The Daily COVID-19 Literature Surveillance Summary

November 25, 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

Transmission & Prevention

- A review by biomedical engineers in Canada discusses the possibility of using animal models including rhesus macaques, hamsters, and ferrets to help guide research on COVID-19 vaccine development. They also describe 8 current vaccine platforms, including 139 vaccine candidates in pre-clinical evaluation and 26 in clinical evaluation, and highlight the importance of introducing an effective COVID-19 vaccine to return to pre-pandemic life.

Management

- Emergency Medicine and Cardiovascular physicians from Mayo Clinic conduct a review reporting an increased risk of cardiac involvement in athletes with COVID-19: they discuss how 10-27.8% of all hospitalized COVID-19 patients have evidence of myocardial injury, of these 78% have arrhythmias, and note that myocarditis accounts for up to 22% of cardiac deaths in young athletes (<35 years old) with increased incidence during exercise. They urge screening for cardiac dysfunction in convalescent COVID-19 patients and recommend providers maintain a high index of suspicion before medical clearance of young athletic patients with COVID-19.

Mental Health & Resilience Needs

- Mental health experts performed a systematic review of 44 studies (54,231 participants across 13 countries) assessing the prevalence of sleep problems during the pandemic and found pooled prevalence of sleep problems was 35.7%, with COVID-19 patients being most affected (74.8%), followed by healthcare workers (36%), and the general public (32.3%), suggesting that sleep problems are common during the pandemic, particularly among COVID-19 patients, and encourage implementing strategies to mitigate adverse effects in these populations.

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UNDERSTANDING THE PATHOLOGY

DO SEX-SPECIFIC IMMUNOBIOLOGICAL FACTORS AND DIFFERENCES IN ANGIOTENSIN CONVERTING ENZYME 2 (ACE2) EXPRESSION EXPLAIN INCREASED SEVERITY AND MORTALITY OF COVID-19 IN MALES?

Vikse J, Lippi G, Henry BM.. Diagnosis (Berl). 2020 Nov 18;7(4):385-386. doi: 10.1515/dx-2020-0054.
Level of Evidence: Other - Review / Literature Review

BLUF

Investigators mainly from Stavanger University Hospital (Norway) and University of Verona (Italy) review the effect of sex-specific factors on the course of SARS-CoV-2 infection to understand the increased severity of COVID-19 in males. They relate that SARS-CoV-2 can be recognized by endosomal toll-like receptor (TLR) 7, whose gene is on the X chromosome, causing release of type I interferons (IFN) and instigating the host's antiviral defense. Further, females have higher CD4 lymphocyte counts than males, which may decrease severity of COVID-19. Conversely, ACE2 has been found to be highly expressed in the male testes, possibly providing a reservoir for SARS-CoV-2. Based on these observations, the investigators hypothesize "that sex-specific immunobiological differences, including timing of type I IFN-response, may contribute at least in part to the observed sex differences in COVID-19 severity and mortality".

ABSTRACT

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome (SARS) coronavirus 2 (SARS-CoV-2), shares similarities with the former SARS outbreak, which was caused by SARS-CoV-1. SARS was characterized by severe lung injury due to virus-induced cytopathic effects and dysregulated hyperinflammatory state. COVID-19 has a higher mortality rate in men both inside and outside China. In this opinion paper, we describe how sex-specific immunobiological factors and differences in angiotensin converting enzyme 2 (ACE2) expression may explain the increased severity and mortality of COVID-19 in males. We highlight that immunomodulatory treatment must be tailored to the underlying immunobiology at different stages of disease. Moreover, by investigating sex-based immunobiological differences, we may enhance our understanding of COVID-19 pathophysiology and facilitate improved immunomodulatory strategies.

IN VITRO

HEALTHY DONOR T CELL RESPONSES TO COMMON COLD CORONAVIRUSES AND SARS-COV-2

Woldemeskel BA, Kwaa AK, Garliss CC, Laeyendecker O, Ray SC, Blankson JN.. J Clin Invest. 2020 Nov 16:143120. doi: 10.1172/JCI143120. Online ahead of print.
Level of Evidence: Other - Mechanism-based reasoning

BLUF

An immunology research team from Johns Hopkins University in Baltimore, USA analyzed T-cell responses against three common cold coronaviruses and SARS-CoV-2 via ELISPOT assay of blood samples from 21 healthy donors (HD) seronegative for SARS-CoV-2 and four patients recovered from COVID-19. They found T-cell specific responses against spike (S) protein of HCoV-229E, HCoV-NL63, HCoV-OC43 in many HDs while only one HD elicited a T-cell response against SARS-CoV-2 S protein (Figures 1, 2). In vitro expansion in this patient showed a wider response against 22 target peptides of HCoV-NL63 that cross-recognized SARS-CoV-2 S protein (Figure 4), and authors recommend further studies of a larger cohort to better assess cross-reactivity in regard to preventing SARS-CoV-2 infection.

