The Daily COVID-19 Literature Surveillance Summary

June 18, 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

- Social psychologists in the United Kingdom argue that under-reaction by the authorities, mismanagement of communication and space, and systemic factors such as poverty are more responsible for avoidable deaths during the COVID-19 pandemic than collective over-reaction and selfishness. This suggests that failure in community leadership plays a larger role in fatalities during emergencies than does collective psychology.
- The director of the WHO Collaborating Center on Public Health Law and Human Rights recommends using the current COVID-19 pandemic to rebuild WHO as a responsive international agency by allocating more funding, ensuring member state compliance with WHO's recommendations, and increasing WHO's freedom to act without political influence.
- A systematic review of COVID-19 research authorship found that women represent 34% of all authors, 29% of first authors, and 26% of last authors in COVID-19 publications. They suggest that this is similar to the underrepresentation of women authorship seen in many research fields and may also hint at gender disparities in COVID-19 data and the global pandemic response.

Epidemiology

- A retrospective study of 936 outpatients who presented with fever to the Tongji Hospital Clinic in Wuhan, China during the peak time period of COVID-19 (January 30 to February 4, 2020) found that 67% of all fever patients tested positive for COVID-19. Additionally, they found that muscle ache and dyspnea were more specific symptoms of COVID-19 than fever and cough.
- A cross-sectional study conducted in Indianapolis found that 3.1% of 2,953 adults tested positive for SARS-CoV-2 by nasopharyngeal swab testing. Of the 81 SARS-CoV-2 positive participants who completed a follow-up interview, 71.6% remained asymptomatic at 14 days while the other 28.4% reported one or more symptoms.
- A study of 1,353 COVID-19 positive children found the three most common symptoms in this population were fever (21.7%), cough (15.4%), and abnormal breathing (8.1%) with the most severe manifestations, such as intubation or myocarditis, occurring in less than 0.7% of patients, and only 1.9% of patients requiring ICU care.

Transmission & Prevention

- An event-study model utilizing data from 15 states plus Washington, D.C. that had implemented mandatory masks in public revealed a statistically significant decrease in daily county-level growth rates of COVID-19 after implementation of mask wearing mandates, suggesting that transmission rates of COVID-19 may decrease as more states mandate face masks in public.

Management

- Guidelines and recommendations for practice during the pandemic include:
  - Convalescent plasma benefits and donation
  - Anticoagulation-related gastrointestinal bleeding
- Pulmonary specialists describe how utilizing nearby hotels for recovering COVID-19 patients discharged from overwhelmed hospitals may be an effective method to meet surging demands citing this approach's success in certain Italian hospitals.
- A retrospective study of 38 COVID-19 patients found that patients who developed severe COVID-19 had a statistically significantly higher CD4/CD8 ratio than patients that did not develop severe COVID-19, which suggests that clinicians may be able to use lymphocyte ratios to predict disease severity.

Adjusting Practice During COVID-19

- Guidelines and recommendations for adjusting clinical practice include management of febrile children younger than 3 years old as well as for empiric antibiotic therapy for children younger than 36 months.
- Three adult COVID-19 patients who suffered ischemic strokes with involvement of large cerebral arteries led Iranian researchers to posit inflammatory response to cytokine release due to SARS-CoV-2 infection as a potential underlying mechanism and recommend that all patients who suffer from

ischemic strokes during the pandemic be tested for SARS-CoV-2 infection, emphasizing the need for further investigation of the link between strokes and COVID-19.

R&D: Diagnosis and Treatments

- A comparative study between two SARS-CoV-2 serology detection methods—chemiluminescence (n=109) and the colloidal gold method (n=60)—using data from 4 clinical trials (n=169 patients with COVID-19) found that for the IgM antibody, the chemiluminescence method had an earlier (by about 1-2 days) positive conversion time, earlier positive results at different stages of COVID-19 disease, and an earlier downward trend in positive results than the colloidal gold method, with similar results for the IgG antibody.
    - The authors suggest that the more sensitive chemiluminescence method may be better suited for high sample detection and early disease diagnosis, such as for suspected patients with negative nucleic acid results, and that the colloidal gold method may be optimal for sporadic cases and emergencies due to its faster return of results and use of less sophisticated equipment.

Mental Health and Resilience Needs

- A review of the mental health impact of the COVID-19 pandemic on the general population, healthcare workers, and vulnerable groups indicated that long-term psychological and social consequences (i.e. exacerbation of existing psychiatric disorders, depression, etc.) could arise in vulnerable individuals during the pandemic and increase the risk for suicidal behaviors.
    - Three different approaches for suicidal preventive interventions (universal, selective, and indicated) were presented and the authors emphasize the importance of further research in mitigating the mental health effects of the pandemic to reduce COVID-19 related suicides.
- Researchers from the Department of Clinical Psychology at Albizu University-Miami discuss the psychological impact of the COVID-19 pandemic, including an increase in interpersonal violence, urging for a catalog of digital mental health resources for both survivors and perpetrators to help with emotional responses to trauma and to develop effective communication strategies.

Silver Linings

- Healthcare reform recommendations are outlined as the current pandemic could be a rare catalyst for major political shifts toward a more efficient and effective system of care, primarily addressing barriers to paying for services and provider reimbursement.

TABLE OF CONTENTS

CLIMATE

COVID-19 IN CONTEXT: WHY DO PEOPLE DIE IN EMERGENCIES? IT'S PROBABLY NOT BECAUSE OF COLLECTIVE PSYCHOLOGY

Drury J, Reicher S, Stott C.. Br J Soc Psychol. 2020 Jun 16. doi: 10.1111/bjso.12393. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

An expert opinion by professors of social psychology in the United Kingdom proposes that under-reaction by the authorities, mismanagement of communication and space, and systemic factors such as poverty are more responsible for avoidable deaths during the COVID-19 pandemic than collective over-reaction and selfishness. This suggests that failure in community leadership plays a larger role in fatalities during emergencies than does collective psychology. Examples of these factors include:

- Not issuing the stay at home warning until March despite COVID-19 risks in January
- Addressing the public as being potential victims initially instead of as potential carriers of disease
- Disadvantaged and low income citizens being unable to take time off work and being forced to utilize overcrowded public transport

ABSTRACT

Notions of psychological frailty have been at the forefront of debates around the public response to the COVID-19 pandemic. In particular, there is the argument that collective selfishness, thoughtless behaviour, and over-reaction would make the effects of COVID-19 much worse. The same kinds of claims have been made in relation to other kinds of emergencies, such as fires, earthquakes, and sinking ships. We argue that in these cases as well as in the case of the COVID-19 pandemic, other factors are better explanations for fatalities - namely under-reaction to threat, systemic or structural factors, and mismanagement. Psychologizing disasters serves to distract from the real causes and thus from who might be held responsible. Far from being the problem, collective behaviour in emergencies - including the solidarity and cooperation so commonly witnessed among survivors - is the solution, one that should be harnessed more effectively in policy and practice.

DISPARITIES

WHERE ARE THE WOMEN? GENDER INEQUALITIES IN COVID-19 RESEARCH AUTHORSHIP

Pinho-Gomes AC, Peters S, Thompson K, Hockham C, Ripullone K, Woodward M, Carcel C.. BMJ Glob Health. 2020 Jul;5(7):e002922. doi: 10.1136/bmjgh-2020-002922.
Level of Evidence: 2 - Systematic review of surveys that allow matching to local circumstances

BLUF

A systematic review by researchers at medical and academic centers in the United Kingdom, the Netherlands, Australia, and the United States on 1 May 2020 found that women represent 34% (95% CI 33% to 35%, p<0.001) of all authors, 29% (95% CI 27% to 32%, p<0.001) of first authors, and 26% (26%, 95% CI 24% to 29%, p<0.001) of last authors in COVID-19 publications (Figure 1). They suggest that this is similar to the underrepresentation of women authorship seen in many research fields and may also hint at gender disparities in COVID-19 data and the global pandemic response.

META-RESEARCH: COVID-19 MEDICAL PAPERS HAVE FEWER WOMEN FIRST AUTHORS THAN EXPECTED

Andersen JP, Nielsen MW, Simone NL, Lewiss RE, Jagsi R.. Elife. 2020 Jun 15;9:e58807. doi: 10.7554/eLife.58807. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

Authors affiliated with medical universities in Denmark and the United States conducted meta-research on 1893 medical papers related to COVID-19 from January 1 - June 5, 2020, to compare rates of female authorship. Based on their analysis of these papers they created a model estimating overall female authorship trends. They estimate female first authorship was reduced in March-April 2020 when compared to May 2020, however "the uncertainty of the estimates make these results inconclusive." Additionally, they estimate that female first authorship was reduced 23% from expected when comparing papers published March-April 2020 to 2019 papers in the same journal. Possible explanations and implications are discussed below.

SUMMARY

The authors believe the data trends might indicate a gender gap in research authorship during the pandemic. As one possible cause for this apparent gap, they posit women may be taking more domestic responsibilities, particularly in the setting of changing professional landscapes with telehealth and virtual teaching. Thus, the authors suggest there may be a need for policies that support female participation in academia and research during the pandemic.

