The Daily COVID-19 Literature Surveillance Summary

August 27, 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

- A group at USC's Keck School of Medicine identified public health concerns of COVID-19 risk in individuals who vape through systematic surveillance on Twitter. They discuss whether this population should be prioritized in COVID-19 screening and whether individuals should stop vaping as a preventive measure. They additionally identified posts sharing unsubstantiated health claims of vaping methods/products used to protect against COVID-19 and discuss the need for additional research in vaping and COVID-19 to combat misinformation.

Epidemiology

- A retrospective single-center study in Wuhan, China including 43 women of child-bearing age (17 pregnant and 26 non-pregnant) with COVID-19 found significantly higher neutrophil%, lymphocyte%, alkaline phosphates, and D-dimer among the pregnant cohort ($p<0.001$; Table 2), but no significant difference in hospitalization time, time from onset to diagnosis, time of viral shedding, or redirected positive tests. This data suggests no indication that pregnant women are more susceptible to severe adverse outcomes of COVID-19.

Understanding the Pathology

- Researchers in Rome, Italy performed molecular human leukocyte antigen (HLA) typing to compare 99 severe COVID-19 patients to over 1000 previously typed individuals and found a significant association between COVID-19 infection severity and HLA alleles DRB1*15:01, DQB1*06:02, and B*27:07. The investigators suggest HLA alleles may be markers of COVID-19 susceptibility but acknowledge a need for larger scale studies to confirm these findings.
- Analysis of single nucleotide polymorphisms (SNPs) and other mutations of sequenced SARS-CoV-2 genomes from 12 countries within the NCBI database found 47 key point mutations within several SARS-CoV-2 proteins (namely Nsp1, spike glycoprotein, and RdRp) that may play a role in SARS-CoV-2 virulence, suggesting that these point mutations or SNPs could aid the development of antiviral therapies for SARS-CoV-2.

Management

- Cardiologists based in Athens, Greece conducted meta-analyses to explore the relationship of smoking with disease severity and mortality of patients hospitalized with COVID-19 in China and the US. The first meta-analysis of 18 studies (n=6210) found that smoking was associated with a slightly increased risk of severe COVID-19—a difference that is more pronounced in younger patients without diabetes. Additional meta-analyses were inconclusive due to the small sample sizes and the findings are limited by poor-quality data and relatively low study heterogeneity.

Adjusting Practice During COVID-19

- UK researchers report the importance of using electronic self-assessments of patient health status or patient reported outcomes in COVID-19 diagnosis, tracking, tracing and symptom monitoring citing multiple benefits of electronic self-assessments.

R&D: Diagnosis & Treatments

- A network meta-analysis of 4 randomized clinical studies including 2,049 moderate/severe COVID-19 patients on the effectiveness of remdesivir in COVID-19 treatment found that both 10-day and 5-day regimens of remdesivir corresponded with greater odds of clinical improvement and greater probabilities of clinical recovery as compared to the placebo group. However, the 5-day regimen resulted in greater odds of clinical improvement when compared to the 10-day regimen.
- A cohort study of 220 COVID-19 patients in Australia found that on-site SARS-CoV-2 RT-PCR testing had a shorter testing turnaround time and isolation period, fewer pathology test orders, and reduced antibiotic use in COVID-19 negative patients, as compared to send away testing. The investigators advocate for on-site COVID-19 testing as a more efficient method than send away testing, suggesting it may reduce healthcare costs and preserve resources.

TABLE OF CONTENTS

CLIMATE

GLOBAL

PUBLIC HEALTH CONCERNS AND UNSUBSTANTIATED CLAIMS AT THE INTERSECTION OF VAPING AND COVID-19

Majmundar A, Allem JP, Cruz TB, Unger JB.. Nicotine Tob Res. 2020 Aug 24;22(9):1667-1668. doi: 10.1093/ntr/ntaa064.
Level of Evidence: 2 - Expert Opinion

BLUF

An expert opinion piece from the department of preventative medicine at USC's Keck School of Medicine identified public health concerns of increased COVID-19 risk in vaping individuals during a systematic surveillance on Twitter. They highlight discussions regarding whether this population should be prioritized in COVID-19 screening and whether they should stop vaping/sharing vape devices as a preventive measure, and point out posts related to unsubstantiated health claims of vaping methods/products used to protect against COVID-19 (outlined below). The authors cite tobacco control experts' suggestions that smokers who contract COVID-19 are at greater risk of suffering complications, in addition to calling for increased vaping/smoking research in relation to COVID-19 infection and continued surveillance of public discourse on the topic.

SUMMARY

Unsubstantiated health claims:
- Vaping devices may protect against COVID-19 by humidifying the lungs.
- These devices may act as delivery vehicles for administering protection from COVID-19 (i.e. organic oregano oil) into the lungs.
- The possible ability of poly-glycerine to destroy COVID-19 airborne pathogen.

RISK ESTIMATION AND PREDICTION OF THE TRANSMISSION OF CORONAVIRUS DISEASE-2019 (COVID-19) IN THE MAINLAND OF CHINA EXCLUDING HUBEI PROVINCE

Wan H, Cui JA, Yang GJ.. Infect Dis Poverty. 2020 Aug 24;9(1):116. doi: 10.1186/s40249-020-00683-6.
Level of Evidence: Other - Modeling

BLUF

An interdisciplinary group of researchers collaborating in China and Switzerland performed a novel dynamic COVID-19 transmission model simulation analysis to assess protective measures (ie., social distancing, restricted travel, contact tracing, PPE) to mitigate the spread of SARS-CoV-2. Findings indicate that the measures put in place by the Chinese government have reduced the intensity of transmission of and prevented growth of positive cases. The simulation data showed:

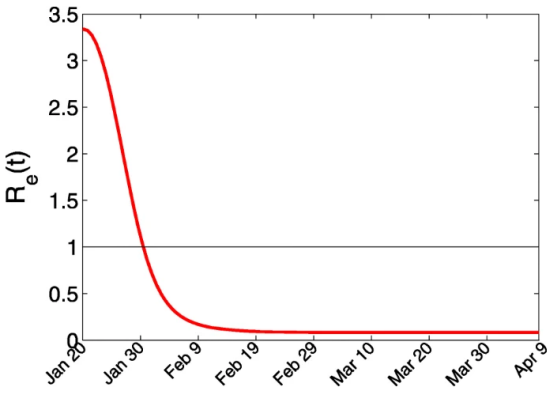
- With protective measures, the effective daily reproduction ratio, Re(t)=0.89 (Figure 5), with a number <1 being significant for showing decreases in transmission intensity
- Scenarios in which population contact rates, c(t)of 20% show that the disease will not rebound (Figure 6, Table 3)

The authors advocate that protective measures minimize COVID-19 infection rates, suggesting the general populous adhere to self-protection and self-isolation during this epidemic to ensure its rapid end.