ABSTRACT

BACKGROUND: The T cell responses to the common cold coronaviruses have not been well characterized. Pre-existing T cell immunity to SARS-CoV-2 has been reported, and a recent study suggested that this was due to cross-recognition of the novel coronavirus by T cells specific for the common cold coronaviruses. METHODS: We used the ELISpot assay to characterize the T cell responses against peptide pools derived from the spike protein of three common cold coronaviruses (HCoV-229E, HCoV-NL63, and HCoV-OC43) and SARS-CoV-2 in 21 healthy donors who were seronegative for SARS-CoV-2 and had no known exposure to the virus. An in vitro expansion culture assay was also used to analyze memory T cell responses. RESULTS: We found responses to the spike protein of the three common cold coronaviruses in many donors. We then focused on HCoV-NL63 and demonstrated broad T cell responses to the spike protein and identified 22 targeted peptides. Interestingly, only one subject had a significant response to SARS-CoV-2 spike or nucleocapsid protein in the ELISpot assay. In vitro expansion studies suggested that T cells specific for the HCoV-NL63 spike protein in this subject could also recognize SARS-CoV-2 spike protein peptide pools. CONCLUSIONS: Healthy donors have circulating T cells specific for the spike proteins of HCoV-NL63, HCoV-229E, and HCoV-OC43. T cell responses to SARS-CoV-2 spike and nucleocapsid proteins were present in only one subject and were potentially the result of cross-recognition by T cells specific for the common cold coronaviruses. Further studies are needed to determine whether this influences COVID-19 outcomes.

FIGURES

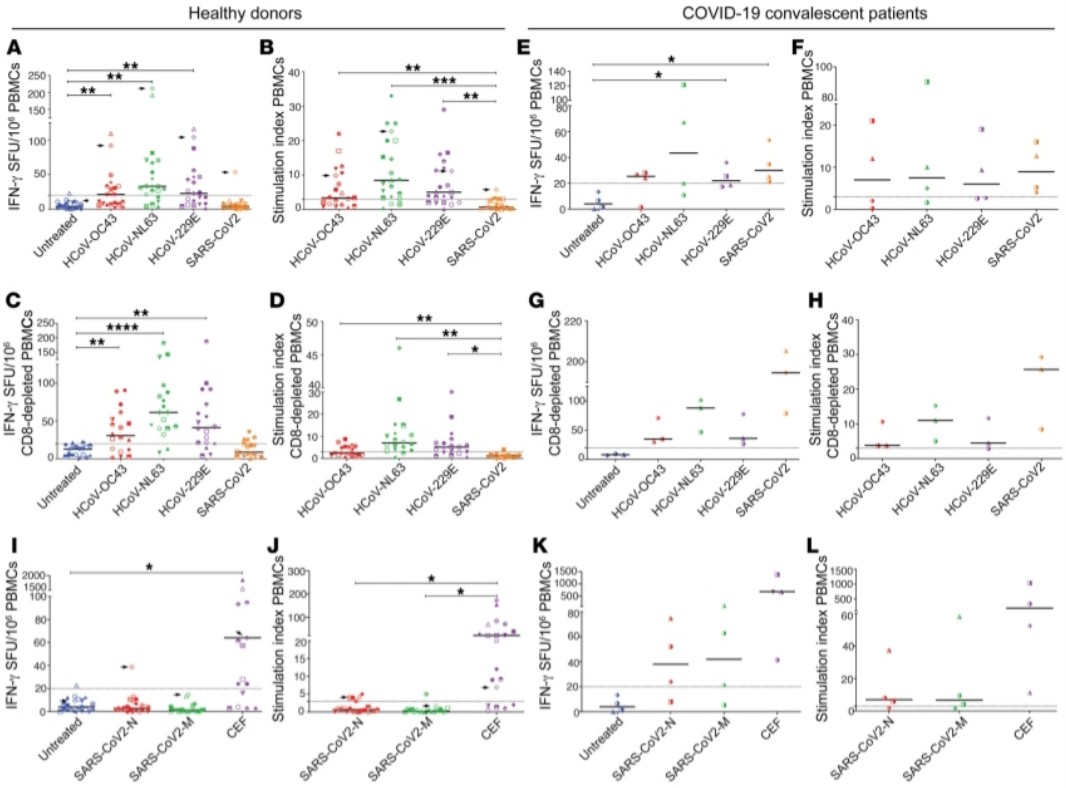

Figure 1: " IFN-γ responses to viral peptide pools from HDs and CCPs. The number of SFU from unfractioned PBMCs (A and E) and CD8+ T cell–depleted PBMCs (C and G) and the corresponding stimulation indices (B, D, F, and H) in response to S protein peptide pools from different viruses are shown. The number of SFU (I and K) and the stimulation indices (J and L) from unfractioned PBMCs in response to CEF and SARS-CoV-2 M and N peptide pools are also shown. Arrows indicate HD9. Each data point represents the mean of 3 replicate values. Horizontal bars represent the median. Statistical comparisons were performed using 1-way ANOVA with Geisser-Greenhouse correction and Dunnett's multiple-comparison test (n = 19–21 for samples from HDs; n = 3–4 for samples from patients with COVID-19). *P = 0.0332, **P = 0.0021, ***P = 0.0002, and ****P < 0.0001".