ABSTRACT

The COVID-19 pandemic has resulted in school closures and distancing requirements that have disrupted both work and family life for many. Concerns exist that these disruptions caused by the pandemic may not have influenced men and women researchers equally. Many medical journals have published papers on the pandemic, which were generated by researchers facing the challenges of these disruptions. Here we report the results of an analysis that compared the gender distribution of authors on 1,893 medical papers related to the pandemic with that on papers published in the same journals in 2019, for papers with first authors and last authors from the United States. Using mixed-effects regression models, we estimated that the proportion of COVID-19 papers with a woman first author was 19% lower than that for papers published in the same journals in 2019, while our comparisons for last authors and overall proportion of women authors per paper were inconclusive. A closer examination suggested that women's representation as first authors of COVID-19 research was particularly low for papers published in March and April 2020. Our findings are consistent with the idea that the research productivity of women, especially early-career women, has been affected more than the research productivity of men.

EPIDEMIOLOGY

SYMPTOMS AND CLINICAL PRESENTATION

ANALYSIS OF 2019 NOVEL CORONAVIRUS INFECTION AND CLINICAL CHARACTERISTICS OF OUTPATIENTS: AN EPIDEMIOLOGICAL STUDY FROM A FEVER CLINIC IN WUHAN, CHINA

Wei Y, Lu Y, Xia L, Yuan X, Li G, Li X, Liu L, Liu W, Zhou P, Wang CY, Zhang H.. J Med Virol. 2020 Jun 16. doi: 10.1002/jmv.26175. Online ahead of print.
Level of Evidence: 4 - Local non-random sample

BLUF

A retrospective study of 936 outpatients who presented with fever to the Tongji Hospital Clinic in Wuhan, China during the peak time period of COVID-19 (January 30 to February 4, 2020) found that 67% of all fever patients tested positive for COVID-19. They found that muscle ache and dyspnea were more specific symptoms of COVID-19, compared to fever and cough, and that low eosinophil count was more prevalent in COVID-19 patients. These findings, in combination with serology and CT imaging, may lead to more accurate and rapid diagnoses of COVID-19 globally.

ABSTRACT

BACKGROUND: Since the outbreak of 2019 novel coronavirus (SARS-CoV-2) pneumonia, thousands of patients with fever or cough were flocked into fever clinic of designated hospitals in Wuhan, China. To date, no data have ever been reported to reflect the prevalence of Corona Virus Disease 2019 (COVID-19) among these outpatients. Moreover, it is almost unknown to discriminate COVID-19 and nucleic acid negative patients based on clinical features in the fever clinics. METHODS: The infectious status of SARS-CoV-2 was estimated among the outpatients. The epidemiological and clinical characteristics were compared between COVID-19 and nucleic acid negative patients. RESULTS: The nucleic acid positive rate for SARS-CoV-2 in the outpatients from our fever clinic was 67 1%, while the majority of COVID-19 patients were mild cases. The predominant initial symptom in those COVID-19 patients was fever (78.2%), followed by cough (15.6%). Very significantly lower number of eosinophils was characterized in COVID-19 patients as compared to that of nucleic acid negative patients. More importantly, the proportion of subjects with eosinophil counts lower than normal levels in COVID-19 patients was much higher than that of nucleic acid negative patients. Fever combined with bilateral ground-glass opacities in CT imaging and eosinophil count below the normal level are probably a valuable indicator of COVID-19 infection in those outpatients. CONCLUSIONS: Those findings may provide critical information for the regions such as Europe and United States that are facing the same situation as Wuhan experienced, and could be valuable to prevent those nucleic acid negative patients from misdiagnosis before antibody testing.

ADULTS

COVID-19 INFECTION ASSOCIATED WITH AUTOIMMUNE HEMOLYTIC ANEMIA

Capes A, Bailly S, Hantson P, Gerard L, Laterre PF.. Ann Hematol. 2020 Jun 16. doi: 10.1007/s00277-020-04137-9. Online ahead of print.
Level of Evidence: Other - Case Report

BLUF

A case study from a group in Belgium reports a 62-year-old male who presented to the emergency room with significant fatigue after a positive COVID-19 test. 14 days after initial respiratory symptoms he developed autoimmune hemolytic anemia. The patient was transferred to the ICU and received eight units of packed red blood cells over the course of one week. After six weeks, the patient is slowly recovering. This case study may suggest that autoimmune hemolytic anemia may be a rare consequence of COVID-19.

SUMMARY

This case report presents a 62-year-old male who reported to the emergency room after a positive COVID-19 test and significant fatigue. Upon physical examination, the patient was febrile with mild dyspnea and low oxygen saturation levels. Bilateral lung infiltrates were found on chest X-ray. His lymphocyte count was 500/uL, he had a slight thrombocytopenia and hemoglobin was low (101,000/uL, 12g/dL respectively), while his LDH was slightly elevated at 307 IU/L. Two weeks after

initial symptoms began, he was transferred to the ICU and intubated. His hemoglobin levels decreased to 6.9 g/dl and his LDH levels rose to 726 IU/L. Additionally, his lymphocyte count decreased to 120/uL and his potassium level was recorded at 6.78 mmol/L. Cell agglutination and schizocytes <1% were seen on blood smear. A Direct Coombs test was carried out which was positive for C3b. Other positive test results were: Cold agglutinations, anti-I, and antinuclear antibodies. Negative tests included: ENA screening, antiphospholipid, and PCR test for atypical bacterial infections, HBV, HCV, and HIV. Ultimately, this patient received 8 units of red packed cells over the course of seven days and has begun to slowly recover.

PREGNANT PERSONS

SEVERE CORONAVIRUS INFECTIONS IN PREGNANCY: A SYSTEMATIC REVIEW

Galang RR, Chang K, Strid P, Snead MC, Woodworth KR, House LD, Perez M, Barfield WD, Meaney-Delman D, Jamieson DJ, Shapiro-Mendoza CK, Ellington SR.. Obstet Gynecol. 2020 Jun 16. doi: 10.1097/AOG.0000000000004011. Online ahead of print.

Level of Evidence: 4 - Case-series or casecontrol studies, or poor quality prognostic cohort study

BLUF

Authors from the Centers for Disease Control and Prevention performed a literature search for information regarding the impact of SARS-CoV, MERS-CoV, and SARS-CoV-2 on pregnancy and neonatal outcomes published before April 23, 2020, which yielded 46 articles meeting the authors requirements for case-level data and comprised 127 total cases (17 SARS-CoV cases, 12 MERS-CoV cases, and 98 SARS-CoV-2 cases; Tables 1 and 2). The results regarding SARS-CoV-2 revealed:

- 6 of the 98 women with COVID-19 required ICU admittance, of whom 5 required mechanical ventilation (Table 3)
- One woman in her third trimester died in the hospital
- 52 neonates were delivered by emergency cesarean due to maternal indications, fetal stress, or other obstetric complications; 4 of were delivered for SARS-CoV-2 infection-control reasons
- Two cases resulted in stillbirth at 34 and 35 weeks and were both associated with severe illness characterized by multiorgan system dysfunction and acute respiratory distress syndrome requiring mechanical ventilation in the mother
- Complications were reported in 7 term neonates and 10 preterm neonates
- One neonate developed respiratory difficulties after birth and died 8 days later
- 7 of 68 neonates tested showed presence of SARS-CoV-2 RNA via RT-PCR

ABSTRACT

OBJECTIVE: To inform the current coronavirus disease 2019 (COVID-19) outbreak, we conducted a systematic literature review of case reports of Middle East respiratory syndrome coronavirus (MERS-CoV), severe acute respiratory syndrome coronavirus (SARS-CoV), and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes COVID-19, during pregnancy and summarized clinical presentation, course of illness, and pregnancy and neonatal outcomes.
DATA SOURCES: We searched MEDLINE and ClinicalTrials.gov from inception to April 23, 2020.
METHODS OF STUDY SELECTION: We included articles reporting case-level data on MERS-CoV, SARS-CoV, and SARS-CoV-2 infection in pregnant women. Course of illness, indicators of severe illness, maternal health outcomes, and pregnancy outcomes were abstracted from included articles. TABULATION, INTEGRATION, AND RESULTS: We identified 1,328 unique articles, and 1,253 articles were excluded by title and abstract review. We completed full-text review on 75, and 29 articles were excluded by full-text review. Among 46 publications reporting case-level data, eight described 12 cases of MERS-CoV infection, seven described 17 cases of SARS-CoV infection, and 31 described 98 cases of SARS-CoV-2 infection. Clinical presentation and course of illness ranged from asymptomatic to severe fatal disease, similar to the general population of patients. Severe morbidity and mortality among women with MERS-CoV, SARS-CoV, or SARS-CoV-2 infection in pregnancy and adverse pregnancy outcomes, including pregnancy loss, preterm delivery, and laboratory evidence of vertical transmission, were reported.
CONCLUSION: Understanding whether pregnant women may be at risk for adverse maternal and neonatal outcomes from severe coronavirus infections is imperative. Data from case reports of SARS-CoV, MERS-CoV, and SAR-CoV-2 infections during pregnancy are limited, but they may guide early public health actions and clinical decision-making for COVID-19 until more rigorous and systematically collected data are available. The capture of critical data is needed to better define how this infection affects pregnant women and neonates. This review was not registered with PROSPERO.