ABSTRACT

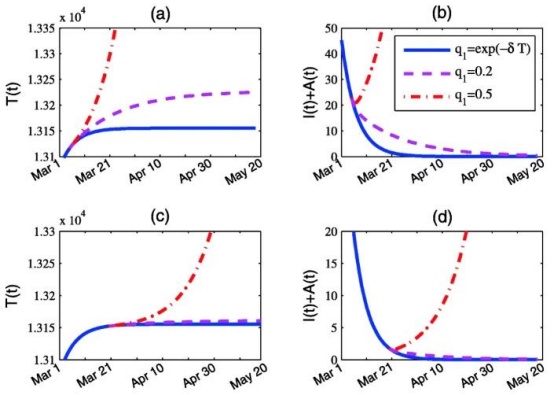
BACKGROUND: In December 2019, an outbreak of coronavirus disease (later named as COVID-19) was identified in Wuhan, China and, later on, detected in other parts of China. Our aim is to evaluate the effectiveness of the evolution of interventions and self-protection measures, estimate the risk of partial lifting control measures and predict the epidemic trend of the virus in the mainland of China excluding Hubei province based on the published data and a novel mathematical model. METHODS: A novel COVID-19 transmission dynamic model incorporating the intervention measures implemented in China is proposed. COVID-19 daily data of the mainland of China excluding Hubei province, including the cumulative confirmed cases, the cumulative deaths, newly confirmed cases and the cumulative recovered cases between 20 January and 3 March 2020, were archived from the National Health Commission of China (NHCC). We parameterize the model by using the Markov Chain Monte Carlo (MCMC) method and estimate the control reproduction number (Rc), as well as the effective daily reproduction ratio-Re(t), of the disease transmission in the mainland of China excluding Hubei province. RESULTS: The estimation outcomes indicate that Rc is 3.36 (95% CI: 3.20-3.64) and Re(t) has dropped below 1 since 31 January 2020, which implies that the containment strategies implemented by the Chinese government in the mainland of China are indeed effective and magnificently suppressed COVID-19 transmission. Moreover, our results show that relieving personal protection too early may lead to a prolonged disease transmission period and more people would be infected, and may even cause a second wave of epidemic or outbreaks. By calculating the effective reproduction ratio, we prove that the contact rate should be kept at least less than 30% of the normal level by April, 2020. CONCLUSIONS: To ensure the pandemic ending rapidly, it is necessary to maintain the current integrated restrict interventions and self-protection measures, including travel restriction, quarantine of entry, contact tracing followed by quarantine and isolation and reduction of contact, like wearing masks, keeping social distance, etc. People should be fully aware of the real-time epidemic situation and keep sufficient personal protection until April. If all the above conditions are met, the outbreak is expected to be ended by April in the mainland of China apart from Hubei province.

Fig. 5



Effective reproduction number

Fig. 6



Comparison of scenarios with different contact rates. The abscissa axis is the time. The blue solid line is the case with no changes (q_1=$exp(-\delta T(t))$); The purple dash line is the case with q_1=0.2; The red dash-dot line is the case with q_1=0.5. **a**–**b** Adjust the contact rate from 5 March 2020; **c**–**d** Adjust the contact rate from 20 March 2020

Table 3 The impact of partial lifting control measures and personal protection

From: Risk estimation and prediction of the transmission of coronavirus disease-2019 (COVID-19) in the mainland of China excluding Hubei province

Starting time of adjustment	Maximum of cumulative confirmed cases	Epidemic period
No adjustment ($\sigma(t)=q_1e^{-\delta T(t)}$)	13 155	70 days
5 March ($\sigma(t)=0.2q_0$)	13 227	110 days
5 March ($\sigma(t)=0.5q_0$)	More than 447 million	More than 365 days
20 March ($\sigma(t)=0.2q_0$)	13 161	77 days
20 March ($\sigma(t)=0.5q_0$)	More than 445 million	More than 365 days

PREGNANT PERSONS

CLINICAL CHARACTERISTICS AND OUTCOMES OF CHILDBEARING-AGE WOMEN WITH COVID-19 IN WUHAN: RETROSPECTIVE, SINGLE-CENTER STUDY

Wei L, Gao X, Chen S, Zeng W, Wu J, Lin X, Zhang H, Mwamaka Sharifu L, Chen L, Feng L, Wang S.. J Med Internet Res. 2020 Aug 24;22(8):e19642. doi: 10.2196/19642.
Level of Evidence: 4 - Case-series or case-control studies, or poor quality prognostic cohort study

BLUF

A retrospective single-center study was conducted in Tongji Hospital in Wuhan, China including 43 child-bearing age women (17 pregnant and 26 non-pregnant; Table 1) with COVID-19 infection from January 19 to March 2, 2020, to investigate potential differences in prognosis in pregnancy. They found significantly higher neutrophil%, lymphocyte%, alkaline phosphates, and D-dimer among the pregnant cohort ($p<0.001$; Table 2), but no significant difference in hospitalization time, time from onset to diagnosis, time of viral shedding, or redirected positive tests, suggesting no indication that pregnant women are more susceptible to severe adverse outcomes of COVID-19.

ABSTRACT

BACKGROUND: Since December 2019, an outbreak of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spread rapidly in Wuhan and worldwide. However, previous studies on pregnant patients were limited. OBJECTIVE: The objective of our study was to evaluate the clinical characteristics and outcomes of pregnant and non-pregnant women with COVID-19. METHODS: This study retrospectively collected epidemiological, clinical, laboratory, imaging, management, and outcome data of 43 childbearing-age women patients (including 17 pregnant and 26 non-pregnant patients) who presented with laboratory confirmed of COVID-19 in Tongji Hospital, Wuhan, China, from January 19 to March 2, 2020. Clinical outcomes were followed up to March 28, 2020. RESULTS: Of 43 childbearing-age women in this study, none developed severe adverse illness and or died. The median ages of pregnant and non-pregnant women were 33.0 and 33.5 years, respectively. Pregnant women had a markedly higher proportion of history exposure to hospitals within two weeks before onset (53% vs 19%, P=.02), and a lower proportion of other family members affected (24% vs 73%%, P=.004). Fever (47% vs 69%) and cough (53% vs 46%) were common onset of symptoms for two groups. Abdominal pain (24%), vaginal bleeding (6%), reduced fetal movement (6%), and increased fetal movement (13%) were observed at onset in pregnant patients. Higher neutrophil and lower lymphocyte percent were observed in pregnant group (79% vs 56%, P<.001; 15% vs 33%, P<.001, respectively). In both groups, we observed elevated concentration of high sensitivity C-reactive protein, erythrocyte sedimentation rate, aminotransferase and lactate dehydrogenase. Concentrations of alkaline phosphatase and D-dimer in pregnant group were significantly higher than those of non-pregnant group (119.0 vs 48.0 U/L, P<.001; 2.1vs 0.3mug/mL, P<.001). Both pregnant (4/10; 40%) and non-pregnant (8/15; 53%) women were tested positive for influenza A virus. A majority of pregnant and non-pregnant groups received antiviral (76% vs 96%) and antibiotic (76% vs 88%) therapy. Additionally, both pregnant (2/11; 18%) and non-pregnant (2/19; 11%) recovered women re-detected positive for SARS-CoV-2 after discharge. CONCLUSIONS: The epidemiology, clinical and laboratory features of pregnant women with COVID-19 were diverse and atypical, which increased the difficulty of diagnosis. Most pregnant women with COVID-19 were mild and moderate, and rarely developed severe pneumonia and severe adverse outcomes. CLINICALTRIAL:

