The Daily COVID-19 Literature Surveillance Summary

September 28, 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

Epidemiology

- Cardiologists and biostatisticians from Denmark conducted a cohort study of 4002 patients to identify severity outcomes between COVID-19 patients (n=688) who were prescribed ibuprofen (42; 15.9%) versus those who were not (646; 17.3%) in a 30-day composite endpoint. The study concluded that there were no significant associations or adverse effects between patients prescribed ibuprofen and COVID-19 severity (p=0.70). Due to several confounding factors, the authors suggest that more studies need to be performed to evaluate this association.

Transmission & Prevention

- Allergy and Immunology experts from México conducted a prospective observational trial of 255 individuals recently vaccinated with mumps, measles, and rubella (MMR) for symptoms of COVID-19 infection and found that 24 eventually tested positive for COVID-19, and 12 were designated as highly probable. Of these patients, all exhibited mild disease leading the authors to suggest that vaccination with a non-SARs-CoV-2 vaccine could potentially minimize the severity of COVID-19 infection.

- A literature review by hematology experts associated with the Australian Red Cross found that although there are no reported instances of transfusion transmission of SARS-CoV-2, there is still potential for transfusion transmission since the virus exists in the blood in low levels. The authors recommend mitigation protocols against the possible risk of COVID-19's transfusion transmissibility at donation centers, such as donor deferral policies based on travel, diseased status, or potential risk of exposure.

- Investigators of medicinal chemistry and nutrition review the antiviral and cytokine-inhibitory mechanisms of lauric acid, enhanced phagocytic activity in high medium-chain triglyceride (MCT) diets, and suppression of several pro-inflammatory cytokines with intermittent fasting. They propose a ketogenic diet with intermittent fasting and supplemental MCT as a potential SARS-CoV-2 prophylaxis or adjuvant therapy for those with infection.

R&D: Diagnosis & Treatments

- Infectious disease experts and immunologists examine the sensitivity and specificity of anti-SARS-CoV-2 antibody tests using five ELISAs, seven colloidal gold lateral flow immunoassays, and ten commercial serological assays on 110 serum samples collected from 87 individuals with known COVID-19 infections and found that tests varied from 60.9% to 87.3% in sensitivity and 82% to 100% in specificity, but it was clear that all tests achieved the highest performance on samples taken at or greater than 20 days after onset of symptoms.

TABLE OF CONTENTS

DISCLAIMER **2**

NOW LIVE! 2

LEVEL OF EVIDENCE **3**

EXECUTIVE SUMMARY **4**

TABLE OF CONTENTS **5**

CLIMATE **6**

Environmental and psychological variables influencing reactions to the COVID-19 outbreak 6

EPIDEMIOLOGY **8**

SYMPTOMS AND CLINICAL PRESENTATION 8

Adults *8*

Association Between Prescribed Ibuprofen and Severe COVID-19 Infection: A Nationwide Register-Based Cohort Study 8

UNDERSTANDING THE PATHOLOGY **10**

Severe colon ischemia in patients with severe coronavirus-19 (COVID-19) 10

IN VITRO 12

Targeting multiple epitopes on the spike protein: a new hope for COVID-19 antibody therapy 12

TRANSMISSION & PREVENTION **13**

Thirty-six COVID-19 cases preventively vaccinated with mumps-measles-rubella vaccine: all mild course 13

Severe acute respiratory syndrome coronavirus-2: implications for blood safety and sufficiency 13

DEVELOPMENTS IN TRANSMISSION & PREVENTION 14

Switching Host Metabolism as an Approach to Dampen SARS-CoV-2 Infection 14

PREVENTION IN THE HOSPITAL 15

Occupational Heat Stress and Practical Cooling Solutions for Healthcare and Industry Workers During the COVID-19 Pandemic 15

MANAGEMENT **16**

The need for improved discharge criteria for hospitalised patients with COVID-19-implications for patients in long term care facilities 16

ADJUSTING PRACTICE DURING COVID-19 ..... **17**

PSYCHIATRY 17

Psychiatry and COVID-19 17

R&D: DIAGNOSIS & TREATMENTS **18**

Is naso-pharyngeal swab always safe for SARS-CoV-2 testing? An unusual, accidental foreign body swallowing 18