Table 1. Maternal Characteristics and Clinical Presentation Among Patients With Middle East Respiratory Syndrome Coronavirus, Severe Acute Respiratory Syndrome Coronavirus, and Severe Acute Respiratory Syndrome Coronavirus 2 Infection

	MERS-CoV (n=12)	SARS-CoV (n=17)	SARS-CoV-2 (n=98)
Age (y)	32 (31–38)	32 (26–34)	30 (28–34)
Comorbidities	4/11 (36)	3/4 (75)	19/69 (28)
Health care worker	4/4 (100)	5/12 (42)	2/2 (100)
Type of exposure			
Household	4/12 (33)	4/11 (36)	15/25 (60)
Community	NR	2/11 (18)	7/25 (28)
Health care–associated	1/12 (8)	NR	NR
Occupational	4/12 (33)	5/11 (45)	NR
Unidentified	3/12 (25)	NR	3/25 (12)
GA at symptom onset or diagnosis (completed wk)	24 (21–33)	19 (5–29)	36 (34–38)
Time from symptom onset to presentation for clinical evaluation (d)	5 (3–6)	3 (2–5)	2 (1–4)
Symptoms			
Fever	7/9 (78)	17/17 (100)	76/92 (83)
Myalgia	2/4 (50)	14/14 (100)	5/21 (24)
Malaise	1/3 (33)	12/13 (92)	14/31 (45)
Chills and rigors	1/3 (33)	13/14 (93)	2/21 (10)
Cough	8/9 (89)	13/16 (81)	34/66 (52)
Headache	1/3 (33)	8/14 (57)	4/15 (27)
Shortness of breath	7/8 (88)	6/15 (40)	12/47 (26)
Runny nose	1/3 (33)	4/13 (31)	5/17 (29)
Sore throat	0/2 (0)	2/13 (15)	7/29 (24)
Diarrhea	0/2 (0)	2/12 (17)	5/42 (12)
Chest pain	1/3 (33)	1/12 (8)	1/24 (4)

MERS-CoV, Middle East respiratory syndrome coronavirus; SARS-CoV, severe acute respiratory syndrome coronavirus; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; NR, not reported; GA, gestation age.
Data are median (interquartile range) or n/N (%).

Table 2. Laboratory Results and Treatment Received Among Patients With Middle East Respiratory Syndrome Coronavirus, Severe Acute Respiratory Syndrome Coronavirus, and Severe Acute Respiratory Syndrome Coronavirus 2 Infection

	MERS-CoV (n=12)	SARS-CoV (n=17)	SARS-CoV-2 (n=98)
Maternal laboratory results			
Anemia	NR	0/3 (0)	7/24 (29)
Leukocytosis	0/1 (0)	6/15 (40)	12/47 (26)
Lymphopenia	1/1 (100)	10/15 (67)	27/50 (54)
Thrombocytopenia	1/1 (100)	6/14 (43)	8/18 (44)
Elevated blood urea nitrogen	1/1 (100)	NR	1/12 (8)
Elevated serum creatinine	1/1 (100)	5/5 (100)	1/17 (6)
Elevated AST	1/1 (100)	1/1 (100)	7/28 (25)
Elevated ALT	1/1 (100)	1/1 (100)	6/28 (21)
Maternal specimen coronavirus testing			
PCR	11/11 (100)	9/15 (60)	98/98 (100)
Antibody testing	1/1 (100)	12/13 (92)	5/5 (100)
Imaging			
Abnormality on chest imaging (X-ray or computerized tomography)	7/7 (100)	16/16 (100)	59/65 (91)
Perinatal specimen coronavirus testing			
Amniotic fluid PCR	NR	0/6 (0)	1/24 (4)
Amniotic fluid antibody testing	NR	0/1 (0)	NR
Cord blood PCR	NR	0/10 (0)	0/24 (0)
Cord blood antibody testing	NR	2/4 (50)	NR
Placental PCR	0/1 (0)	0/12 (0)	0/12 (0)
Breast milk PCR	NR	0/2 (0)	0/8 (0)
Breast milk antibody testing	NR	1/2 (50)	NR
Treatment(s)			
Antibiotics	2/3 (67)	16/16 (100)	46/49 (94)
Antivirals	2/4 (50)	13/15 (87)	43/57 (75)
Intravenous hydrocortisone	0/1 (0)	11/13 (85)	1/30 (3)
Methylprednisolone	1/2 (50)	10/13 (77)	12/30 (40)
Oral prednisolone	0/1 (0)	11/13 (85)	0/29 (0)
Dexamethasone or betamethasone	1/2 (50)	0/1 (0)	4/31 (13)

MERS-CoV, Middle East respiratory syndrome coronavirus; SARS-CoV, severe acute respiratory syndrome coronavirus; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; NR, not reported; AST, aspartate aminotransferase; ALT, alanine aminotransferase; PCR, polymerase chain reaction.
Data are n/N (%).

Table 3. Maternal and Newborn Outcomes Among Patients With Middle East Respiratory Syndrome Coronavirus, Severe Acute Respiratory Syndrome Coronavirus, and Severe Acute Respiratory Syndrome Coronavirus 2 Infection

	MERS-CoV (n=12)	SARS-CoV (n=17)	SARS-CoV-2 (n=98)
Duration of hospitalization (d)	19 (13–28)	21 (15–27)	2 (0–17)
Hospitalization events			
Admitted to ICU	7/11 (64)	6/12 (50)	6/42 (14)
Mechanically ventilated	5/9 (56)	7/14 (50)	5/41 (12)
Renal failure	2/4 (50)	4/4 (100)	3/32 (9)
Disseminated intravascular coagulopathy	0/2 (0)	3/3 (100)	0/29 (0)
Sepsis	1/4 (25)	2/3 (67)	1/30 (3)
Maternal death	3/11 (27)	3/17 (18)	1/89 (1)
GA at pregnancy completion (completed wk)	35 (32–38)	31 (26–36)	37 (35–38)
Pregnancy outcome			
Live birth			
GA 37 weeks or more	5/10 (50)	3/17 (18)	57/94 (61)
GA less than 37 weeks	3/10 (30)	6/17 (35)	35/94 (37)
Spontaneous abortion or termination	NR	6/17 (35)	NR
Stillbirth	2/10 (20)	2/17 (12)	2/94 (2)
Route of delivery			
Vaginal	1/5 (20)	10/16 (63)	12/84 (14)
Cesarean	4/5 (80)	6/16 (38)	72/84 (86)
Postpartum hemorrhage	0/1 (0)	0/2 (0)	1/18 (6)
Neonatal death	1/4 (25)	0/6 (0)	1/49 (2)
Neonatal complications*	0/5 (0)	2/10 (20)	17/54 (31)
Neonatal specimen coronavirus testing			
PCR	0/1 (0)	0/7 (0)	7/68 (10)
Antibody testing	0/1 (0)	0/6 (0)	1/13 (8)
Birth weight (g)			
GA 37 weeks or more	3,140 (3,140–3,140)	3,086 (1,985–3,145)	3,250 (3,070–3,530)
GA less than 37 weeks	1,015 (240–1,790)	1,395 (1,035–1,650)	2,570 (2,050–2,890)

MERS-CoV, Middle East respiratory syndrome coronavirus; SARS-CoV, severe acute respiratory syndrome coronavirus; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; ICU, intensive care unit; GA, gestational age; NR, not reported; PCR, polymerase chain reaction.

Data are median (interquartile range) or n/N (%).

* Neonatal complications include those requiring immediate medical intervention after delivery (eg, respiratory distress, necrotizing enterocolitis, patent ductus arteriosus).

TRANSMISSION & PREVENTION

SEROEPIDEMIOLOGIC STUDY DESIGNS FOR DETERMINING SARS-COV-2 TRANSMISSION AND IMMUNITY

Clapham H, Hay J, Routledge I, Takahashi S, Choisy M, Cummings D, Grenfell B, Metcalf CJE, Mina M, Barraquer IR, Salje H, Tam CC.. Emerg Infect Dis. 2020 Jun 16;26(9). doi: 10.3201/eid2609.201840. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

This review highlights the strength and limitations of different types of serological studies and discusses different methods of utilizing serologic data to determine the global transmission of SARS-COV-2 (Table). The authors suggest that certain types of epidemiologic study may be most effective at different phases of the outbreak and in different settings. The authors call for the development of a shared platform to effectively and efficiently disseminate seroepidemiologic data.

ABSTRACT

Serologic studies are crucial for clarifying dynamics of the coronavirus disease pandemic. Past work on serologic studies (e.g., during influenza pandemics) has made relevant contributions, but specific conditions of the current situation require adaptation. Although detection of antibodies to measure exposure, immunity, or both seems straightforward conceptually, numerous challenges exist in terms of sample collection, what the presence of antibodies actually means, and appropriate analysis and interpretation to account for test accuracy and sampling biases. Successful deployment of serologic studies depends on type and performance of serologic tests, population studied, use of adequate study designs, and appropriate analysis and interpretation of data. We highlight key questions that serologic studies can help answer at different times, review strengths and limitations of different assay types and study designs, and discuss methods for rapid sharing and analysis of serologic data to determine global transmission of severe acute respiratory syndrome coronavirus 2.