FIGURES

Variables	Total (N=43)	Pregnancy (n=17)	Nonpregnancy (n=26)	*P* value
Age (years), median (IQR)	33.0 (30.0-37.0)	33.0 (30.0-35.0)	33.5 (31.0-38.0)	.28
Gestational age on admission, n (%)				
First trimester	N/A[a]	1 (6)	N/A	N/A
Second trimester	N/A	3 (18)	N/A	N/A
Third trimester	N/A	13 (76)	N/A	N/A
Health care workers, n (%)	8 (19)	3 (18)	5 (19)	.77
Hospital exposure within 2 weeks before onset, n (%)	14 (33)	9 (53)	5 (19)	.02
Other family members affected, n (%)	23 (53)	4 (24)	19 (73)	.004
Time from onset of symptom to first outpatient visit (days), median (IQR)	3.5 (1.0-7.0)	2.0 (0.9-10.8)	4.0 (1.0-7.0)	.75
Clinical classification, n (%)				.54
Mild	3 (7)	2 (12)	1 (4)	
Moderate	35 (81)	13 (76)	22 (85)	
Severe	5 (12)	2 (12)	3 (12)	
Critical	0 (0)	0 (0)	0 (0)	
Symptoms at onset, n (%)				
Fever	26 (60)	8 (47)	18 (69)	.15
Chills and rigors	2 (5)	0 (0)	2 (8)	.67
Headache	1 (2)	0 (0)	1 (4)	.83
Dizziness	1 (2)	1 (6)	0 (0)	.83
Fatigue	5 (12)	1 (6)	4 (15)	.93
Cough	21 (49)	9 (53)	12 (46)	.66
Expectoration	9 (21)	3 (18)	6 (23)	.96
Chest tightness	5 (12)	2 (12)	3 (12)	.64
Shortness of breath	2 (5)	1 (6)	1 (4)	.67
Myalgia	1 (2)	0 (0)	1 (4)	.83
Diarrhea	5 (12)	1 (6)	4 (15)	.64
Asymptomatic	4 (9)	2 (12)	2 (8)	.93
Abdominal pain	N/A	4 (24)	N/A	N/A
Vaginal bleeding	N/A	1 (6)	N/A	N/A
Reduced fetal movements	N/A	1 (6)	N/A	N/A
Increased fetal movement	N/A	2 (13)	N/A	N/A

Table 1: Epidemiological and clinical features of pregnant and nonpregnant women with the coronavirus disease.

TODO: ERROR EMBEDDING IMAGE: https://covid19lst.qualtrics.com/jfe/file/F_3noBzc7Sbg3IOQq

Table 2. Laboratory and imaging features of pregnant and nonpregnant women with the coronavirus disease.

Variables	Total (N=43)	Pregnancy (n=17)	Nonpregnancy (n=26)	*P* value
Management, n (%)				
Antiviral therapy	38 (88)	13 (76)	25 (96)	.14
Antibiotic therapy	36 (84)	13 (76)	23 (88)	.54
Glucocorticoid therapy	9 (21)	4 (24)	5 (19)	.96
Immunoglobulin	4 (9)	1 (6)	3 (12)	.93
Cough-suppressant therapy	24 (56)	6 (35)	18 (70)	.03
Oxygen support (nasal cannula)	20 (47)	6 (35)	14 (54)	.23
Mechanical ventilation	0 (0)	0 (0)	0 (0)	N/A[a]
Noninvasive	0 (0)	0 (0)	0 (0)	N/A
Invasive	0 (0)	0 (0)	0 (0)	N/A
Continuous renal replacement therapy	0 (0)	0 (0)	0 (0)	N/A
Extracorporeal membrane oxygenation	0 (0)	0 (0)	0 (0)	N/A
Clinical outcomes				
Intensive care unit admission, n (%)	0 (0)	0 (0)	0 (0)	N/A
Acute respiratory distress syndrome, n (%)	0 (0)	0 (0)	0 (0)	N/A
Disseminated intravascular coagulation, n (%)	0 (0)	0 (0)	0 (0)	N/A
Renal failure, n (%)	0 (0)	0 (0)	0 (0)	N/A
Heart failure, n (%)	0 (0)	0 (0)	0 (0)	N/A
Secondary bacterial pneumonia, n (%)	0 (0)	0 (0)	0 (0)	N/A
Sepsis, n (%)	0 (0)	0 (0)	0 (0)	N/A
Death, n (%)	0 (0)	0 (0)	0 (0)	N/A
Time of hospitalization (days), median (IQR)	22.0 (14.0-28.0)	17.0 (11.0-28.0)	22.0 (15.5-26.5)	.53
Time from onset to diagnosis (days), median (IQR)	9.5 (6.3-17.0)	4.0 (2.0-17.0)	10.0 (7.5-17.0)	.09
Time of viral shedding after onset of symptom (days), median (IQR)	25.0 (19.0-29.0)	24.0 (14.0-26.0)	26.0 (20.0-29.0)	.21
Redetected positive for discharged patients, n/N (%)	2/30 (7)	2/11 (18)	2/19 (11)	.61

Table 3: Clinical treatment and outcomes of pregnant and nonpregnant women with the coronavirus disease.

HLA ALLELES FREQUENCIES AND SUSCEPTIBILITY TO COVID-19 IN A GROUP OF 99 ITALIAN PATIENTS

Novelli A, Andreani M, Biancolella M, Liberatoscioli L, Passarelli C, Colona VL, Rogliani P, Leonardis F, Campana A, Carsetti R, Andreoni M, Bernardini S, Novelli G, Locatelli F.. HLA. 2020 Aug 22. doi: 10.1111/tan.14047. Online ahead of print.
Level of Evidence: 4 - Case-series, case-control, or historically controlled studies

BLUF

Interdisciplinary researchers in Rome, Italy performed Next Generation Sequencing (NGS) molecular human leukocyte antigen (HLA) typing comparing COVID-19 patients (n=99) to previously typed individuals (n=1017) and found a significant association (after application of Bonferroni's correction) between COVID-19 infection and HLA alleles DRB1*15:01, DQB1*06:02, and B*27:07 (Table 1). Authors suggest HLA alleles may be markers of COVID-19 susceptibility but acknowledge a need for larger scale studies to confirm these findings.