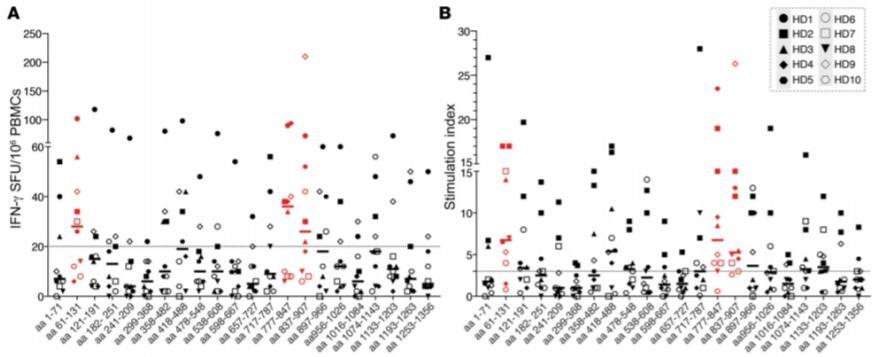

Figure 2: ". Breadth of T cell responses to HCoV-NL63 S protein. The numbers of SFU per million PBMCs (A) and stimulation indices (B) generated for pools of 10 peptides are shown for 10 HDs. Horizontal bars indicate the median. Pools that elicited the most potent responses are highlighted in red".

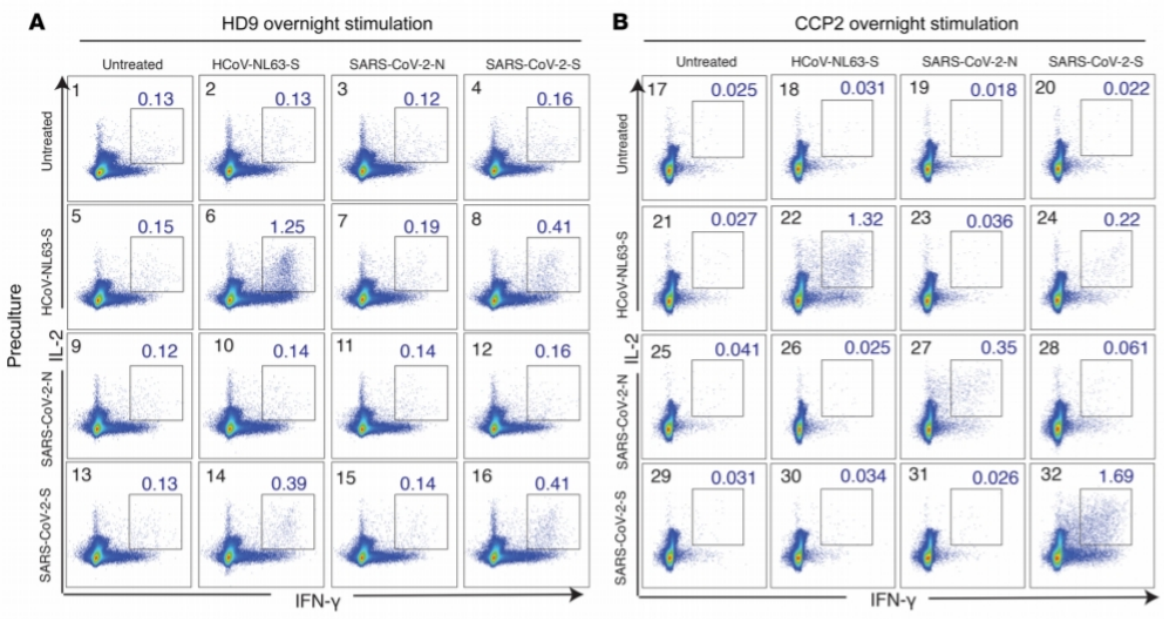

Figure 4: " Cross-recognition of HCoV-NL63 and SARS-CoV-2 S protein peptide pools in HD9 and CCP2. PBMCs from HD9 (A) and CCP2 (B) were precultured with peptide pools (shown in rows) for 10–12 days and then stimulated for 12 hours with peptide pools (shown in columns). The percentage of cells that coexpressed IL-2 (y axis) and IFN-γ (x axis) is shown above the gated box in the upper right corner of each plot".

DEVELOPMENTS IN TRANSMISSION & PREVENTION

COVID-19 BASICS AND VACCINE DEVELOPMENT WITH A CANADIAN PERSPECTIVE

Liu M, Chen X.. Can J Microbiol. 2020 Nov 2. doi: 10.1139/cjm-2020-0421. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

A review by biomedical engineers from the University of Saskatchewan and University of Calgary in Canada discusses the possibility of using animal models including rhesus macaques, hamsters, and ferrets to help guide research on COVID-19 vaccine development. They also describe 8 current vaccine platforms, including 139 vaccine candidates in pre-clinical evaluation and 26 in clinical evaluation (see summary). Authors highlight the importance of introducing an effective COVID-19 vaccine to return to pre-pandemic life, and hope this review adds to the growing knowledge on vaccine development.