FIGURES

Table

Describing different study designs, questions they could answer, and issues with study design and execution during the coronavirus disease pandemic

Study type	Brief description	Questions study could answer	Issues with interpretation and representativeness	Issues with conducting during a pandemic
Cross-sectional	A sample of the population has serum samples collected at 1 time point	Background cross-reactivity (if started before pandemic); current proportion of population that have been infected; proportion of population that is immune (if a correlate of protection defined); infection fatality ratio (with information on cases or deaths in the same population	For the different modes of collection (e.g., blood banks, residual sera, and volunteers), different issues can bias the sample included in the study that must be assessed	Blood banks might have fewer participants, residual sera studies in hospitals might have fewer samples or over representation of severe acute respiratory syndrome coronavirus 2 infections
Cohort	The same persons are followed up over time, with serum samples collected at regular intervals, and information on disease in intervening periods	Background cross-reactivity (if started before pandemic); ratio of asymptomatic to symptomatic infections; waning of antibody levels, correlates, and duration of protection; changes in infection dynamics over time	Attrition can make analysis and interpretation difficult, biases in which participants are retained across sampling rounds	Challenges in collecting and continuing cohort during outbreak; attrition
Targeted populations	Populations with particularly high exposures, such as those around index patients or healthcare workers, have serum samples taken either cross-sectionally or in a targeted cohort	Attack rates; ratio of asymptomatic to Symptomatic infections; proportion of population infected, correlates, and duration of protection	Targeted populations such because healthcare workers might have different infection exposure rates and intensity from the general population	Potentially logistically difficult to collect samples in household studies

PREVENTION IN THE COMMUNITY

COMMUNITY USE OF FACE MASKS AND COVID-19: EVIDENCE FROM A NATURAL EXPERIMENT OF STATE MANDATES IN THE US

Lyu W, Wehby GL.. Health Aff (Millwood). 2020 Jun 16:101377hlthaff202000818. doi: 10.1377/hlthaff.2020.00818. Online ahead of print.
Level of Evidence: 4 – Modeling

BLUF

In this event-study model, health policy experts from the University of Iowa analyze data from 15 states plus Washington, D.C. that had implemented mandatory masks in public between 8 April and 15 May, 2020 in order to compare pre- and post-mandated changes in the growth rate of COVID-19 cases (Supplemental Exhibit 1). The results revealed a statistically significant decrease in daily county-level growth rates of COVID-19 post-mandates, suggesting that transmission rates of COVID-19 may decrease as more states mandate face masks in public.

Percentage decrease in COVID-19 growth rate after mandate:
- 0.9% Day 1-5
- 1.1% Day 6-10
- 1.4% Day 11-15
- 1.7% Day 16-20
- 2.0% Day 21 and after

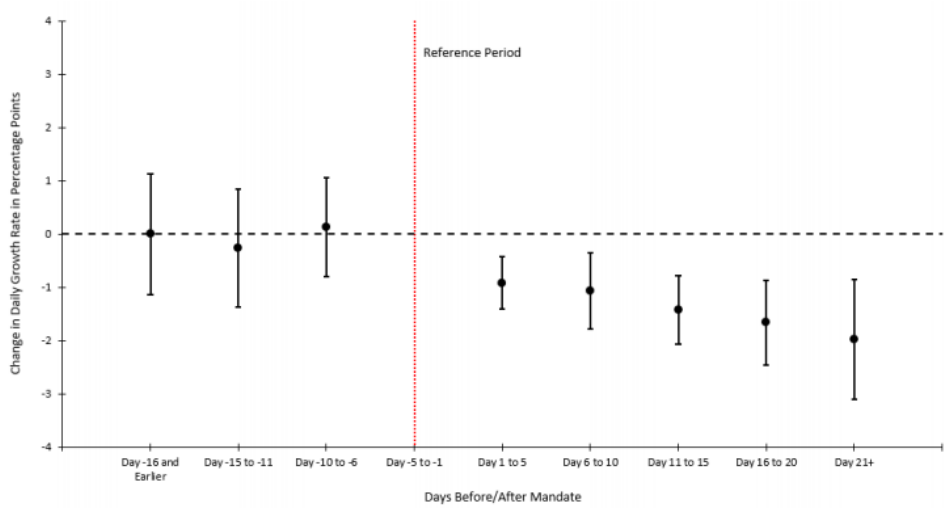
ABSTRACT

State policies mandating public or community use of face masks or covers in mitigating novel coronavirus disease (COVID-19) spread are hotly contested. This study provides evidence from a natural experiment on effects of state government mandates in the US for face mask use in public issued by 15 states plus DC between April 8 and May 15. The research design is an event study examining changes in the daily county-level COVID-19 growth rates between March 31, 2020 and May 22, 2020. Mandating face mask use in public is associated with a decline in the daily COVID-19 growth rate by 0.9, 1.1, 1.4, 1.7, and 2.0 percentage-points in 1-5, 6-10, 11-15, 16-20, and 21+ days after signing, respectively. Estimates suggest as many as 230,000-450,000 COVID-19 cases possibly averted By May 22, 2020 by these mandates. The findings suggest that requiring face mask use in public might help in mitigating COVID-19 spread. [Editor's Note: This Fast Track Ahead Of Print article is the accepted version of the peer-reviewed manuscript. The final edited version will appear in an upcoming issue of Health Affairs.].

FIGURES

SUPPLEMENTAL EXHIBIT 1

Event Study Estimates of Effects of States Mandating Face Mask Use in Public on Daily County-Level Growth Rate of COVID-19 Cases.



Supplemental Exhibit 1. SOURCE Authors' analysis of US county-level COVID-19 case data between March 31 and May 22 of 2020. NOTES This graph shows the event-study estimates and the 95% confidence intervals of the effects of states mandating the use of facial covers/masks in public on county-level daily growth rate of COVID-19 cases over different periods before and after signing the mandate. The reference period is the first five days before the mandate was signed. The model controls for major COVID-19 mitigation policies as time-varying (closure of K-12 schools, county-level or statewide shelter-in-place orders, non-essential business closure, closure of restaurant for dining in, closure of gyms or movies theaters), COVID-19 tests per 100,000, county fixed effects and day fixed effects. The model is estimated by least squares weighted by the county 2019 population and the standard errors are robust to heteroscedasticity and clustered at state level.

SHOULD I BE WORRIED ABOUT CARRYING THE VIRUS THAT CAUSES COVID-19 HOME ON MY CLOTHES?

Howard-Jones A, Almuzam S, Britton P, Isaacs D, Kesson A, Khatami A, Marais B, Nayda C, Outhred A, Yuso J.. J Paediatr Child Health. 2020 Jun 16. doi: 10.1111/jpc.14938. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

This article describes how the viral load of SARS-CoV-2 dramatically decreases or becomes undetectable after several hours on environmental surfaces including tissue paper, wood, glass, money, steel, plastic, and cardboard. The authors suggest that the risk of bringing COVID-19 home on clothes and other surfaces is "so low that we consider it negligible."

MANAGEMENT

ACUTE CARE

INCREASED CD4/CD8 RATIO AS A RISK FACTOR FOR CRITICAL ILLNESS IN CORONAVIRUS DISEASE 2019 (COVID-19): A RETROSPECTIVE MULTICENTRE STUDY

Pallotto C, Suardi LR, Esperti S, Tarquini R, Grifoni E, Meini S, Valoriani A, Di Martino S, Cei F, Sisti E, Piani F, Botta A, Salomoni E, Baragli F, Blanc P.. Infect Dis (Lond). 2020 Jun 16:1-3. doi: 10.1080/23744235.2020.1778178. Online ahead of print.
Level of Evidence: 4 - Case-series or casecontrol studies, or poor quality prognostic cohort study

BLUF

A retrospective study of 38 COVID-19 patients at two hospitals in Central Italy from March 9th, 2020 to April 30th, 2020 found that patients who developed severe COVID-19 had a statistically significantly higher CD4/CD8 ratio than patients that did not develop severe COVID-19 (Figure 1). Since these tests were administered within 48-hours of hospital admission, this study suggests that clinicians may be able to use lymphocyte ratios to predict disease severity.

FIGURES

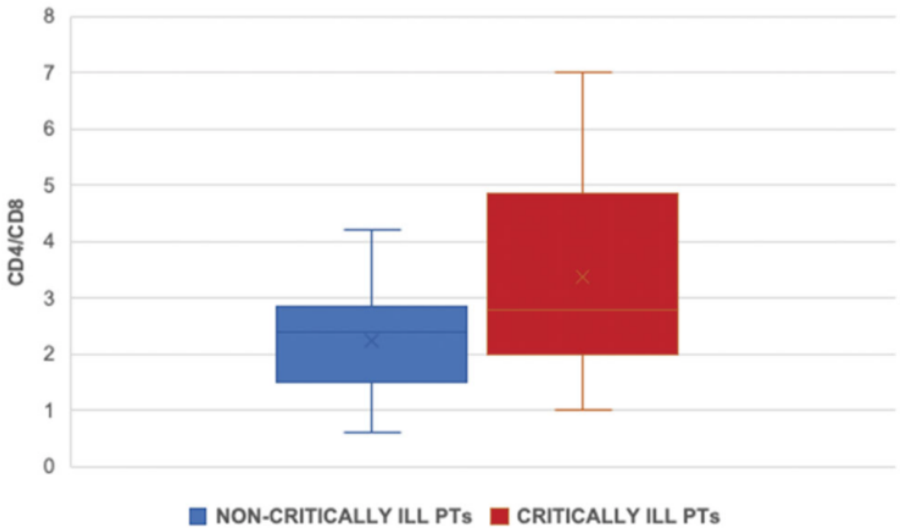


Figure 1. CD4/CD8 ratio in critically ill and non-critically ill COVID- 19 patients; p = 0.0444.