ABSTRACT

With the aim to individuate alleles that may reflect a higher susceptibility to the disease, in the present study we analyzed the HLA allele frequency distribution in a group of 99 Italian patients affected by a severe or extremely severe form of COVID-19. After the application of Bonferroni's correction for multiple tests, a significant association was found for HLA-DRB1*15:01, -DQB1*06:02 and -B*27:07, after comparing the results to a reference group of 1017 Italian individuals, previously typed in our laboratory. The increased frequencies observed may contribute to identify potential markers of susceptibility to the disease, although controversial results on the role of single HLA alleles in COVID-19 patients have been recently reported. This article is protected by copyright. All rights reserved.

FIGURES

Healthy Italian individuals (2034 haplotypes)			COVID-19 Italian patients (198 haplotypes)				
Allele	N	F %	Allele	N	F %	p	pc
B*27:07	2	0.10	B*27:07	4	2.02	0.00001	0.004
B*58:01	41	2.02	B*58:01	10	5.05	0.01317	ns
C*06:02	228	11.21	C*06:02	9	4.55	0.005356	ns
DRB1*07:01	291	14.31	DRB1*07:01	17	8.59	0.0339	ns
DRB1*15:01	94	4.62	DRB1*15:01	20	10.10	0.0015	0.048
DQB1*06:02	74	3.64	DQB1*06:02	15	7.58	0.0001	0.0016

Table 1. Comparison of HLA allele frequencies between a group of 99 COVID-19 patients and a group of 1017 Italian individuals. N, number of alleles; F %, allele frequency, in percent; p, value of Chi Square statistic analysis; pc, statistic value after Bonferroni's Correction, ns, not significant.

OVERWHELMING MUTATIONS OR SNPS OF SARS-COV-2: A POINT OF CAUTION

Vankadari N.. Gene. 2020 Aug 20;752:144792. doi: 10.1016/j.gene.2020.144792. Epub 2020 May 20.
Level of Evidence: Other - Mechanism-based reasoning

BLUF

A microbiologist affiliated with Monash University in Australia reviewed single nucleotide polymorphisms (SNPs) and mutations of sequenced SARS-CoV-2 genomes from 12 countries within the NCBI database as of March 24, 2020. The author relates 47 key point mutations or SNPs within several SARS-CoV-2 proteins (namely Nsp1, spike glycoprotein, and RdRp) that may play a role in SARS-CoV-2 virulence (Figure 1), suggesting that these point mutations or SNPs could aid the development of antiviral therapies for SARS-CoV-2.

FIGURES

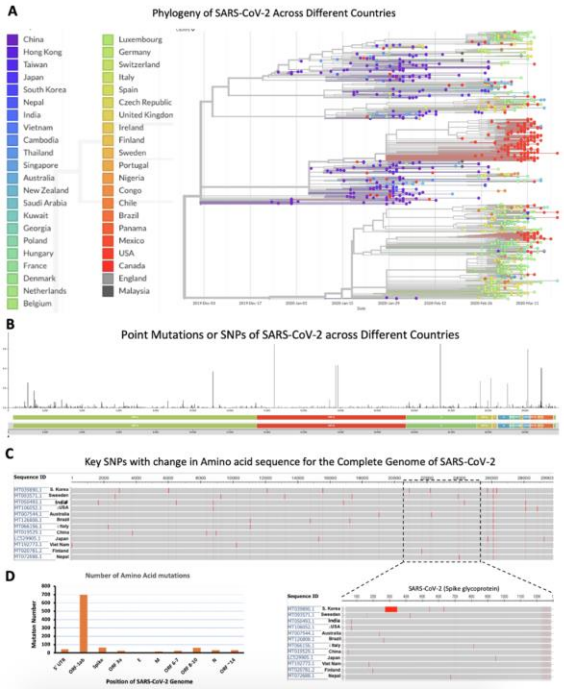


Fig. 1.(A) Phylogenetic tree showing the evolution of SARS-CoV-2 from the initial origin China (2020/01/17). The tree represents the mutations or SNPs that resulted in the evolution of current SARS-CoV-2 in the last three months. Individual countries are colored in as shown in the color key. (B) Position and number of SNPs across are the genome is denoted with bar graph. (C) The key mutations with change in amino acid observed across the whole genome of 12 countries are listed and highlighted in red lines. Enlarged view showing the mutations occurred in spike glycoprotein. (D) Bar graph depicting the number of mutations and position is complete genome.

EMERGENCY MEDICINE

PRESENTATIONS OF STROKE AND ACUTE MYOCARDIAL INFARCTION IN THE FIRST 28 DAYS FOLLOWING THE INTRODUCTION OF STATE OF EMERGENCY RESTRICTIONS FOR COVID-19

Mitra B, Mitchell RD, Cloud GC, Stub D, Nguyen M, Nanayakkara S, Miller JP, O'Reilly G, Smit V, Cameron PA.. Emerg Med Australas. 2020 Aug 24. doi: 10.1111/1742-6723.13621. Online ahead of print.
Level of Evidence: 4 - Local non-random sample

BLUF

A retrospective cohort study conducted at a single tertiary care center in Melbourne, Australia compared the number and outcomes of acute stroke and acute myocardial infarction patients from March 26th to April 23rd 2020 to patients from the same time period in 2019 (Table 1). Median time from symptom onset to presentation, median time to primary reperfusion intervention, mortality rate, and length of hospital stay were all not significantly different (Table 2) suggesting that at this center, emergency pandemic measures did not lead to delays in treatment for these patients.

ABSTRACT

OBJECTIVES: To determine if Victorian state of emergency (SOE) measures to combat COVID-19 were associated with delayed presentations or management of acute stroke and acute myocardial infarction (AMI). METHODS: This was a retrospective, pre- and post-implementation study using data from an adult, tertiary cardiology and neurosciences centre with 24-hour capacity for endovascular procedures. All primary presentations with acute stroke or AMI during the first 28 days of Stage 2 and 3 SOE restrictions (26 March to 23 April 2020) were compared to an equivalent period without restrictions (26 March to 23 April 2019). The primary outcome variable was time from onset of symptoms to emergency department (ED) presentation. RESULTS: There were 52 (1.6% of all ED presentations) patients that met inclusion criteria during the SOE period and 57 (1.0%) patients in the comparator period. Patients were equally matched for demographics, disease severity and prior history of stroke or AMI. Median time from symptom onset to presentation was 227 (93-1183) mins during the SOE period and 342 (119-1220) mins during the comparator period (p=0.24). Among eligible patients with ischaemic stroke or ST-elevation AMI, median time to primary reperfusion intervention was 65 (37-78) mins during SOE and 44 (39-60) mins in the comparator period (p=0.54). There were no differences in mortality at hospital discharge (9.6% vs 10.5%) and hospital LOS (5.4 vs 4.3 days). CONCLUSIONS: In the first 28 days, SOE measures to combat COVID-19 were not associated with delays in presentation or life-saving interventions for patients with acute stroke and AMI. This article is protected by copyright. All rights reserved.