CURRENT DIAGNOSTICS 18

Comparative assessment of multiple COVID-19 serological technologies supports continued evaluation of point-of-care lateral flow assays in hospital and community healthcare settings 18

ACKNOWLEDGEMENTS **22**

ENVIRONMENTAL AND PSYCHOLOGICAL VARIABLES INFLUENCING REACTIONS TO THE COVID-19 OUTBREAK

Rubaltelli E, Tedaldi E, Orabona N, Scrimin S.. Br J Health Psychol. 2020 Sep 19. doi: 10.1111/bjhp.12473. Online ahead of print.
Level of Evidence: 3 - Non-randomized controlled cohort/follow-up study

BLUF

Developmental and Social Psychologists from University of Padova, Italy conducted a pair of temporally isolated cross-sectional survey-based studies in Italy from 24 February to 29 February 2020 (time of first COVID-19 deaths in Italy) and from 10 March to 20 March 2020 (after Italy's government implemented a full lockdown) to study media coverage and public perception of COVID-19 protective behaviors (Summary). While this study is likely not representative of the population as a whole due to selection bias (Table 1), the authors suggest that state action and media coverage likely affect public anxiety and behaviors related to preventing spread of the virus.

SUMMARY

The study helped to determine the impact that media outlets, risk perception, state anxiety, and emotional regulation played in encouraging individuals to undertake protective behaviors to reduce the spread of SARS-CoV-2. Particular findings include:

1) the state anxiety was higher at the second time point,
2) the risk perception positively correlated with the number of protective behaviors taken at both time points,
3) the media exposure and the rate of infected cases per million Italian citizens correlated with risk perception in the second time point (Table 2 and Table 3).

ABSTRACT

OBJECTIVE: The COVID-19 outbreak in Italy caused a major health emergency and high uncertainty. We studied how media outlets, risk perception, state anxiety, and emotion regulation impacted peoples' reactions and undertaking of protective behaviours aimed at reducing the spread of the virus. DESIGN: Data were collected in two cross-sectional waves (N = 992 at T1; N = 1031 at T2): at the beginning of the outbreak and once the national lockdown was imposed. METHODS: Participants completed online surveys on their perception of the COVID-19 outbreak. Moreover, they were asked to self-report on their emotion regulation, state anxiety, and protective behaviours. RESULTS: Media exposure and wave predicted risk perception. An interaction between wave, risk perception, and emotion regulation predicted the number of protective behaviours people undertook. Specifically, in the second wave, the number of protective behaviours was predicted by risk perception only among those who were ineffective at regulating emotions. Instead, effective regulators undertook the same number of behaviours regardless of their level of risk perception. In the second wave, we also found that the risk perception by emotion interaction predicting protective behaviours was mediated by state anxiety. CONCLUSIONS: The present study provides important insights on how people experienced the early stages of the outbreak. This information could prove valuable in the coming months to understand who might have been more impacted by the stress caused by the COVID-19 pandemic and the consequent restrictive measures.

FIGURES

	Wave 1			Wave 2					
	M	*SD*	Range	*M*	*SD*	Range	*t*	*d*	95% C.I.
Emotion reg.	4.91	.73	2.43–6.80	4.88	.75	2.13–6.83	−.85	.04	[−0.04, 0.09]
Risk perception	41.94	26.88	0–100	66.33	23.66	0–100	−21.69***	.96	[−26.60, −22.19]
Media exposure	2.59	1.49	0–8	3.42	1.58	0–8	−12.13***	.54	[−0.96, −0.70]
Behaviours	1.40	1.01	0–5	2.65	.98	0–5	−28.39***	1.26	[−1.34, −1.17]
Cases per million	4.41	2.09	2.18–14.69	211.93	88.01	121.98–590.67	−74.24***	3.33	[−.212.99, −202.03]

Note. *$p < .05$; **$p < .01$; ***$p < .001$.