MEDICAL SUBSPECIALTIES

GASTROENTEROLOGY

PPIS AND BEYOND: A FRAMEWORK FOR MANAGING ANTICOAGULATION-RELATED GASTROINTESTINAL BLEEDING IN THE ERA OF COVID-19

Patel P, Sengupta N.. Dig Dis Sci. 2020 Jun 15. doi: 10.1007/s10620-020-06408-x. Online ahead of print.
Level of Evidence: 1 - Guidelines and Recommendations

BLUF

Authors at the University of Chicago Medical Center discuss the risk of gastrointestinal bleeding (GIB) secondary to anticoagulant therapy in COVID-19 patients. They cite a retrospective study (citation below) which found co-therapy with proton-pump inhibitors (PPI) can reduce GIB (HR 0.52, 95% CI 0.28–0.94, p = 0.03). Based on this and additional evidence that

COVID-19 increases thromboembolism risk, and thus treatment with anticoagulants, they raise concerns these patients may be uniquely susceptible to GIB and subsequent readmission. They propose an algorithm to further assess GIB risk and make judicious management adjustments (Figure 1). The authors believe this algorithm along with H. pylori testing and eradication with limited use of antiplatelet medications could minimize future complications for patients undergoing anticoagulation therapy. *Of note, this research was not conducted specifically on COVID-19 patients.

ABSTRACT

Coronavirus disease of 2019 (COVID-19) can be associated with high morbidity and mortality; patients with severe clinical manifestations may develop significant coagulopathy as well as unexpected thromboembolic complications. In response, centers are increasingly treating selected patients with intermediate-dose prophylactic or even therapeutic dose anticoagulation in order to prevent potentially catastrophic thrombotic complications. With this changing practice, the authors suspect that inpatient gastrointestinal consult teams across the country will be frequently managing COVID-19 patients with gastrointestinal bleeding (GIB). In order to reduce potentially avoidable hospital readmissions for GIB while improving patient outcomes, it is imperative to appropriately risk-stratify patients prior to initiation of anticoagulation. In this review, we discuss how to appropriately identify high-risk patients for GIB and how to mitigate GIB risk with proton-pump inhibitor co-therapy, medication reconciliation, and Helicobacter pylori testing and treating in this complex and morbid population.

FIGURES

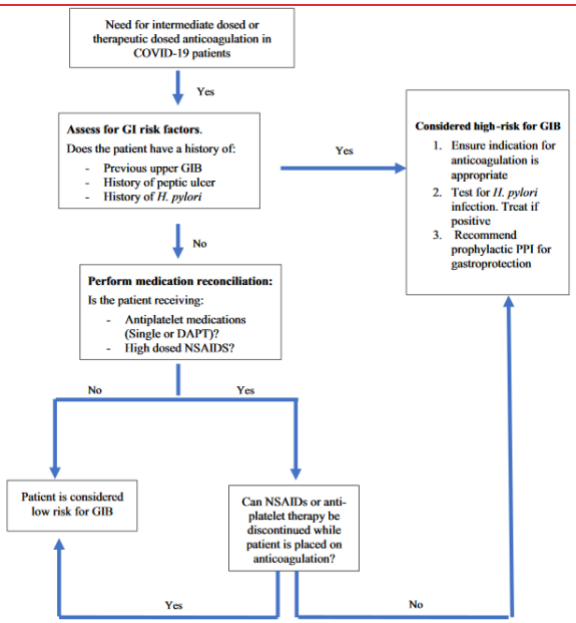


Fig. 1. Proposed algorithm to assess risk of GIB in COVID-19 patients undergoing intermediate dosed or therapeutic dosed anticoagulation

SURGICAL SUBSPECIALTIES

GENERAL SURGERY

NON-OPERATIVE MANAGEMENT OF ACUTE APPENDICITIS IN A PEDIATRIC PATIENT WITH CONCOMITANT COVID-19 INFECTION

Jones BA, Slater BJ.. J Pediatr Surg Case Rep. 2020 Aug;59:101512. doi: 10.1016/j.epsc.2020.101512. Epub 2020 May 31.
Level of Evidence: Other - Case Report

BLUF

A 13 year old female who received care at a hospital in Chicago was diagnosed with acute appendicitis and was also found to be SARS-CoV-2 positive during her workup. The patient was managed non-operatively with IV antibiotics to minimize risk of operative harm to the patient as well as transmission to the surgical team. Her appendicitis symptoms improved and she was discharged home.

ABSTRACT

Introduction: In late December 2019, reports emerged from Wuhan, China of a novel corovonavirus SARS-CoV-2, which caused severe acute respiratory distress syndrome referred to as COVID-19. As the virus spread, reports of severe perioperative complications, including fatalities, began to emerge in the literature. We present a case of a previously healthy patient who developed classic symptoms of appendicitis. The patient was also found to be positive for COVID-19. Given the risks to both the patient and surgical team, we elected to pursue a non-operative management strategy for this patient with appendicitis. Materials and methods: A 13 year old female with COVID-19 presented with a day of right lower quadrant abdominal pain. A computerized tomography (CT) scan diagnosed uncomplicated appendicitis. The patient was successfully treated non-operatively with antibiotics and discharged home. Conclusion: To our knowledge, this case illustrates the first report of a pediatric patient with concomitant appendicitis and COVID-19 infection. We have been able to utilize a non-operative management strategy to effectively treat the patient's acute appendicitis, while protecting her from the risks of undergoing a general anesthetic as well as the operative team. We hope this report can provide others with a potential management strategy for similar patients.

OBGYN

APPROPRIATE CARE FOR NEONATES BORN TO MOTHERS WITH COVID-19 DISEASE

Thi Tran H, Thi Kim Nguyen P, Thi Li H, Hoang Minh Le C, Giang HTN, Nguyen Thi Thu P, Murray J.. Acta Paediatr. 2020 Jun 16. doi: 10.1111/apa.15413. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

A review from Vietnamese and American researchers surveyed cases of COVID-19 positive mothers and their neonates in China. They found insufficient evidence that SARS-CoV-2 infection causes congenital anomalies in neonates. Neither did they find evidence that it can be delivered to a neonate via vertical transmission. Initially, practices in Wuhan, China separated neonates and COVID-19 positive mothers directly after birth and adhered to strict formula feeding to prevent spread of the virus. Further evidence has shown that maternal antibodies against SARS-CoV-2 can be delivered to the neonate through breastmilk, suggesting that the benefit of breastmilk and skin-to-skin contact directly after birth outweighs the risks of COVID-19 transmission.

ABSTRACT

The global COVID-19 pandemic has been associated with high rates of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission, morbidity and mortality in the general population. Evidence-based guidance on caring for babies born to mothers with COVID-19 is needed. There is currently insufficient evidence to suggest vertical transmission between mothers and their newborn infants. However, transmission can happen after birth from mothers or other carers. Based on the currently available data, prolonged skin-to-skin contact and early and exclusive breastfeeding remain the best strategies to reduce the risks of morbidity and mortality for both the mother with COVID-19 and her baby.

GASTROENTEROLOGY

COVID-19 HEATH CRISIS: LESS COLORECTAL RESECTIONS AND YET NO MORE PERITONITIS OR BOWEL OBSTRUCTION AS A COLLATERAL EFFECT?

Collard MK, Lefèvre JH, Batteux F, Parc Y; APHP / Universities / Inserm COVID-19 research collaboration.. Colorectal Dis. 2020 Jun 16. doi: 10.1111/codi.15199. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

Researchers associated with the Assistance Publique-Hôpitaux de Paris in Paris, France write a letter to the editor comparing surgical activities from 14 public hospitals in France. They compared records from 3/12/2020 - 4/29/2020 and 3/14/2019 - 05/01/2019 and found a 61% reduction in overall gastrointestinal surgical procedures, 67% for planned colorectal surgery, and a 48% reduction in emergency procedures (Table 1). The authors believe the reduction cannot be fully attributed to factors such as patients transferred to private systems, decrease in road accidents, or deferral of non-essential procedures and use of non-surgical treatments. They suggest people also became fearful of going to a hospital and hesitated to seek medical attention and recommend that these factors be accounted for in future studies and in considering colorectal cancer prognosis.

ABSTRACT

Because of the rapid worldwide propagation of COVID-19 (coronavirus disease 2019), each health care system had to urgently adapt with all efforts aimed to maximize the capacity of treatment for infected patients. With this in mind, the President of the French Republic declared on March 12, 2020: "Non-essential hospital care will be postponed, i.e. surgical procedures that are not urgent." But, in spite of the effort deployed by each hospital to provide a sufficient capacity of treatment for patients requiring a surgical procedure as an emergency, we have observed that the management of these patients have been largely affected, not because of a lack of resources but because of a surprising lack of patients.

FIGURES

Subgroup of surgery	2019 period (Number of procedures)	2020 period (Number of procedures)	Percentage variation
Major planned procedures			
Colorectal surgery	681	322	-53%
Segmental colectomy	183	117	-36%
Low anterior rectal resection	78	56	-28%
Total colectomy or coloproctectomy	14	15	+7%
Colostomy/ileostomy closure, reversal of Hartmann's procedure	160	63	-61%
Proctology	170	28	-84%
Others	76	43	-43%
Parietal surgery	567	44	-92%
Hepato-bilio-pancreatic surgery (cholecystectomy excluded)	271	164	-39%
Bariatric surgery	199	8	-96%
Oesogastric surgery excluding bariatric surgery	110	53	-52%
Common emergencies procedures			
Appendectomy on emergency	335	163	-51%
Proctology	226	64	-72%
Cholecystectomy on emergency	159	82	-48%
Peritonitis or intra-abdominal abscess	149	65	-56%
Small or large bowel surgery	114	61	-46%
Parietal surgery	93	45	-52%
Liver transplantation	54	39	-28%
Cutaneous or subcutaneous abscess	75	32	-57%

Table 1. Variation in the number of the major planned and emergency surgical procedures between 2019 and 2020 periods.