SUMMARY

Animal models for potential utility in COVID-19 vaccine development:
- Rhesus macaques show protective humoral and cellular immunity against re-exposure to SARS-CoV-2
- Infected hamsters demonstrate the ability to transmit SARS-CoV-2 to naive hamsters
- Ferrets display airborne transmission of SARS-CoV-2 through direct and indirect contact with naive ferrets
- Authors propose animal models can help evaluate immune response and viral challenge for protection efficacy

The 8 vaccine platforms under development for SARS-CoV-2 vaccine include:
- RNA and DNA
- Replicating and non-replicating viral vector
- Inactivated and live-attenuated virus
- Protein subunit and virus-like particle (VLP)

ABSTRACT

The ongoing coronavirus disease 2019 (COVID-19) pandemic is a rapidly evolving situation. New discoveries about COVID-19 and its causative virus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), continue to deepen the understanding of this novel disease. As there is currently no COVID-19 specific treatment, isolation is the most effective method to prevent transmission. Moreover, development of a safe and effective COVID-19 vaccine will be instrumental in reinstating pre-COVID-19 conditions. As of July 31, 2020, there are at least 139 vaccine candidates from around the globe are in preclinical evaluation, with another 26 undergoing clinical evaluation. This paper aims to review the basics of COVID-19, including epidemiology, basic biology of SARS-CoV-2, and transmission. We also review COVID-19 vaccine development, including animal models, platforms under development, and vaccine development in Canada.

MANAGEMENT

MEDICAL SUBSPECIALTIES

CARDIOLOGY

IMPLICATIONS OF SARS-COV-2-ASSOCIATED MYOCARDITIS IN THE MEDICAL EVALUATION OF ATHLETES

Raukar NP, Cooper LT.. Sports Health. 2020 Nov 17:1941738120974747. doi: 10.1177/1941738120974747. Online ahead of print.
Level of Evidence: 2 - Review / Literature Review

BLUF

Emergency Medicine and Cardiovascular physicians from Mayo Clinic conduct a review reporting an increased risk of cardiac involvement in athletes with COVID-19. Specifically, they discuss how 10-27.8% of all hospitalized COVID-19 patients have evidence of myocardial injury, and of these 78% have arrhythmias. The authors note that myocarditis accounts for up to 22% of cardiac deaths in young athletes (<35 years old) with increased incidence during exercise. They urge screening for cardiac dysfunction in convalescent COVID-19 patients and recommend providers maintain a high index of suspicion before medical clearance of young athletic patients with COVID-19.

ABSTRACT

CONTEXT: Myocarditis is a known cause of death in athletes. As we consider clearance of athletes to participate in sports during the COVID-19 pandemic, we offer a brief review of the myocardial effects of SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) through the lens of what is known about myocarditis and exercise. All athletes should be queried about any recent illness suspicious for COVID-19 prior to sports participation. EVIDENCE ACQUISITION: The PubMed database was evaluated through 2020, with the following keywords: myocarditis, COVID-19, SARS-CoV-2, cardiac, and athletes. Selected articles identified through the primary search, along with position statements from around the world, and the relevant references from those articles, were reviewed for pertinent clinical information regarding the identification, evaluation, risk stratification, and management of myocarditis in patients, including athletes, with and without SARS-CoV-2. STUDY DESIGN: Systematic review. LEVEL OF EVIDENCE: Level 3. RESULTS: Since myocarditis can present with a variety of symptoms, and can be asymptomatic, the sports medicine physician needs to have a heightened awareness of athletes who may have had COVID-19 and be at risk for myocarditis and should have a low threshold to obtain further cardiovascular testing. Symptomatic athletes with SARS-CoV-2 may require cardiac evaluation including an electrocardiogram and possibly an echocardiogram. Athletes with cardiomyopathy may benefit from cardiac magnetic resonance imaging in the recovery phase and, rarely, endocardial biopsy. CONCLUSION: Myocarditis is a known cause of sudden cardiac death in athletes. The currently reported rates of cardiac involvement of COVID-19 makes myocarditis a risk, and physicians who clear athletes for participation in sport as well as sideline personnel should be versed with the diagnosis, management, and clearance of athletes with suspected myocarditis. Given the potentially increased risk of arrhythmias, sideline personnel should practice their emergency action plans and be comfortable using an automated external defibrillator.

POLYMERASE CHAIN REACTION ASSAYS REVERTED TO POSITIVE IN 25 DISCHARGED PATIENTS WITH COVID-19

Yuan J, Kou S, Liang Y, Zeng J, Pan Y, Liu L.. Clin Infect Dis. 2020 Nov 19;71(16):2230-2232. doi: 10.1093/cid/ciaa398.
Level of Evidence: 3 - Local non-random sample

BLUF

Infectious disease researchers from Shenzhen Third People's Hospital conducted a cohort study between January 23 - February 21, 2020 to assess COVID-19 testing parameters and viral recrudescence. Findings show that of 172 patients who recovered from COVID-19 (two consecutive negative SARS-CoV-2 RT-PCR tests before discharge), 25 patients without signs of symptoms tested positive about 7.32 ± 3.86 days after their last negative test (Table 1). The authors advise providers repeat viral RT-PCR testing several days apart to ensure viral clearance since RT-PCR test results can fluctuate between positive and negative during COVID-19 recovery.

ABSTRACT

We report the observation that 14.5% of COVID-19 patients had positive RT-PCR testing again after discharge. We describe correlations between laboratory parameters and treatment duration (r= -0.637; p=0.002) and time to virus recrudescence (r= 0.52; p=0.008) respectively, suggesting the need for additional measures to confirm illness resolution in COVID-19 patients.