Table 2. Descriptive statistics and differences between wave 1 and wave 2 for the main study variables

	Wave 2				
	Emotion reg.	Risk perception	Media exposure	Behaviours	Cases per million
Wave 1					
Emotion reg.	---	−.04	.02	.08**	−.03
Risk perception	−.01	---	.08**	.18***	.13***
Media exposure	.03	.05	---	.15***	.00
Behaviours	.00	.20***	.14***	---	.11***
Cases per million	.02	.05	−.01	−.03	---

Note. *$p < .05$; **$p < .01$; ***$p < .001$.

Table 3. Correlations between the main study variables split by wave (wave 1 in the bottom left side and wave 2 in the top right side of the correlation matrix)

Table 1. Characteristics of the participants and response to main survey items in the two waves of the study[a]

Characteristics	Wave 1 (*N* = 992)	Wave 2 (*N* = 1031)	Difference
Age, year (range)	30.95 (18–72)	30.63 (18–75)	0.566
Gender			
Female, no. (%)	671 (67.64%)	701 (67.99%)	0.148
Highest level of education			
Primary school, no. (%)	0 (0%)	1 (0.09%)	0.679
Middle school, no. (%)	36 (3.63%)	50 (4.85%)	
High school, no. (%)	427 (43.04%)	460 (44.62%)	
Bachelor's degree, no. (%)	333 (33.57%)	303 (29.39%)	
Master's degree, no. (%)	170 (17.14%)	187 (18.14%)	
Specialization/Doctorate, no. (%)	26 (2.62%)	30 (2.91%)	
Income			
>10,000 (%)	75 (7.56%)	65 (6.30%)	0.043
10,000–19,999 (%)	180 (18.15%)	190 (18.43%)	
20,000–29,999 (%)	12 (1.21%)	9 (0.87%)	
30,000–39,999 (%)	239 (24.09%)	260 (25.22%)	
40,000–49,999 (%)	144 (14.52%)	153 (14.84%)	
50,000–59,999 (%)	83 (8.37%)	93 (9.02%)	
60,000–69,999 (%)	49 (4.94%)	50 (4.85%)	
70,000–79,999 (%)	29 (2.92%)	29 (2.81%)	
80,000–89,999 (%)	28 (2.82%)	27 (2.62%)	
90,000–99,999 (%)	14 (1.41%)	17 (1.65%)	
100,000–109,999 (%)	4 (0.40%)	3 (0.29%)	
110,000–119,999 (%)	10 (1.01%)	7 (0.68%)	
120,000–129,999 (%)	3 (0.30%)	3 (0.29%)	
130,000–139,999 (%)	1 (0.10%)	3 (0.29%)	
140000–149,999 (%)	2 (0.20%)	0 (0%)	
>150,000 (%)	3 (0.30 %)	1 (0.10%)	
Prefer not to say (%)	116 (11.70%)	121 (11.74%)	
Political orientation			
Extreme left wing, no. (%)	23 (2.32%)	26 (2.52%)	2.473*
Left wing, no. (%)	273 (27.52%)	285 (27.64%)	
Centre-left wing, no. (%)	273 (27.52%)	335 (32.50%)	
Centre wing, no. (%)	151 (15.22%)	152 (14.74%)	
Centre-right wing, no. (%)	144 (14.52%)	142 (13.77%)	
Right wing, no. (%)	117 (11.79%)	85 (8.25%)	
Extreme right wing, no. (%)	11 (1.11%)	6 (0.58%)	
Religiosity, 7-points scale (SD)	2.927 (1.78)	2.944 (1.824)	0.204
Trust authorities, 1–7 scale (SD)	3.957 (1.415)	4.250 (1.357)	4.765***
Symptoms reported in the last 48 hours			
Coughing, no. (%)	205 (20.67%)	176 (17.07%)	4.273*
Runny nose, no. (%)	313 (31.55%)	283 (27.45%)	4.096*
Fever, no. (%)	32 (3.23%)	17 (1.65%)	5.319*
General malaise, no. (%)	143 (14.42%)	123 (11.93%)	2.734
Sore throat, no. (%)	122 (12.30%)	123 (11.93%)	0.064
Headache, no. (%)	290 (29.23%)	257 (24.93%)	4.752*