FIGURES

	SOE period (n=52)	Comparator period (n=57)	p-value
Age (years)	71.1 (16.0)	74.7 (14.3)	0.21
Sex: **- Male** **- Female**	 35 (67.3%) 17 (32.7%)	 48 (84.2%) 9 (15.8%)	0.04
After-hours presentation	22 (42.3%)	18 (31.6%)	0.25
Ambulance transport	42 (80.8%)	46 (80.7%)	0.99
COVID-suspect	10 (19.2%)	0 (0%)	<0.001
Prior AMI or stroke	7 (13.5%)	14 (24.6%)	0.14
Severity of disease: **- Median NIHSS*** **- Peak Troponin†**	 3 (2-10) 9139 (173-45231)	 4 (2-14) 4540 (719-16783)	 0.34 0.68

Table 1: Baseline characteristics; *Among patients with stroke; †Among patient with AMI

	SOE period (n=52)	Comparator period (n=57)	p-value
Time from onset of symptoms to presentation (mins; median and IQR)	227 (93-1183)	342 (119-1220)	0.24
Onset of symptoms to presentation of over 24h	11 (21.6%)	14 (24.6%)	0.67
Time to CTB* (mins; median and IQR)	52 (21-97)	65 (45-90)	0.11
Time to primary reperfusion intervention (mins; median and IQR): All eligible stroke and STEMI (n=20) - Eligible ischaemic stroke† (n=5) - Eligible STEMI (n=15) - NSTEMI (n=25)	 65 (37-78) 67 (37-97) 40.6 (29.3-45.1) 340 (89-1301)	 44 (39-60) 60 (46-212) 64.7 (37.5-76.0) 830 (144-3831)	 0.54 0.56 0.30 0.58
Death in hospital	5 (9.6%)	6 (10.5%)	0.99
LOS in hospital‡	3 (2-6)	4 (2-6.5)	0.39

Table 2. Outcome measures; * Among patients with acute stroke; †Eligible for thrombolysis or endovascular procedure; ‡Excludes 2 patients who were inpatients at the time of reporting

CRITICAL CARE

IMPACT OF SMOKING STATUS ON DISEASE SEVERITY AND MORTALITY OF HOSPITALIZED PATIENTS WITH COVID-19 INFECTION: A SYSTEMATIC REVIEW AND META-ANALYSIS

Karanasos A, Aznaouridis K, Latsios G, Synetos A, Plitaria S, Tousoulis D, Toutouzas K.. Nicotine Tob Res. 2020 Aug 24;22(9):1657-1659. doi: 10.1093/ntr/ntaa107.
Level of Evidence: 1 - Systematic review of inception cohort studies

BLUF

Cardiologists based in Athens, Greece conducted meta-analyses to explore the relationship of smoking with disease severity and mortality of patients hospitalized with COVID-19 in China and the US. The first meta-analysis of 18 studies (n=6210) found that smoking was associated with a slight increased risk of severe COVID-19 (OR = 1.34, CI = 1.07-1.67, I^2 = 45%; Figure 1), and younger patients without diabetes were more associated with severe COVID-19 (Figure 3). Meta-analyses of 5 studies (n=838) and 2 studies (n=465) addressing smoking and risk of mortality with COVID-19 were inconclusive due to the small sample sizes. Overall, the findings are limited by poor-quality data and relatively low study heterogeneity, but do suggest possible negative effects of smoking on COVID-19 severity, particularly in young patients without diabetes.

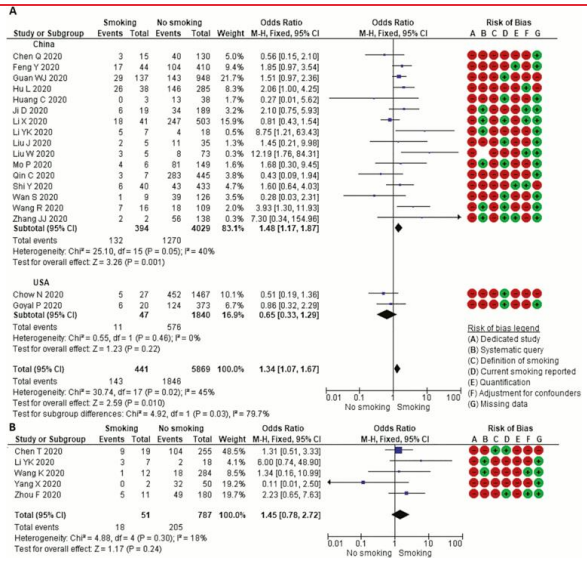


Figure 1: Forest plot and risk of bias tables examining in hospitalized COVID-19 patients the association of smoking with (A) the composite end point of disease severity in China and in US regions and (B) mortality. Boxes represent odds ratio (OR) and lines represent the 95% confidence interval [CI] for individual studies. Diamonds and their width represent pooled ORs and the 95% CI, respectively.

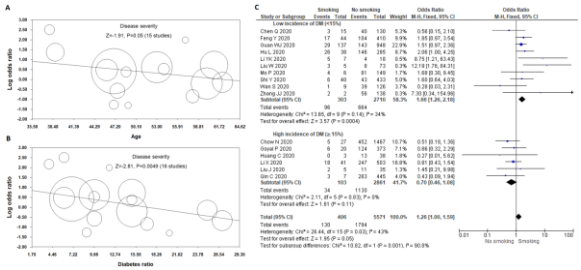


Figure 3: A. Meta-regression plot for age. B. Meta-regression plot for diabetes. C. Forest plot examining in hospitalized patients with COVID-19 infection the association of smoking status with the composite outcome of disease severity stratified by low or high incidence of diabetes. Boxes represent the OR and lines represent the 95% CI for individual studies. Diamonds and their width represent the pooled ORs and the 95% CI, respectively. DM=diabetes mellitus

PATIENT-REPORTED OUTCOMES: CENTRAL TO THE MANAGEMENT OF COVID-19

Aiyegbusi OL, Calvert MJ.. Lancet. 2020 Aug 22;396(10250):531. doi: 10.1016/S0140-6736(20)31724-4. Epub 2020 Aug 10.
Level of Evidence: Other - Expert Opinion

BLUF

UK Researchers affiliated with the National Institute for Health Research Birmingham Biomedical Research Centre at the University of Birmingham report the importance of using electronic self-assessments of patient health status or patient reported outcomes (PROs) in COVID-19 diagnosis, tracking, tracing and symptom monitoring (Figure 1). The authors cite multiple benefits of electronic self-assessments, including:
- providing support for those in home isolation
- detecting rapid deterioration in health status before changes in clinical parameters
- identifying individuals in need of help with remote symptom monitoring
- assessing quality of life
- detecting adverse events during COVID-19 trials
- providing information on safety and tolerability from the patient's view

Based on these observations, the authors suggest that electronic self-assessments of PROs can help manage COVID-19 in the current pandemic as well as be a possible tool for future pandemics.