FIGURES

Table 1. Baseline Characteristics of the 25 Discharged Patients With Newly Positive Results on Reverse Transcription–Polymerase Chain Reaction

	Groups by Age Range (Case Numbers)				
	≤14 Years (n = 6)	20–40 Years (n = 13)	41–60 Years (n = 6)	Total (N = 25)	*P*
Sex (males, females), n	1, 5	4, 9	3, 3	8, 17	NS
Symptom of first admission to hospital, n (%)					
Fever	3 (50)	9 (69.23)	5 (83.33)	17 (68)	NS
Cough	2 (33.33)	9 (69.23)	4 (66.67)	15 (60)	NS
Symptom of second admission to hospital, n (%)					
Mild cough	2 (33.33)	3 (18.75)	3 (50)	8 (32)	
Laboratory parameters before discharge, mean (SD)					
Lymphocyte count, 10^9 cells/L	3.61 (1.52)	1.62 (0.46)	1.51 (0.43)	2.07 (1.19)	.001
LDH level, U/L	218.40 (49.85)	156.50 (29.74)	188 (40.42)	180.24 (44.5)	.025
CRP level, mg/L	0.84 (0.85)	6.77 (5.05)	5.30 (4.78)	4.90 (4.79)	NS
IL6 level, pg/mL	2.49 (0.93)	3.3.0 (1.94)	3.41 (0.81)	3.19 (1.40)	NS
D-dimer level, μg/mL	0.29 (0.14)	0.36 (0.29)	0.43 (0.27)	0.37 (0.26)	NS
Clinical features, mean (SD), days					
Length of first hospital stay	15 (2.83)	15.23 (3.35)	16 (5.83)	15.36 (3.81)	NS
Antivirus treatment durations	13.33 (3.93)	13.46 (4.31)	13.5 (4.46)	13.44 (4.08)	NS
Time from negative PCR test to discharge	3.67 (2.50)	2.17 (1.53)	2.83 (1.72)	2.71 (1.88)	NS
Time from positive again to last negative	8.33 (5.61)	6.77 (3.40)	7.5 (3.21)	7.32 (3.86)	NS
Time from positive again to last discharge	4.67 (4.23)	5.92 (4.72)	4.67 (2.94)	5.32 (4.13)	NS
Time from positive again to second hospitalization	1.33 (1.51)	1.85 (2.12)	2.67 (2.07)	1.92 (1.96)	NS
Time from readmission to negative again	1 (0)	2.69 (2.06)	3.67 (2.07)	2.73 (2.03)	NS

Data are presented as mean (SD) or n (%) unless otherwise indicated, determined using 1-way analysis of variance.
Abbreviations: CRP, C-reactive protein; IL6, interleukin-6; LDH, lactate dehydrogenase; NS, not significant; PCR, polymerase chain reaction.

EVALUATION OF THE TRUVIAN EASY CHECK COVID-19 IGM/IGG LATERAL FLOW DEVICE FOR RAPID ANTI-SARS-COV-2 ANTIBODY DETECTION

Chan CW, Shahul S, Coleman C, Tesic V, Parker K, Yeo KJ.. Am J Clin Pathol. 2020 Nov 2:aqaa221. doi: 10.1093/ajcp/aqaa221. Online ahead of print.
Level of Evidence: 5 - Mechanism-based reasoning

BLUF

A diagnostic accuracy study by a multidisciplinary team affiliated with University of Chicago Medical Center evaluated performance of the Truvian Easy Check Device, a 10 minute rapid test, in detecting anti-SARS-CoV-2 IgM or IgG antibodies (Figure 1) from COVID-19 patients (confirmed via RT-PCR; n=99) versus healthy control patients (n=56). They found the device compared well to the Roche Elecsys antibody assay with 98.6% concordance (Figure 3), and clinical performance showed 96.6% sensitivity, 98.2% specificity (Table 1), and overall accuracy of 98.1%. Authors acknowledge this study is limited by lack of external validity, but suggest the Truvian Easy Check Device may offer a simple, reliable, and rapid option for SARS-CoV-2 detection.

ABSTRACT

OBJECTIVES: To evaluate the analytical and clinical performance of the Truvian Easy Check coronavirus disease 2019 (COVID-19) IgM/IgG anti-severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antibody test.Serologic assays have become increasingly available for surveillance through the Food and Drug Administration emergency use authorization in the ongoing COVID-19 global pandemic. However, widespread application of serologic assays has been curbed by reports of faulty or inaccurate tests. Therefore, rapid COVID-19 antibody tests need to be thoroughly validated prior to their implementation. METHODS: The Easy Check device was analytically evaluated and its performance was compared with the Roche Elecsys anti-SARS-CoV-2 antibody assay. The test was further characterized for cross-reactivity using sera obtained from patients infected by other viruses. Clinical performance was analyzed with polymerase chain reaction-confirmed samples and a 2015 prepandemic reference sample set. RESULTS: The Easy Check device showed excellent analytical performance and compares well with the Roche Elecsys antibody assay, with an overall concordance of 98.6%. Clinical performance showed a sensitivity of 96.6%, a specificity of 98.2%, and an overall accuracy of 98.1%. CONCLUSIONS: The Easy Check device is a simple, reliable, and rapid test for detection of SARS-CoV-2 seropositivity, and its performance compares favorably against the automated Roche Elecsys antibody assay.