ADULTS

ASSOCIATION BETWEEN PRESCRIBED IBUPROFEN AND SEVERE COVID-19 INFECTION: A NATIONWIDE REGISTER-BASED COHORT STUDY

Kragholm K, Gerds TA, Fosbøl E, Porsborg Andersen M, Phelps M, Butt JH, Østergaard L, Bang CN, Pallisgaard J, Gislason G, Schou M, Køber L, Torp-Pedersen C.. Clin Transl Sci. 2020 Sep 24. doi: 10.1111/cts.12904. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

Cardiologists and biostatisticians from Copenhagen, Denmark conducted a cohort study using patient data (n=4002) from the Danish National Patient Registry between February 2020 and May 16, 2020 to identify severity outcomes between COVID-19 patients (n=688) who were prescribed ibuprofen (42; 15.9%) versus those who were not (646; 17.3%) in a 30-day composite endpoint (Table 3). The study concluded that there were no significant associations or adverse effects between patients prescribed ibuprofen and COVID-19 severity (p=0.70; Table 4). Due to several confounding factors (ie., limited data on the medications used during hospitalization and whether the prescribed ibuprofen was continued or discontinued), the authors suggest that more studies need to be performed to evaluate this association.

ABSTRACT

Recommendations regarding ibuprofen use in relation to coronavirus disease 2019 (COVID-19) have been conflicting. We examined risk of severe COVID-19 between ibuprofen-prescribed and non-ibuprofen COVID-19 patients in a nationwide register-based study of COVID-19 patients in Denmark between end of February 2020 and May 16, 2020. Patients with heart failure (n=208), <30 years (n=575), and prescribed other non-steroidal anti-inflammatory drugs (n=57) were excluded. Patients with ibuprofen prescription claims between January 1, 2020, and before COVID-19 diagnosis or April 30, 2020 (last available prescription) were compared to patients without ibuprofen prescription claims. Outcome was a 30-day composite of severe COVID-19 diagnosis with acute respiratory syndrome, intensive care unit admission, or death. Absolute risks and average risk ratios comparing outcome for ibuprofen versus non-ibuprofen patients standardized to the age, sex, and comorbidity distribution of all patients were derived from multivariable Cox regression. Among 4,002 patients, 264 (6.6%) had ibuprofen prescription claims before COVID-19. Age, sex and comorbidities were comparable between the two study groups. Standardized absolute risks of the composite outcome for ibuprofen-prescribed versus non-ibuprofen patients were 16.3% [95% CI 12.1-20.6] versus 17.0% [95% CI 16.0-18.1], P=0.74. The standardized average risk ratio for ibuprofen-prescribed versus non-ibuprofen patients was 0.96 [95% CI 0.72-1.23]. Standardized absolute risks of the composite outcome for patients with ibuprofen prescription claims >14 days before COVID-19 versus <=14 days of COVID-19 were 17.1% [95% CI 12.3-22.0] versus 14.3% [95% CI 7.1-23.1]. In conclusion, in this nationwide study, there was no significant association between ibuprofen prescription claims and severe COVID-19.

FIGURES

Table 3. Absolute risks and average risk ratio of the 30-day composite outcome for COVID-19 patients with versus without recent ibuprofen prescription claims prior to COVID-19

Ibuprofen group	Unadjusted absolute risk [95% CI]	Age- and sex-adjusted absolute risk [95% CI]	Fully adjusted absolute risk [95% CI]	Standardized average risk ratio [95% CI]
No ibuprofen prescription claim	17.3% [16.1-18.6]	17.0% [15.9-18.0]	17.0% [16.0-18.1]	Ref
Ibuprofen prescription claim	16.0% [11.8-20.5]	16.6% [12.7-21.1]	16.3% [12.1-20.6]	0.96 [0.72-1.23]

The 30-day composite outcome consisted of severe COVID-19 diagnosis, intensive care unit admission, or death. The average risk ratio was standardized to the age, sex, and comorbidity distribution of all patients. Abbreviations: COVID-19, coronavirus 2019; CI, confidence interval; Ref, reference.