COMPARISON AND APPLICATION OF DIFFERENT IMMUNOASSAY METHODS FOR THE DETECTION OF SARS-COV-2

He J, Hu P, Gao Y, Zheng S, Xu C, Liu R, Fang L, Li R, Han C, An J, Dong J, Deng G, Sun L, Lv Y.. J Med Virol. 2020 Jun 16. doi: 10.1002/jmv.26187. Online ahead of print.
Level of Evidence: 3 - Non -randomized controlled cohort/follow-up study

BLUF

Authors at the Center for Medical Device Evaluation in China performed a comparative study between two SARS-CoV-2 serology detection methods—chemiluminescence (n=109) and the colloidal gold method (n=60)—using data from 4 clinical trials (n=169 patients with COVID-19). For the IgM antibody, the chemiluminescence method had an earlier (by about 1-2 days) positive conversion time, earlier positive results at different stages of COVID-19 disease, and an earlier downward trend in positive results than the colloidal gold method (Figure 1). Similar results were seen for the IgG antibody: earlier positive conversion time and increased slope (rate) of positive results (Figure 2). Based on these results, the authors suggest that the more sensitive chemiluminescence method may be better suited for high sample detection and early disease diagnosis, such as for suspected patients with negative nucleic acid results; the colloidal gold method may be optimal for sporadic cases and emergency due to its faster return of results and use of less sophisticated equipment.

ABSTRACT

The detection data of IgM and IgG antibodies in 169 patients with coronavirus disease (COVID-19) were analyzed to evaluate differences in clinical performance between the colloidal gold method and chemiluminescence method. In this study, chemiluminescence detection of IgM antibody showed a positive conversion earlier (about 1~2 days earlier), positive conversion rates higher in different stages of disease, and a trend of declining positive rate later than colloidal gold method. For IgG antibody, the chemiluminescence method showed a positive conversion earlier and the positive rate climbing more quickly than the colloidal gold method. No obvious negative-converting tendency of IgG detection was observed within 35 days after the onset of disease. Although colloidal gold method is generally less sensitive than chemiluminescence method, it shows advantages of shorter turn-around time, more simple procedure and no special equipment required. The two methodologies can be chosen according to different laboratory conditions. A reasonable understanding of the performance of reagents with different methodologies can help in clinical disease diagnosis effectively and assist in the diagnosis of the progression of COVID-19, for which the dynamic changes of antibody will provide reliable evidence.

FIGURES

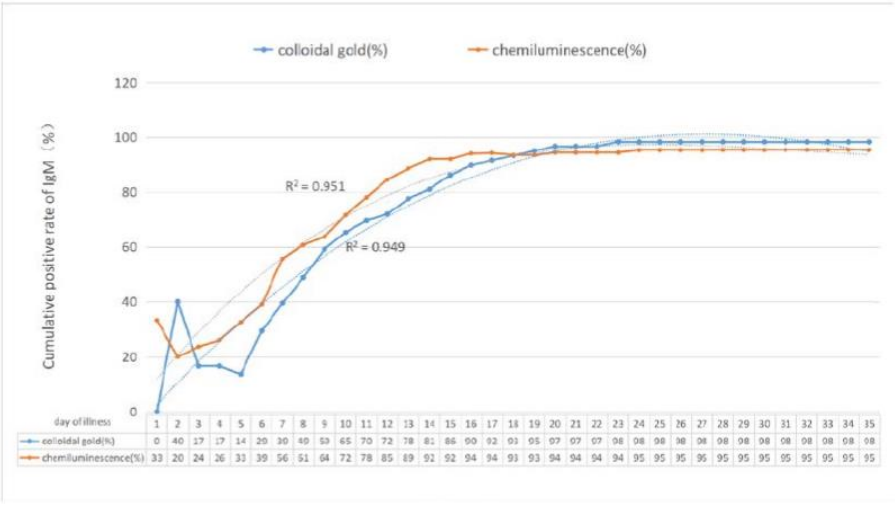


Figure 1. IgM Antibody Cumulative Positive Rate Comparing Chemiluminescence and Colloidal Gold Method

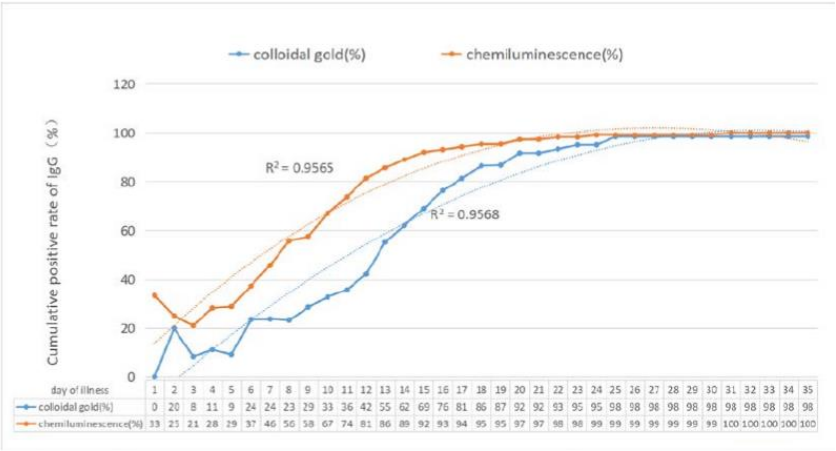


Figure 2. IgG Antibody Cumulative Positive Rate Comparing Chemiluminescence and Colloidal Gold Method

DEVELOPMENTS IN DIAGNOSTICS

DEVELOPMENT OF AN AUTOMATIC INTEGRATED GENE DETECTION SYSTEM FOR NOVEL SEVERE ACUTE RESPIRATORY SYNDROME-RELATED CORONAVIRUS (SARS-COV 2)

Li Y, Li J, Zhang Y, Dai L, Li L, Liu J, Zhang S, Wu X, Hu Y, Qin C, Jiang T, Kang X.. Emerg Microbes Infect. 2020 Jun 16:1-24. doi: 10.1080/22221751.2020.1782774. Online ahead of print.
Level of Evidence: 4 - Case-control studies, or “poor or non-independent reference standard

BLUF

A team from Beijing, China designed an integrated protocol for extracting RNA and performing qRT-PCR for the detection of SARS-CoV-2 in human samples (Figures 1-2).
Using the Sansure SARS-CoV-2 nucleic acid detection kit as a gold standard, this method was tested on 266 clinical samples, yielding a sensitivity of 97.62% (95% CI: 0.9320-0.9951) and specificity of 100%. This work may allow for a simpler method of diagnosis of COVID-19, requiring less skill and time; however, equipping remote or underserved regions with this technology remains a challenge.

ABSTRACT

In December 2019, Wuhan, China suffered a serious outbreak of a novel coronavirus infectious disease (COVID) caused by novel severe acute respiratory syndrome-related coronavirus (SARS-CoV 2). To quickly identify the pathogen, we designed and screened primer sets, and established a sensitive and specific qRT-PCR assay for SARS-CoV 2; the lower limit of detection(LOD) was 14.8 (95% CI : 9.8-21) copies per reaction. We combined this qRT-PCR assay with an automatic integration system for nucleic acid extraction and amplification, thereby establishing an automatic integrated gene detection system (AIGS) for SARS-CoV 2. Cross reactive analysis performed in 20 other respiratory viruses and 37 nasopharyngeal swabs confirmed a 100% specificity of the assay. Using two fold diluted SARS-CoV 2 culture, the LOD of AIGS was confirmed to be 365copies/ml(95% CI: 351-375), which was Comparable to that of conventional q RT-PCR(740copies/ml, 95% CI: 689-750). Clinical performances of AIGS assay were assessed in 266 suspected COVID-19 clinical respiratory tract samples tested in parallel with a commercial kit. The clinical sensitivity of AIGS test was 97.62% (95%CI:0.9320-0.9951) based on the commercial kit test result , and concordance analysis showed a high agreement in SARS-CoV-2 detection between the two assays, Pearson R was 0.9623 (95% CI:0.9523-0.9703).The results indicated that this AIGS could be used for rapid detection of SARS-CoV 2. With the advantage of simple operation and less time consuming, AIGS could be suitable for SARS-CoV2 detection in primary medical institutions, thus would do a great help to improve detection efficiency and control the spread of COVID-19.

FIGURES

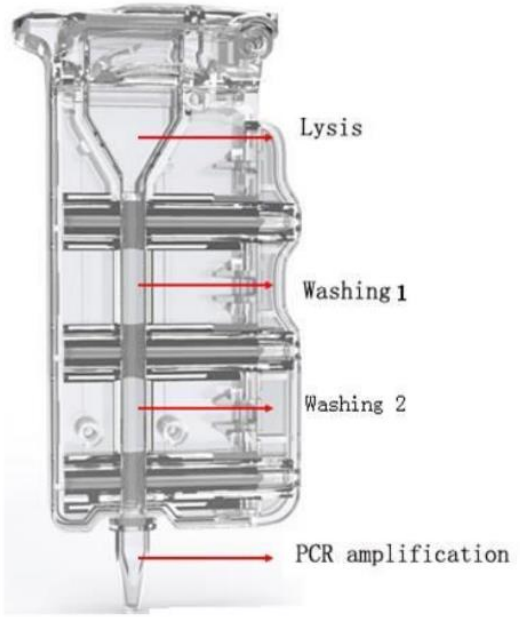


Figure 1: schematic of AIGS cartridge. The cartridge consists of the lysis area, washing area 1, washing area 2, and PCR amplification area; adjacent areas are separated by silicone oil and a plunger seal. The virus was lysed with detergent in the lysis area, and DNA/RNA bound to the magnetic beads under the high-salt conditions in the lysate. The magnet inside the instrument attracted the magnetic beads and pulled them into washing areas 1 and 2 for RNA/DNA extraction. Finally, the magnetic beads were dragged into the PCR amplification area nucleic acids amplification and detection.