FIGURES

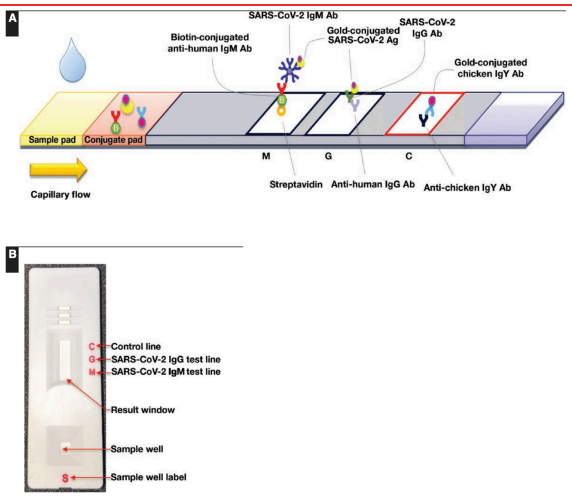

Figure 1. Design schematic of the Truvian Easy Check COVID-19 IgM/IgG test device. A, The device is an implementation of immunochromatography that relies on capillary flow of sample across immobilized anti-human IgM, anti-human IgG, and control (anti-chicken IgY) antibodies (Ab). Detection is achieved by secondary binding via gold-conjugated antigens (Ag). B, Macro design of the test device. Figure used with permission from Truvian

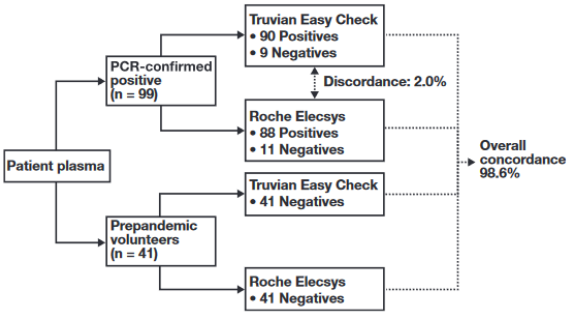

Figure 3. Comparison of the Truvian Easy Check and Roche Elecsys anti-SARS-CoV-2 antibody assays. A total of 140 patient samples (99 COVID-19-positive, PCR-confirmed samples and 41 prepandemic volunteer samples) were tested using both the Easy Check and Roche Elecsys assays, yielding an overall concordance rate of 98.6% between the two serologic tests. Among the 99 COVID-19-positive, PCR-confirmed samples, there were 2 samples for which the Easy Check assay resulted as positive, whereas the Roche Elecsys assay resulted as negative.

Table 1

Cross-Reactivity of the Truvian Easy Check Test Against Other Common Viruses[a]

Sera Sample	Truvian IgM Reactivity		Truvian IgG Reactivity	
	Positive	Negative	Positive	Negative
OC43 CV[c]	0	8	0	8
229E CV[c]	0	2	0	2
OC43 CV + 229E CV[c]	0	1	0	1
NL63 CV[c]	0	7	0	7
HKU1 CV[c]	0	4	0	4
HKU1 CV + RSV[c]	0	1	0	1
Rhinovirus[c]	0	2	0	2
HepBS[d]	0	5	0	5
HCV[d]	0	5	0	5
HIV[d]	0	5	0	5
Total	0	40	0	40

COI, cutoff index ; CV, coronavirus; HCV, hepatitis C virus; HepBS, hepatitis B surface antigen; PCR, polymerase chain reaction; RSV, respiratory syncytial virus.

[a]Zero cross-reactivity was observed with 40 samples from patients infected with hepatitis B, hepatitis C, HIV, or a common, non-SARS-CoV-2 respiratory virus and confirmed by either antibody or PCR positivity. OC43, 229E, NL63, and HKU1 are common strains of other CVs.

[b]Negative result is defined as both individual and mean COIs < 1.0.

[c]PCR-positive.

[d]Antibody-positive.

SLEEP PROBLEMS DURING COVID-19 PANDEMIC BY POPULATION: A SYSTEMATIC REVIEW AND META-ANALYSIS

Jahrami H, BaHammam AS, Bragazzi NL, Saif Z, Faris M, Vitiello MV.. J Clin Sleep Med. 2020 Oct 27. doi: 10.5664/jcsm.8930. Online ahead of print.

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

BLUF

Mental health experts performed a systematic review of 44 studies between November 1, 2019 and July 5, 2020 assessing prevalence of sleep problems during the pandemic (Figure 1). Meta-analysis included 54,231 participants across 13 countries and found pooled prevalence of sleep problems was 35.7%, with COVID-19 patients being most affected (74.8%) followed by healthcare workers (36%) and the general public (32.3%)(Table 2, Figure 2). The authors suggest sleep problems are common during the pandemic, particularly among COVID-19 patients, and encourage implementing strategies to mitigate adverse effects in these populations.