Table 4. Absolute risks and average risk ratio of the 30-day composite endpoint for patients with ibuprofen prescription claims >14 days versus ≤14 days before COVID-19 diagnosis

Ibuprofen group	Unadjusted absolute risk [95% CI]	Age- and sex-adjusted absolute risk [95% CI]	Fully adjusted absolute risk [95% CI]	Standardized average risk ratio [95% CI]
ibuprofen prescription claim >14days before COVID-19	16.0% [10.9-21.2]	16.0% [11.7-20.9]	16.0% [11.9-20.9]	Ref
Ibuprofen prescription claim ≤14days before COVID-19	15.5% [7.0-25.0]	14.6% [7.7-22.6]	14.4% [6.7-23.0]	0.90 [0.39-1.57]

The composite outcome consisted of severe COVID-19 diagnosis, intensive care unit admission, or death. The average risk ratio was standardized to the age, sex, and comorbidity distribution of all patients. Abbreviations: COVID-19, coronavirus disease 2019; CI, confidence interval; Ref, reference.

SEVERE COLON ISCHEMIA IN PATIENTS WITH SEVERE CORONAVIRUS-19 (COVID-19)

Almeida Vargas A, Valentí V, Sánchez Justicia C, Martínez Regueira F, Martí Cruchaga P, Luján Colás J, Aliseda Jover D, Esteban Gordillo S, Cienfuegos JA, Rotellar Sastre F.. Rev Esp Enferm Dig. 2020 Sep 21;112. doi: 10.17235/reed.2020.7329/2020. Online ahead of print.
Level of Evidence: Other - Case Report

BLUF

Physicians from the Universidad de Navarra, the Institute of Health Research of Navarra (IdisNA) and Instituto de Salud Carlos III describe 3 patients presenting with colonic ischemia that was thought to be associated with a SARS-CoV-2-induced hypercoaguable state and disseminated intravascular coagulation (Table 1). As the findings of these cases (summarized below) were limited in that intestinal pathologic analysis was unavailable, the authors propose that further investigation on SARS-CoV-2 pathogenesis and its impact on the gastrointestinal tract are needed.

SUMMARY

Details regarding the 3 cases are listed below:

Case 1: A 76-year-old male with hypertension, presenting with SARS-CoV-2 pneumonia, required mechanical ventilation and was treated with lopinavir/ritonavir, hydroxychloroquine, corticosteroids, ceftriaxone and prophylactic anticoagulation via low molecular weight heparin (LMWH). Following multiple episodes of hematochezia in ICU, he was diagnosed with necrotizing pancreatitis, signs of colonic ischemia (Figure 1), high D-dimer and expired 24 hours later.

Case 2: A 68-year-old male with hypertension and diabetes mellitus 2 (DM2), presenting with bilateral SARS-CoV-2 pneumonia, required mechanical ventilation and was treated with lopinavir/ritonavir, hydroxychloroquine, Ciprofloxacin, Azithromycin and prophylactic anticoagulation via low molecular weight heparin (LMWH). The patient died 12 days post-op following laparotomy for fecaloid peritonitis, gangrenous perforation of the cecum and diffuse ischemia of the bowel and colon.

Case 3: A 56-year-old male with hypertension and diabetes mellitus 2 (DM2), presenting with SARS-CoV-2 pneumonia with subsequent respiratory failure and severe systemic inflammatory response syndrome (SIRS), required mechanical ventilation and was treated with lopinavir/ritonavir, hydroxychloroquine, Levofloxacin, corticosteroids and prophylactic anticoagulation via low molecular weight heparin (LMWH). Following a diagnosis of pneumoperitoneum and colonic pneumatosis (Figure 2), the patient died 24 hours after diagnosis.

ABSTRACT

COVID-19 is associated with severe coagulopathy. We present three cases of colonic ischemia that can be attributed to the hypercoagulable state related with SARS-CoV2 and disseminated intravascular coagulation. Three males aged 76, 68 and 56 with respiratory distress presented episodes of rectal bleeding, abdominal distension and signs of peritoneal irritation. Endoscopy (case 1) and computed tomography angiography revealed colonic ischemia. One patient (case 2) in which a computed tomography (CT) scan showed perforation of the gangrenous cecum underwent surgery. D-dimer levels were markedly increased (2,170, 2,100 and 7,360 ng/ml) in all three patients. All three patients died shortly after diagnosis.

