .05$; ** $p < .01$.

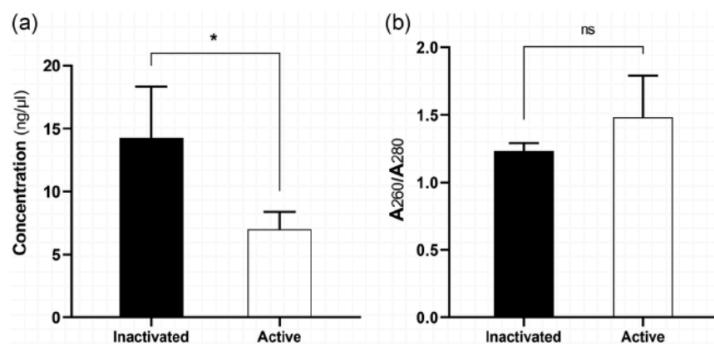


FIGURE 1 The effect of thermal inactivation on the integrity of extracted-RNA. To evaluate the effect of SARS-CoV-2 inactivation through heat treatment, suspected specimens of the upper respiratory tract from 36 hospitalized patients were divided into two (inactivated and active) group. Inactivated samples were incubated at 60°C for 30 min and subsequently, RNA extraction was performed for both inactivated and active samples. The concentration and purity of extracted-RNAs were determined using a NanoDrop Spectrophotometer. (a) The concentration of extracted-RNA was higher in inactivated samples than active samples ($p = .028$). (b) No significant differences were found between A_{260}/A_{280} in inactivated and active samples ($p = .421$). Significant p values were calculated using the paired t test after passing the normality test (Kolmogorov-Smirnov). Values are the mean \pm SEM (error bars). ns, nonsignificant; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2. * $p < .05$

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