ABSTRACT

STUDY OBJECTIVES: No systematic review or meta-analysis has yet been conducted to examine the impact of the pandemic on the prevalence of sleep problems among the general population, healthcare workers, or COVID-19 patients. Therefore, this systematic review was conducted to assess the impact and prevalence of sleep problems among those categories. METHODS: APA PsycINFO; Cochrane; Cumulative Index to Nursing and Allied Health Literature (CINAHL); EBSCOhost; EMBASE; Google Scholar; MEDLINE; ProQuest Medical; ScienceDirect; Scopus; and Web of Science from 01 November 2019 to 05 July 2020. Additionally, four preprints servers (medRxiv.org; Preprints.org; psyarxiv.com; arXiv.org; biorxiv.org) were also searched for papers accepted after peer-review but not yet published and indexed. There was no language restriction. The random-effect models meta-analysis model were used with the DerSimonian and Laird methodology. RESULTS: Forty-four papers, involving a total of 54,231 participants from 13 countries, were judged relevant and contributed to the systematic review and meta-analysis of sleep problems during COVID-19. The global pooled prevalence rate of sleep problems among all populations was 35.7% [95%CI 29.4-42.4%]. COVID-19 patients appeared to be the most affected group, with a pooled rate of 74.8% [95%CI 28.7-95.6%]. Healthcare workers and the general population had comparative rates of sleep problems with rates of 36.0% [95%CI 21.1-54.2%] and 32.3% [95%CI 25.3-40.2%], respectively. CONCLUSIONS: The prevalence of sleep problems during the COVID-19 pandemic is high and approximately affect 40% of people from the general and healthcare populations. COVID-19 active patients appeared to have higher prevalence rates of sleep problems.

FIGURES

Component	K	N	Random-Effects Meta-Analysis		Heterogeneity			Moderators		
			Pooled Results [95% CI]	Forest Plot	I^2	τ^2	Q	Age	Sex (%Male)	Publication Bias
Sleep problems (all populations, all measures*)	40	53489	35.7% [29.4%-42.4%]		99.5%	0.8	7477 (39)	NS	NS	Kendall's P=0.70, Egger's P=0.72
Sleep problems (general population, all measures)	26	46751	32.3% [25.3%-40.2%]		99.5%	0.8	6137 (25)	NS	NS	Kendall's P=0.80; Egger's P=0.90
Sleep problems (healthcare workers, all measures)	11	4854	36.0% [21.1%-54.2%]		99%	1.6	1043 (10)	NS	NS	Kendall's P=0.70; Egger's P=0.80
Sleep problems (COVID-19 patients, all measures)	3	932	74.8% [28.7%-95.6%]		96%	2.7	50 (2)	P=0.001	P=0.001	Kendall's P=0.60; Egger's P=0.80
Sleep problems (all populations, PSQI only)	18	20570	39.6% [29.6%-50.6%]		99.5%	0.8	2933 (17)	NS	NS	Kendall's P=0.80; Egger's P=0.42
Sleep problems (general population, PSQI only)	9	16516	37.9% [25.2%-52.4%]		99.6%	0.8	2018 (8)	P=0.001	NS	Kendall's P=0.80; Egger's P=0.42
Sleep problems (healthcare workers, PSQI only)	8	4854	39.7% [21.2%-61.6%]		97%	1.6	853 (7)	NS	NS	Kendall's P=1.0; Egger's P=0.96
Sleep problems (general population, SD)	6	8538	25.2% [9.3%-52.6%]		99.7%	2.2	1774 (5)	NS	NS	Kendall's P=0.85; Egger's P=0.96
Sleep problems (general population, ISI)	3	7220	29.7% [11.9%-56.9%]		99.6%	1.1	531 (2)	NS	NS	Kendall's P=0.60; Egger's P=0.71
Mean sleep quality (all populations, PSQI)	15	9230	7.1 [6.3-8.0]		99.1%	2.4	1716 (14)	NS	NS	Kendall's P=0.08; Egger's P=0.045
Mean sleep quality (general population, PSQI)	4	4722	6.0 [5.3-6.8]		98%	0.6	182 (3)	NS	P=0.04	Kendall's P=1.0; Egger's P=0.47
Mean sleep quality (healthcare workers, PSQI)	9	4483	7.7 [6.1-9.2]		99%	5.4	1358 (9)	NS	NS	Kendall's P=0.14; Egger's P=0.13
Mean (C1) subjective sleep quality (healthcare workers, PSQI)	6	2897	1.3 [0.3-2.3]	-	99.8%	1.5	1219 (5)	NS	NS	Kendall's P=0.34; Egger's P=0.02
Mean (C2) sleep latency (healthcare workers, PSQI)			1.5 [0.9-2.2]	-	99.8%	0.7	2662 (5)	NS	NS	Kendall's P=0.57; Egger's P=0.38
Mean (C3) sleep duration (healthcare workers, PSQI)			0.9 [-0.2-2.0]	-	99.9%	2.0	17713 (5)	NS	NS	Kendall's P=0.34; Egger's P=0.34
Mean (C4) habitual sleep efficiency (healthcare workers, PSQI)			0.9 [-0.1-1.9]	-	99.9%	1.5	13197 (5)	NS	NS	Kendall's P=0.85; Egger's P=0.40
Mean (C5) sleep disturbances (healthcare workers, PSQI)			1.4 [0.4-3.0]	-	99.9%	1.0	9829 (5)	NS	NS	Kendall's P=0.60; Egger's P=0.20
Mean (C6) use of sleep-promoting medications (healthcare workers, PSQI)			0.7 [-0.4-1.8]	-	99.9%	1.2	14010 (5)	NS	NS	Kendall's P=0.85; Egger's P=0.15
Mean (C7) daytime dysfunction (healthcare workers, PSQI)			1.0 [-0.1-2.0]	-	99.9%	2.0	17641 (5)	NS	NS	Kendall's P=0.85; Egger's P=0.72