Figure 2: AIGS flow chart. A: add 10ul magnetic beads ; B: add 200ul sample to each cartridge; C: Inserting the cartridge into detection site ; D: result analysis. Thermal cycling conditions were as follows: reverse transcription, 56 °C for15 min; initial denaturation, 94 °C for 1 min; and 40 cycles of 95 °C for 10 sec and 58 °C for 30 sec. The amplification curve was displayed on the screen in real time while the amplification program ran.

DEVELOPMENTS IN TREATMENTS

DECOY ACE2-EXPRESSING EXTRACELLULAR VESICLES THAT COMPETITIVELY BIND SARS-COV-2 AS A POSSIBLE COVID-19 THERAPY

Inal JM.. Clin Sci (Lond). 2020 Jun 26;134(12):1301-1304. doi: 10.1042/CS20200623.
Level of Evidence: 5 - Review / Literature Review

BLUF

The author from the United Kingdom discusses how mesenchymal/stromal stem cell derived extracellular vesicles (MSC-EVs) could potentially be used for COVID-19 treatment by expressing angiotensin-converting enzyme 2 (ACE2) which binds the spike (S) proteins of SARS-CoV-2, competitively inhibiting the virus in alveolar cells (Figure 1). This treatment would result in increased phagocytosis, anti-inflammatory effects, and overall reduced lung injury. This article suggests that testing this therapy utilizing "human ACE2 transgenic mouse models" should be prioritized.

ABSTRACT

The novel strain of coronavirus that appeared in 2019, SARS-CoV-2, is the causative agent of severe respiratory disease, COVID-19, and the ongoing pandemic. As for SARS-CoV that caused the SARS 2003 epidemic, the receptor on host cells that promotes uptake, through attachment of the spike (S) protein of the virus, is angiotensin-converting enzyme 2 (ACE2). In a recent article published by Batlle et al. (Clin. Sci. (Lond.) (2020) 134, 543-545) it was suggested that soluble recombinant ACE2 could be used as a novel biological therapeutic to intercept the virus, limiting the progression of infection and reducing lung injury. Another way, discussed here, to capture SARS-CoV-2, as an adjunct or alternative, would be to use ACE2+-small extracellular vesicles (sEVs). A competitive inhibition therapy could therefore be developed, using sEVs from engineered mesenchymal stromal/stem cells (MSCs), overexpressing ACE2.

FIGURES

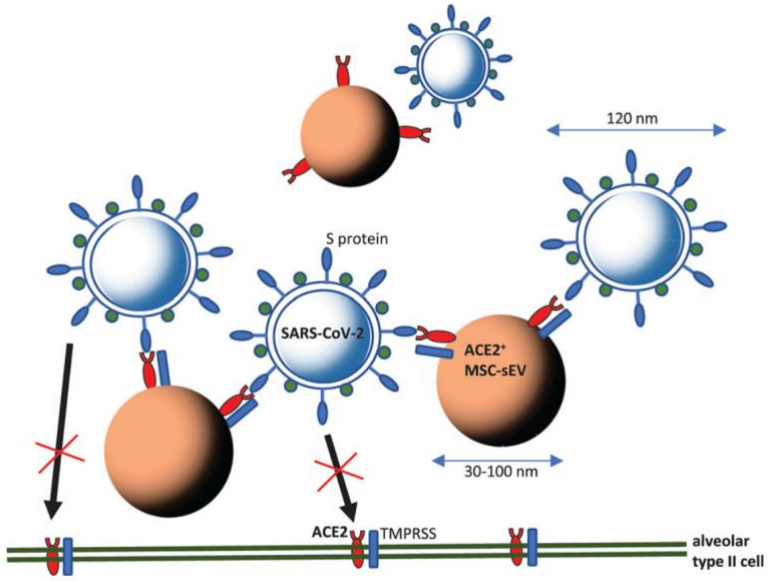


Figure 1. Schematic for ACE2-expressing small EVs binding SARS-CoV-2

Binding of SARS-CoV-2 S protein through ACE2 expressed on MSC-derived sEVs to competitively inhibit binding to ACE2 on alveolar type II cells and thereby limit infection. This could be tested using a human ACE2 transgenic mouse model and as a preliminary proof of concept study using sEVs from the tumour cell line, A549, a known model of alveolar type II cells [26] and thus a ready source of ACE2+ sEVs.

MONOCLONAL ANTIBODIES FOR PREVENTION AND TREATMENT OF COVID-19

Marovich M, Mascola JR, Cohen MS.. JAMA. 2020 Jun 15. doi: 10.1001/jama.2020.10245. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

Authors from the National Institute of Health promote further exploration of monoclonal antibodies during the COVID-19 pandemic. They argue that monoclonal antibodies targeting viral surface spike glycoproteins could provide both therapeutic and preventative value, and predict that clinical trials involving monoclonal antibody therapy in the near future will advance our control of the pandemic.

IGY - TURNING THE PAGE TOWARD PASSIVE IMMUNIZATION IN COVID-19 INFECTION (REVIEW)

Constantin C, Neagu M, Diana Supeanu T, Chiurciu V, A Spandidos D.. Exp Ther Med. 2020 Jul;20(1):151-158. doi: 10.3892/etm.2020.8704. Epub 2020 Apr 30.
Level of Evidence: Other - Review / Literature Review

BLUF

This literature review investigates immunoglobulin Y (IgY) as a potential candidate for passive immunization in COVID-19 infection. The authors discuss IgY's activity against bacterial infections (pseudomonas, salmonella), diagnostic applications (enzyme-linked immunosorbent assay), anti-viral activity in in vitro and in vivo models (SARS, influenza, etc; Table 1), and the

low-cost and non-invasive purification process from egg yolk by which it can be isolated for use. Based on these observations, the authors suggest that IgY should be investigated as a potential therapeutic option for COVID-19.

ABSTRACT

The world is facing one of the major outbreaks of viral infection of the modern history, however, as vaccine development workflow is still tedious and can not control the infection spreading, researchers are turning to passive immunization as a good and quick alternative to treat and contain the spreading. Within passive immunization domain, raising specific immunoglobulin (Ig)Y against acute respiratory tract infection has been developing for more than 20 years. Far from being an obsolete chapter we will revise the IgY-technology as a new frontier for research and clinic. A wide range of IgY applications has been effectively confirmed in both human and animal health. The molecular particularities of IgY give them functional advantages recommending them as good candidates in this endeavor. Obtaining specific IgY is sustained by reliable and nature friendly methodology as an alternative for mammalian antibodies. The aria of application is continuously enlarging from bacterial and viral infections to tumor biology. Specific anti-viral IgY were previously tested in several designs, thus its worth pointing out that in the actual COVID-19 pandemic context, respiratory infections need an enlarged arsenal of therapeutic approaches and clearly the roles of IgY should be exploited in depth.

FIGURES

Table I. Main studies focusing on *in vitro* and *in vivo* models using anti-viral IgY.

Pathogen	IgY preparation	Model type	Effect	Refs.
Pandemic influenza virus A/H1N1	Ostrich immunized with swine influenza virus vaccine strain	MDCK cells infected with pandemic virus	Neutralizing of viral infectivity in the cells	(82)
Influenza B virus	Hens immunized with IBV	MDCK cells BALB/c mouse model	Neutralization of IBV in MDCK cells Reducing viral replication in the lungs	(83)
Influenza A virus	Hens immunized with H1N1 virus	MDCK cells Mouse model	Neutralizing of viral infectivity in the cells *In vivo* protection by reducing the infectious titer of the virus in the lung	(84)
Viruses H1N1, H3N2, and H5N1 strain	Hens immunized with whole inactivated H1N1, H3N2, and H5N1	MDCK cell BALB/c and C.B-17 mice	Neutralization of viruses in MDCK cells 100% protection against challenge with H5N1 and A/Puerto Rico/8/34 H1N1	(85)
SARS	SPF chickens immunized with inactivated SARS coronavirus	VERO E6 cells	Neutralizing SARS coronavirus viral infectivity in the cells	(78)
BRSV related to human syncytial virus	Hens immunized with BRSV	MDCK cells infected with A51908 BRSV strain	Neutralization of viruses in MDCK cells	(86)

IgY, immunoglobulin Y; SARS, severe acute respiratory syndrome; SPF, specific pathogen-free; BRSV, bovine respiratory syncytial virus.

Table 1. Various studies employing anti-viral IgY

MENTAL HEALTH & RESILIENCE NEEDS

COVID-19'S IMPACT ON HEALTHCARE WORKFORCE

ARE WOMEN STILL "THE OTHER"? GENDERED MENTAL HEALTH INTERVENTIONS FOR HEALTH CARE WORKERS IN SPAIN DURING COVID-19

López-Atanes M, Recio-Barbero M, Sáenz-Herrero M.. Psychol Trauma. 2020 Jun 15. doi: 10.1037/tra0000751. Online ahead of print.
Level of Evidence: Other - Opinion

BLUF

Spain has implemented mental health interventions to aid healthcare workers in coping with the COVID-19 pandemic; however, these interventions do not address the disparities among different genders, especially among women, who make up the majority of front line COVID-19 care providers and the majority of those reporting depressive symptoms. The authors suggest that these interventions "should apply gender sensitivity and recognize that specific stressors may differ between genders."