FIGURES

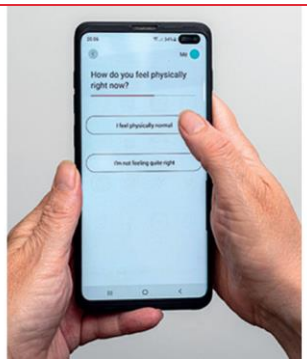


Figure 1: Electronic patient-reported outcomes measure to assist with diagnosis, tracking and remote monitoring of sympoms

EFFECTIVENESS OF REMDESIVIR FOR THE TREATMENT OF HOSPITALIZED COVID-19 PERSONS: A NETWORK META-ANALYSIS

Jiang Y, Chen D, Cai D, Yi Y, Jiang S.. J Med Virol. 2020 Aug 19. doi: 10.1002/jmv.26443. Online ahead of print.
Level of Evidence: 1 - Systematic review of randomized trials or n-of-1 trials

BLUF

Physicians from the School of Public health (Shenzhen) at Sun Yat-sen University, Guangdong Provincial Center for Disease Control and Prevention, and the School of Population and Public Health at University of British Columbia performed a network meta-analysis (n=4 randomized clinical studies including 2,049 moderate/severe COVID-19 patients) on the effectiveness of remdesivir in COVID-19 treatment. They found that both 10-day and 5-day regimens of remdesivir corresponded with greater odds of clinical improvement and greater probabilities of clinical recovery as compared to the placebo group. However, the 5-day regimen resulted in greater odds of clinical improvement when compared to the 10-day regimen (Figure 1; OR: 1.33, CI: 1.01-1.76). Based on these findings, the authors suggest that a 5-day remdesivir regimen may be beneficial in the treatment of severe COVID-19 patients.

ABSTRACT

INTRODUCTION: Several randomized clinical trials (RCTs) that investigated the effectiveness of remdesivir for the treatment of Covid-19 have generated inconsistent evidence. The present study aimed to synthesize available RCT evidence using network meta-analyses (NMAs). METHODS: Both blinded and open-label RCTs in PubMed database from inception to June 7, 2020 that contained "remdesivir", "Covid-19", and "trial" in the abstracts conducted on hospitalized Covid-19 persons were identified and screened. The studies must have at least one remdesivir arm and evaluated one of the pre-specified outcomes. The outcomes were clinical improvement between days 10-15 after randomization and clinical recovery during the follow-up period. The identified literature was supplemented with relatively recent studies that were known to the researchers if not already included. Frequentist NMAs with random effects were conducted. RESULTS: Both 10-day and 5-day remdesivir regimens were associated with higher odds of clinical improvement [odds ratio (OR) of 10-day regimen: 1.35, 95% confidence interval (CI): 1.09 - 1.67); OR of 5-day regimen: 1.81, CI: 1.32 - 2.45] and higher probabilities of clinical recovery [relative risk (RR) of 10-day regimen: 1.24, CI: 1.07 - 1.43); RR of 5-day regimen: 1.47, CI: 1.16 - 1.87] compared with placebo. CONCLUSIONS: Remdesivir may have clinical benefits among hospitalized Covid-19 persons. This article is protected by copyright. All rights reserved.

FIGURES

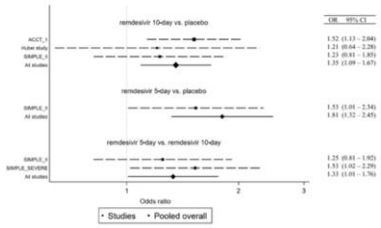


Figure 1: Base-case results of the clinical improvement NMA. OR, odds ratio; CI, confidence interval.

CIRCULATING ENDOTHELIAL CELLS AS A MARKER OF ENDOTHELIAL INJURY IN SEVERE COVID -19

Guervilly C, Burtey S, Sabatier F, Cauchois R, Lano G, Abdili E, Daviet F, Arnaud L, Brunet P, Hraiech S, Jourde-Chiche N, Koubi M, Lacroix R, Pietri L, Berda Y, Robert T, Degioanni C, Velier M, Papazian L, Kaplanski G, Dignat-George F.. J Infect Dis. 2020 Aug 19:jiaa528. doi: 10.1093/infdis/jiaa528. Online ahead of print.
Level of Evidence: 4 - Case-control studies, or "poor or non-independent reference standard

BLUF

A retrospective study of COVID-19 patients (n=99) conducted at Public Assistance-Marseille Hospital (APHM) in France by interdisciplinary researchers found that patients admitted to the intensive care unit (ICU; n=19) had significantly increased

numbers of circulating endothelial cells (CEC) when compared to non-ICU patients (p=0.002; Figure 1A), and increased CEC were also correlated with inflammatory cytokines (IL-6, IP-10) and disease severity but negatively correlated with lymphocyte and platelet counts (Figure 1B, 1C). Authors suggest CEC could serve as a clinical biomarker for disease severity and provide justification for therapies aimed at SARS-CoV-2 induced endothelial injury supplementing inflammation control.

ABSTRACT

Beside the commonly described pulmonary expression of the coronavirus disease 2019 (COVID-19), major vascular events have been reported. The objective of this study was to investigate whether increased levels of circulating endothelial cells (CEC) might be associated with severe forms of COVID-19. Ninety-nine patients with COVID-19 were enrolled in this retrospective study. Patients in the intensive care units (ICU) had significantly higher CEC counts than non-ICU patients and the extent of endothelial injury was correlated with putative markers of disease severity and inflammatory cytokines. Altogether, these data provide in vivo evidence that endothelial injury is a key feature of COVID-19.

FIGURES

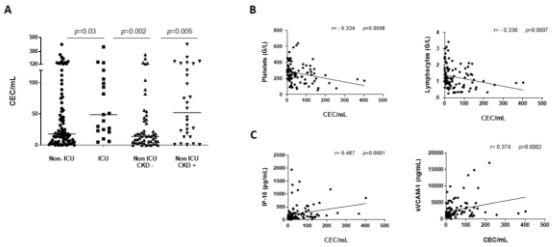


Figure 1. CEC enumeration in patients with COVID-19. (A) CEC/mL values in Non-ICU patients (n=80), ICU patients (n=19), Non-ICU Non-CKD patients (Non-ICU CKD -, n=52), patients with CKD (Non ICU CKD +, n=28). (B) Correlations between CEC count and platelets and lymphocytes. (C) Correlations between CEC count and IP-10 and sVCAM-1.
CEC: circulating endothelial cells. COVID-19=coronavirus disease 2019. ICU: intensive care unit. IP-10: interferon gamma-induced protein 10. sVCAM-1: soluble vascular cell adhesion molecule-1.