Gender		Male	Male	Male
Age (years)		76	68	56
Comorbidities		Hypertension	Hypertension Type II diabetes Dyslipidemia	Hypertension Type II diabetes COPD Dyslipidemia Obesity (class I)
Days since disease onset		21	13	21
Intensive Care Unit (days)		17	12	21
Days to diagnosis of MI		15	11	19
Complications of Covid-19		Multifocal pneumonia Acute kidney injury (AKIN II) Hematochezia	Bilateral pneumonia *Staphylococcus aureus* pneumonia Paralytic ileus	Multifocal bilateral pneumonia Acute kidney injury (AKIN II) Necrotizing pulmonary Aspergillosis Paralytic ileus Pulmonary embolism
Acute gastro-intestinal symptom		Rectal bleeding	Acute abdomen	Acute abdomen
Vital signs in acute episode				
Blood pressure (mm Hg)		99/41	92/32	115/62
Heart rate (beats per min)		62	60	119
Temperature (°C)		36.9	38.6	38.4
Additional diagnostic tests				
Endoscopy		Ischemic colitis	Pneumoperitoneum	Pneumoperitoneum
CT scan		Ischemic colitis Necrotizing pancreatitis	Bowel perforation Pneumatosis intestinalis	Bowel perforation Distension of small bowel and right colon Pneumatosis intestinalis Segmental pulmonary embolism
Laboratory results in acute episode	Reference ranges			
Hemoglobin (g/dl)	*14-17*	9.4	11.4	10.6
White blood cell count (cells x 10^9/l)	*4.8-10.8*	11	15.1	13
Lymphocyte (cells x 10^9/l)	*1.2-4*	0.45	0.42	0.54
Platelets (cells x 10^9/l)	*150-450*	109	269	325
C-reactive protein (mg/dl)	*0.0-0.50*	0.38	31.6	0.1
Procalcitonin (ng/dl)	*0.0-0.50*	0.07	0.9	0.24
D-dimer (ng/ml)	*150-500*	2,170	2,100	7,360
Fibrinogen (mg/dl)	*150-350*	224	886	-
Ferritin(ng/ml)	*30-400*	1,059	1,842	3,665
Lactic acid (mmol/l)	*0.50-2.00*	1.48	1.8	5.69
Lactate deshydrogensase (U/l)	*135-225*	384	348	649
Alanine aminotransferase (U/l)	*0-41*	37	72	108
Aspartate aminotransferase (U/l)	*1-40*	77	24	135
Alkaline phosphatase (U/l)	*40-129*	120	62	57
Gamma glutamyltransferase (U/l)	*0-60*	486	40	136
Ferritin (ng/ml)		1,059		

Table 1: Baseline characteristics and laboratory findings of cases 1, 2 and 3

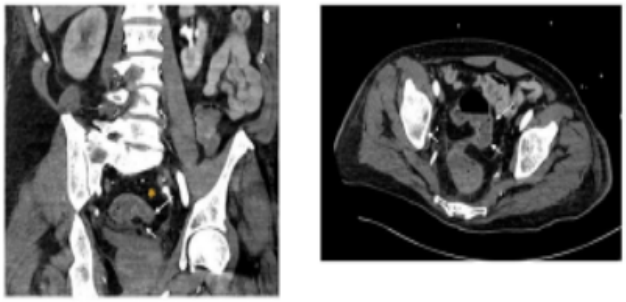

Figure 1. Case 1. Coronal and axial CT of the pelvis with IV contrast showing wall thickening of the sigma (long arrow), mesenteric stranding (*) and ascites (short arrow)

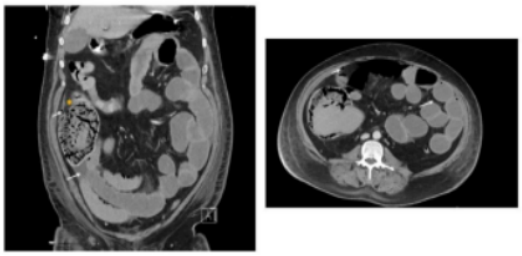

Figure 2. Case 3. Coronal (A) and axial (B) CT of the abdomen with IV contrast showing small bowel distension and pneumatosis intestinalis (arrow).