ABSTRACT

During the COVID-19 pandemic, Spain ranked 1st in number of infected health workers. Despite the fact that up to 75% of them were women, psychological interventions to prevent distress usually lacked a gender perspective and a biopsychosocial approach. (PsycInfo Database Record (c) 2020 APA, all rights reserved).

IMPACT ON PUBLIC MENTAL HEALTH

THE IMPLICATIONS OF COVID-19 FOR THE MENTAL HEALTH CARE OF OLDER ADULTS: INSIGHTS FROM EMERGENCY DEPARTMENT SOCIAL WORKERS

Xiang X, Ning Y, Kayser J.. J Gerontol Soc Work. 2020 Jun 16:1-3. doi: 10.1080/01634372.2020.1779160. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

The authors express concerns that the current COVID-19 pandemic could exacerbate mental health problems in older adults due to anxiety and paranoia, isolation from younger family members, care being given remotely, delays to high-quality care, and financial concerns. Therefore, it is important for social workers to document the measures implemented to provide care for the elderly during this time and to collect data so the extent of the negative impact on mental health during the COVID-19 pandemic can be properly evaluated.

SUMMARY

The COVID-19 pandemic has caused unprecedented anxiety in the population, and older adults are at a higher risk due to the higher prevalence of mental health concerns and their greater risk of developing severe illness from COVID-19. Many older adults live alone, which furthers the negative impact that measures such as social distancing can have. In light of the stressors that the COVID-19 pandemic has created, it is important for social workers that take care of the elderly population to document the measures that they have taken that have been successful and collect data which will help estimate and minimize the negative psychological impact that the COVID-19 pandemic has had on older people.

THE IMPACT OF THE COVID-19 PANDEMIC ON SUICIDE RATES

Sher L.. QJM. 2020 Jun 15:hcaa202. doi: 10.1093/qjmed/hcaa202. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

This review conducted by a physician from New York investigates the mental health impact of the COVID-19 pandemic on the general population, healthcare workers, and vulnerable groups. The author stresses that long-term psychological and social consequences (i.e. exacerbation of existing psychiatric disorders, depression, etc) could arise in vulnerable individuals during the pandemic and increase the risk for suicidal behaviors (Figure 1). Based on this observation and other findings of the review, the author presents three different approaches for suicidal preventive interventions (universal, selective, and indicated) and urges further research in mitigating the mental health effects of the pandemic to reduce COVID-19 related suicides.

SUMMARY

Specific findings of this review include, but are not limited to, the following:

- Multiple studies show that the pandemic is related to distress, anxiety, fear of infection, depression, and insomnia in the general population, with health care workers especially affected.
- Social isolation and social disengagement as a result of the pandemic are associated with increased suicidal ideation and suicide attempts, most prominently among individuals with pre-existing mental health conditions.
- Universal approach to suicide prevention is suggested for the general population and encourages staying connected via phone or video chat, healthy eating, exercise, and access to suicide prevention helplines, most prominently in the outpatient primary care setting.
- Selective approach to suicide prevention is suggested for populations at increased risk for suicide (previous psychiatric disorders, emotional distress, frontline healthcare workers, elderly) involving maintenance of treatment regimen, increased contact with mental health professionals, telehealth resource accessibility, and limiting access to social media news.
- Indicated approach to suicide prevention is recommended for individuals with high risk/risk factors for suicide that require special attention and follow-up with mental health professionals.

ABSTRACT

Multiple lines of evidence indicate that the COVID-19 pandemic has profound psychological and social effects. The psychological sequelae of the pandemic will probably persist for months and years to come. Studies indicate that the COVID-19 pandemic is associated with distress, anxiety, fear of contagion, depression, and insomnia in the general population and among health care professionals. Social isolation, anxiety, fear of contagion, uncertainty, chronic stress, and economic difficulties may lead to the development or exacerbation of depressive, anxiety, substance use, and other psychiatric disorders in vulnerable populations including individuals with pre-existing psychiatric disorders and people who reside in high COVID-19 prevalence areas. Stress-related psychiatric conditions including mood and substance use disorders are associated with suicidal behavior. COVID-19 survivors may also be at elevated suicide risk. The COVID-19 crisis may increase suicide rates during and after the pandemic. Mental health consequences of the COVID-19 crisis including suicidal behavior are likely to be present for a long time and peak later than the actual pandemic. To reduce suicides during the COVID-19 crisis it is imperative to decrease stress, anxiety, fears and loneliness in the general population. There should be traditional and social media campaigns to promote mental health and reduce distress. Active outreach is necessary, especially for people with a history of psychiatric disorders, COVID-19 survivors, and older adults. Research studies are needed of how mental health consequences can be mitigated during and after the COVID-19 pandemic.

FIGURES

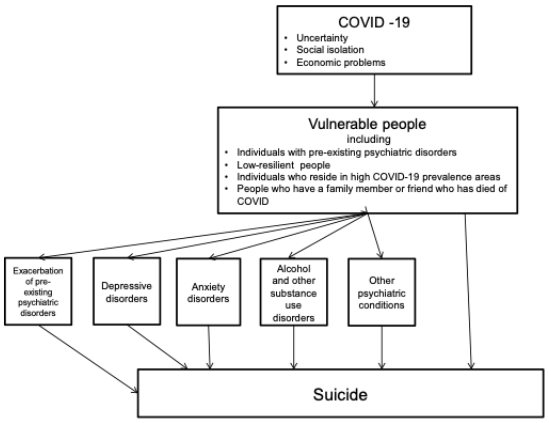


Figure 1: Suicidal behavior in vulnerable populations in the COVID-19 era

Figure 1. Suicidal behavior in vulnerable populations in the COVID-19 era.

CORONAVIRUS AND INTERPERSONAL VIOLENCE: A NEED FOR DIGITAL MENTAL HEALTH RESOURCES

Carballea D, Rivera RM.. Psychol Trauma. 2020 Jun 15. doi: 10.1037/tra0000849. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

Researchers from the Department of Clinical Psychology at Albizu University-Miami discuss the psychological impact of the COVID-19 pandemic, including an increase in interpersonal violence. Authors urge for a catalog of digital mental health resources for both survivors and perpetrators to help with emotional responses to trauma and to develop effective communication strategies.

ABSTRACT

Since the declaration of COVID-19 restrictions and lockdowns, countries across the world have seen an increase in reports of interpersonal violence. During these trying times, digital mental health resources tailored to interpersonal violence are needed. Through the use of online platforms such as websites, mobile applications, and social media, survivors and perpetrators alike can access tools that help them manage stressors induced by the coronavirus as well as practice emotional regulation techniques and communication strategies at home. (PsycInfo Database Record (c) 2020 APA, all rights reserved).

HETEROGENEOUS MENTAL HEALTH CONSEQUENCES OF COVID-19: COSTS AND BENEFITS

Mancini AD.. Psychol Trauma. 2020 Jun 15. doi: 10.1037/tra0000894. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

In this editorial, a psychologist from Pace University in New York argues that the COVID-19 pandemic has had a profound effect on the mental health of populations around the world. Overall, the author emphasizes that we must remain acutely aware of the toll that the COVID-19 pandemic will have on mental health while also understanding some people may actually experience improved mental health during this time.

SUMMARY

A psychologist from Pace University in New York argues that the COVID-19 pandemic has had a profound effect on the mental health of populations around the world. The author specifically argues the following three points:
- The pandemic will undoubtedly affect certain populations differently, and the specific health effects within populations will be variegated as well.
- The maintenance and degree of social relationships will substantially effect mental health outcomes.
- There will be a subset of people who will see an improvement in their mental health status, likely due to improvements in some social environments.

Ultimately, the author emphasizes that "we must remain vigilant to the potential harms, but we should not lose sight of the ways the pandemic may positively impact social and psychological functioning."

ABSTRACT

In this commentary, I argue that the mental health impact of COVID-19 will show substantial variation across individuals, contexts, and time. Further, one key contributor to this variation will be the proximal and long-term impact of COVID-19 on the social environment. In addition to the mental health costs of the pandemic, it is likely that a subset of people will experience improved social and mental health functioning. (PsycInfo Database Record (c) 2020 APA, all rights reserved).

SILVER LININGS

HEALTH CARE POLICY AFTER THE COVID-19 PANDEMIC

Fuchs VR.. JAMA. 2020 Jun 12. doi: 10.1001/jama.2020.10777. Online ahead of print.
Level of Evidence: Other - Opinion

BLUF

This author from the Stanford Institute of Economic Policy Research proposed ideas for healthcare reform, primarily addressing barriers to paying for services and provider reimbursement. The author makes the following recommendations and observations:

1. A flat tax on consumption where "high-income individuals pay more because they consume more, but everyone gets similar health insurance regardless of income."
2. "Capitation [fixed payment per patient] reimbursement provides incentives to use resources efficiently, unlike fee-for-service reimbursement that provides incentives for overuse."
3. A risk-adjusted capitation fee would allow for increased reimbursement with higher risk groups and vice versa for lower risk groups.

While the author acknowledges political obstacles may exist, particularly from high-income earners; they believe the current pandemic could be a rare catalyst for major political shifts toward a more efficient and effective system of care.

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