CURRENT DIAGNOSTICS

IMPACT OF ON-SITE COMPARED TO SEND-AWAY TESTING FOR SARS-COV-2 ON DURATION OF ISOLATION AND RESOURCE UTILIZATION

Roberts A, Wong G, Kotsanas D, Francis MJ, Stuart RL, Graham M, Rogers BA.. Infect Control Hosp Epidemiol. 2020 Aug 24:1-15. doi: 10.1017/ice.2020.433. Online ahead of print.
Level of Evidence: 3 - Non -randomized controlled cohort/follow-up study

BLUF

This cohort study of 220 patients conducted at Monash Health in Victoria, Australia from March 1 to March 27, 2020 by infectious disease specialists and microbiologists found on-site SARS-CoV-2 RT-PCR testing had a shorter testing turnaround time (TAT) and isolation period (p<0.001; Tables 1,2), fewer pathology test orders, and reduced antibiotic use in COVID-19 negative patients, as compared to send away testing. Authors advocate for on-site COVID-19 testing as a more efficient method than send away testing, suggesting it may reduce healthcare costs and preserve resources.

ABSTRACT

Rapid detection and isolation of COVID-19 patients is the only means of reducing hospital transmission. We describe the impact of implementation of on-site SARS-CoV-2 RT-PCR testing on reduction in result turnaround time, isolation duration, pathology test ordering and antibiotic use in patients who do not have COVID-19.

FIGURES

	Send-away RT-PCR tests (n=65)	Early on-site RT-PCR tests (n=54)	Established on-site PCR tests (n=123)	P-value
Median report TAT – hrs (IQR)	70.4 (46.5-111.5)	24.3 (19.4-44.2)	16.1 (14.4-19.1)	<0.001
Median time to notification to clinician – hrs (IQR)*	47.3 (41.5-77.8)	37.6 (25.4-47.1)	19.7 (16.3-23.8)	<0.001
Location of testing				
ED or Outpatient Clinic – no. (%)	48 (74)	46 (85)	100 (81)	0.274
Hospital Ward – no. (%)	17 (26)	8 (15)	23 (19)	
Specimen type				
Nasopharyngeal swab – no. (%)	58 (89)	52 (96)	119 (97)	0.120
Lower airway (endotracheal aspirate or sputum) – no. (%)	7 (11)	2 (4)	4 (3)	
Indications for testing				
Respiratory symptoms – no. (%)	58 (89)	49 (91)	98 (80)	0.084
Fever – no. (%)	46 (71)	22 (41)	77 (63)	0.003
Contact of a known case – no. (%)	10 (15)	7 (6)	8 (15)	0.054
Repeat testing – no. (%)	10 (15)	4 (7)	10 (8)	0.260

Table 1. Characteristics of performed SARS-CoV-2 RT-PCR tests.

	Send-away RT-PCR tests (n=55)	Early on-site RT-PCR tests (n=51)	Established on-site RT-PCR tests (n=118)	P-value
Median time to cessation of isolation – hrs (IQR)	**66.8 (47.1-97.0)**	**39.8 (26.9-47.7)**	**21.9 (18.6-27.8)**	**<0.001**
Median total number of routine blood tests performed during isolation – no. (IQR)	7 (4-11)	4 (3-7)	4 (2-7)	<0.001
Median rate of routine blood tests[1] performed per day in isolation – no. (IQR)	2.5 (1.5-4.1)	2.9 (1.7-4.6)	4.1 (2.0-6.3)	0.006
Median total number of microbiological investigations performed during isolation – no. (IQR)	1 (0-3)	1 (0-2)	1(0-2)	0.085
Median rate of microbiological investigations[2] performed per day in isolation – no. (IQR)	0.5 (0-1.0)	0.5 (0-1.4)	0.7(0-1.8)	0.6802
Median total number of diagnostic imaging investigations performed during isolation – no. (IQR)	1 (0-1)	1 (0-1)	1 (0-1)	0.193
Median rate of diagnostic imaging[3] investigations performed per day in isolation – no. (IQR)	0.3 (0-0.6)	0.9 (0-1.3)	0.5 (0-1.0)	0.009
Received antibiotics[4] in isolation – no. (%)	48 (87)	45 (88)	79 (67)	0.001
Received oseltamivir in isolation – no. (%)	33 (60)	40 (78)	108 (92)	<0.001

[1]Each full blood examination, urea, electrolytes, creatinine, liver function tests and C-reactive protein performed on a patient was considered a routine blood test

[2]Each sputum culture, blood culture and urine culture performed on a patient was considered a microbiological investigation

[3]Any diagnostic imaging investigation was included

[4]Antibiotics given for treatment of the acute presentation (i.e. long-term antibiotics prophylaxis, if present, was not included)

Table 2. Time spent in isolation and isolation-based outcomes.

ADVANCES IN VIRAL DIAGNOSTIC TECHNOLOGIES FOR COMBATING COVID-19 AND FUTURE PANDEMICS

Zhu N, Wong PK.. SLAS Technol. 2020 Aug 24:247263032095379 8. doi: 10.1177/2472630320953798. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

A review study by biomedical engineers from Pennsylvania State University discusses current diagnostic methods for detecting COVID-19, assessing reverse transcription polymerase chain reaction, isothermal amplification, antigen tests, serological tests, clustered regularly interspaced short palindromic repeats (CRISPR), high throughput sequencing, and viral cultures (Figure 1) in terms of target, assay time, lag time, sensitivity, specificity, result, and point-of-care (Table 1). This article suggests that diagnostic technologies such as CRISPR and other engineering platforms must continue to be developed in terms of speed, availability, and accuracy in order to improve diagnostic abilities during the COVID-19 era and for future pandemics.

ABSTRACT

The emergence of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) threatens the health of the global population and challenges our preparedness for pandemic threats. Previous outbreaks of coronaviruses and other viruses have suggested the importance of diagnostic technologies in fighting viral outbreaks. Nucleic acid detection techniques are the gold standard for detecting SARS-CoV-2. Viral antigen tests and serological tests that detect host antibodies have also been developed for studying the epidemiology of COVID-19 and estimating the population that may have immunity to SARS-CoV-2. Nevertheless, the availability, cost, and performance of existing viral diagnostic technologies limit their practicality, and novel approaches are required for improving our readiness for global pandemics. Here, we review the principles and limitations of major viral diagnostic technologies and highlight recent advances of molecular assays for COVID-19. In addition, we discuss emerging technologies, such as clustered regularly interspaced short palindromic repeats (CRISPR) systems, high-throughput sequencing, and single-cell and single-molecule analysis, for improving our ability to understand, trace, and contain viral outbreaks. The prospects of viral diagnostic technologies for combating future pandemic threats are presented.