K = number of studies, N = number of participants, I^2 = statistic describing the percentage of variation across studies due to heterogeneity rather than chance, τ-squared = the extent of variation among the effects observed in different studies (between-study variance) in a random-effects meta-analysis, Cochran's Q = calculated as the weighted sum of squared differences between individual study effects and the pooled effect across studies, with the weights being those used in the pooling method, CI = confidence interval, Moderators = a method of moments estimator for random effect multivariate meta-analysis. Publication bias was not observed in Funnel plot. *Measures used to estimate sleep problems were: AIS = Athens Insomnia Scale; GAD-7 = General Anxiety Disorder-7; HADS = Hospital Anxiety and Depression Scale; ISI = Insomnia Severity Index; PCL5 = Posttraumatic Stress Disorder Checklist For DSM-5; PHQ-9 = Patient Health Questionnaire-9; PSQ = Psychological Stress Questionnaire; PSQI = Pittsburgh Sleep Quality Index RASS = Richmond Agitation Sedation Scale; RD = Researcher-developed; SDS = Self-Rating Depression Scale; and SNS = Subjective Neurological Symptoms. NS = not significant.

Table 2. Meta-analysis of sleep problems during COVID-19: by population and by research measure.

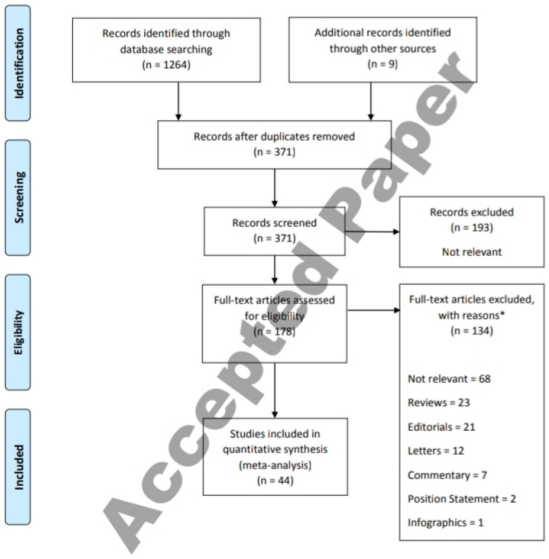

Figure 1. PRISMA flow diagram of study inclusion.

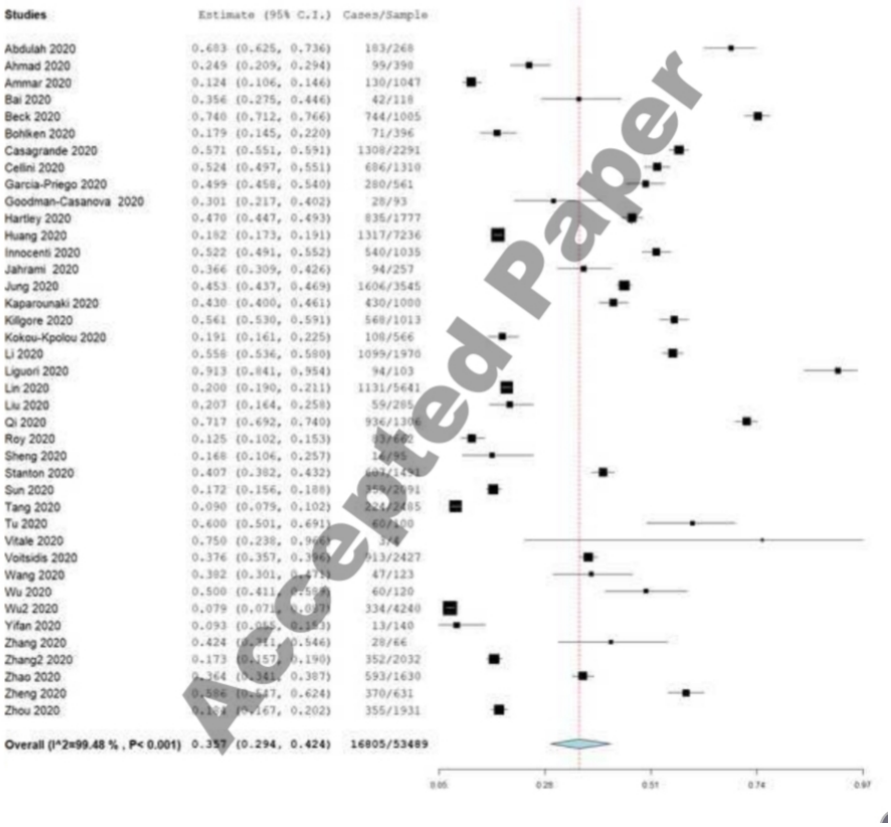

Figure 2. Meta-analysis of the prevalence of sleep problems (all populations, all measures). Cases refer to persons with positive sleep problem.

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