FIGURES

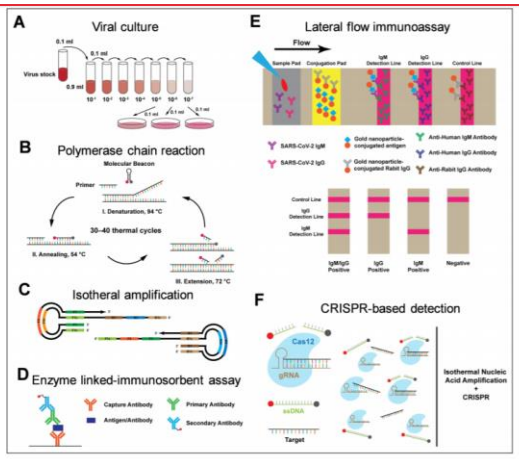


Figure 1. Common viral diagnostic schemes. (**A**) Viral culture for measuring virus titer by infecting host cells. (**B**) Real-time reverse transcription PCR (qRT-PCR) for measuring a target RNA. (**C**) Loop-mediated isothermal amplification (LAMP) for amplifying target nucleic acid with four to six sets of primers at a constant temperature. (**D**) Enzyme linked-immunosorbent assay (ELISA) for detecting viral antigen and host immunoglobulin M (IgM) and G (IgG) with a sandwiched antibody scheme. (**E**) Lateral flow immunoassay for capturing host IgM and IgG from patient's blood. (**F**) Clustered regularly interspaced short palindromic repeats (CRISPR)-based detection for recognizing amplified targets by forming a Cas–SARS-CoV-2–gRNA (CRISPR-associated protein–severe acute respiratory syndrome coronavirus 2–guide RNA) that cleaves a single-stranded, fluorescence reporter.

Table 1. Comparison of COVID-19 Diagnostic Tests.

Assays	Target	Assay time	Lag time	Sensitivity	Specificity	Result	Point-of-care
qRT-PCR	RNA	30–120 min	N/A	High	High	Quantitative	Possible
Isothermal amplification	RNA	5–30 min	N/A	High	High	Quantitative	Yes
Antigen tests	Nucleocapsid protein	15–120 min	>6 d	Low	Intermediate	Semiquantitative	Possible
Serological tests	IgM and IgG	~15 min	>15 d	Low	Intermediate	Qualitative	Yes
CRISPR	RNA	~30 min	N/A	High	High	Qualitative	Possible
High-throughput sequencing	RNA	Hours to days	N/A	N/A	N/A	Quantitative	No
Viral culture	Virulence	Days to weeks	N/A	N/A	N/A	Quantitative	No

COVID-19: Coronavirus disease 2019; CRISPR: clustered regularly interspaced short palindromic repeats; IgG: immunoglobulin G; IgM: immunoglobulin M; qRT-PCR: real-time reverse transcription PCR.

SARS-COV-2 CORONAVIRUS NUCLEOCAPSID ANTIGEN-DETECTING HALF-STRIP LATERAL FLOW ASSAY TOWARD THE DEVELOPMENT OF POINT OF CARE TESTS USING COMMERCIALLY AVAILABLE REAGENTS

Grant BD, Anderson CE, Williford JR, Alonzo LF, Glukhova VA, Boyle DS, Weigl BH, Nichols KP.. Anal Chem. 2020 Aug 18;92(16):11305-11309. doi: 10.1021/acs.analchem.0c01975. Epub 2020 Aug 5.
Level of Evidence: 5 - Mechanism-based reasoning

BLUF

Biomolecular researchers from the state of Washington conducted a mechanistic study to develop rapid care tests using commercial antibodies (originally manufactured to target SARS-CoV-1) that detected SARS-CoV-2 proteins on a half-strip lateral flow assay (LFA) at a minimum of 0.65 ng/mL and 3.03 ng/mL for different protein samples (Figure 2). Although the authors suggest LFA tests can rapidly and affordably detect COVID-19 in clinics, they urge for further studies on similar tests to prove its specificity for SARS-CoV-2 and accuracy at clinically relevant levels of the virus.

ABSTRACT

The SARS-CoV-2 pandemic has created an unprecedented need for rapid diagnostic testing to enable the efficient treatment and mitigation of COVID-19. The primary diagnostic tool currently employed is reverse transcription polymerase chain reaction (RT-PCR), which can have good sensitivity and excellent specificity. Unfortunately, implementation costs and logistical problems with reagents during the global SARS-CoV-2 pandemic have hindered its universal on demand adoption. Lateral flow assays (LFAs) represent a class of diagnostic that, if sufficiently clinically sensitive, may fill many of the gaps in the current RT-PCR testing regime, especially in low- and middle-income countries (LMICs). To date, many serology LFAs have been developed, though none meet the performance requirements necessary for diagnostic use cases, primarily due to the relatively long delay between infection and seroconversion. However, based on previously reported results from SARS-CoV-1, antigen-based SARS-CoV-2 assays may have significantly better clinical sensitivity than serology assays. To date, only a very small number of antigen-detecting LFAs have been developed. Development of a half-strip LFA is a useful first step in the development of any LFA format. In this paper we present a half-strip LFA using commercially available antibodies for the detection of SARS-CoV-2. We have tested this LFA in buffer and measured an LOD of 0.65 ng/ mL (95% CI of 0.53 to 0.77 ng/mL) ng/mL with recombinant antigen using an optical reader with sensitivity equivalent to a visual read. Further development, including evaluating the appropriate sample matrix, will be required for this assay approach to be made useful in a point of care setting, though this half-strip LFA may serve as a useful starting point for others developing similar tests.

FIGURES

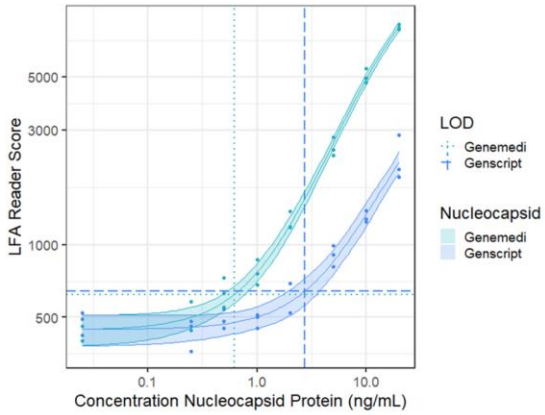


Figure 2: Dose response curve for a half-strip LFA using nucleocapsid protein from two commercially available sources, as measured using a commercially available optical LFA reader. The LOD for the Genemedi N protein was 0.65 ng/mL (95% CI of 0.53 to 0.77 ng/mL) and for the Genscript N protein was 3.03 ng/mL (95% CI of 0.00 to 7.44 ng/mL). Raw data for this graph are presented in the SI.

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