TARGETING MULTIPLE EPITOPES ON THE SPIKE PROTEIN: A NEW HOPE FOR COVID-19 ANTIBODY THERAPY

Sun Y, Kobe B, Qi J.. Signal Transduct Target Ther. 2020 Sep 19;5(1):208. doi: 10.1038/s41392-020-00320-6.
Level of Evidence: 5 - Review / Literature Review

BLUF

Investigators from the Chinese Academy of Sciences and University of Queensland (Brisbane) describe Liu et al., 2020's study that identified potential neutralizing monoclonal antibodies (mAbs) to different epitopes on SARS-CoV-2 spike protein. Specifically, Liu et al., 2020 identified the epitope sites of these mAbs to to the N terminal domain (NTD) and the receptor binding domain (RBD) on the spike-trimer and found particularly strong neutralizing mAbs against a "patch" on the N terminal domain (NTD). Additionally, they used electron microscopy to model the binding of different mAbs to epitope sites on the spike-trimer NTD and RBD (Figure 1). These neutralizing mAbs may assist in developing clinical therapies, specifically "mAb cocktail therapies," for SARS-CoV-2 infection.

FIGURES

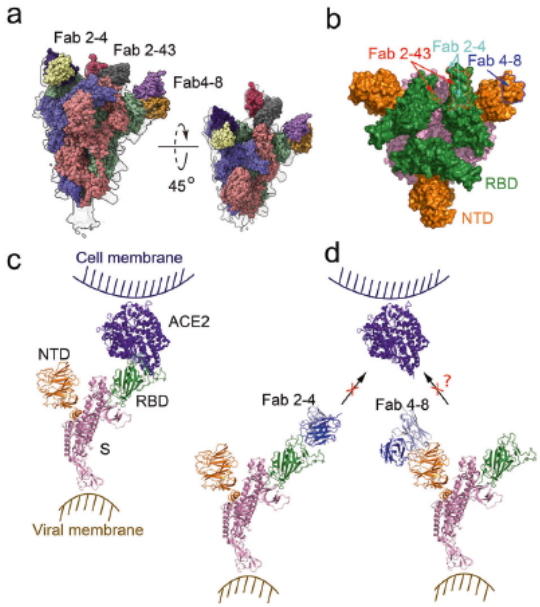

Fig. 1 Neutralizing mAbs targeting different epitopes on SARS-CoV-2 S inhibit virus infection. a A structural model for SARS-CoV-2 S in complex mAbs Fab 2-4, Fab 4-8, and Fab 2-43. b Target regions of Fab 2-4, Fab 4-8, and Fab 2-43. c SARS-CoV-2 S (for clarification, only one S monomer is shown) binds to ACE2 receptor. d The RBDdirected Fab 2-4 inhibits virus infection via blocking SARS-CoV-2 S binding to ACE2 receptor; the NTD-directed Fab 4-8 inhibits virus infection via unknown mechanisms

TRANSMISSION & PREVENTION

THIRTY-SIX COVID-19 CASES PREVENTIVELY VACCINATED WITH MUMPS-MEASLES-RUBELLA VACCINE: ALL MILD COURSE

Larenas-Linnemann DE, Rodríguez-Monroy F.. Allergy. 2020 Sep 7. doi: 10.1111/all.14584. Online ahead of print.
Level of Evidence: 3 - Non-randomized controlled cohort/follow-up study

BLUF

Allergy and Immunology experts from Médica Sur, México conducted a prospective observational trial of a cohort of 255 individuals recently vaccinated with mumps, measles, and rubella (MMR) for symptoms of COVID-19 infection. Of these 255 participants, 24 eventually tested positive for COVID-19 and 12 were designated as highly probable. Of these patients, all exhibited mild disease leading the authors to suggest that vaccination with a non-SARs-CoV-2 vaccine could potentially minimize the severity of COVID-19 infection.

SUMMARY

The researchers propose that a non-SARs-CoV-2 vaccine could potentially minimize the severity of COVID-19 infection due to trained immunity: They posit that the MMR vaccine primes the immune system and subsequent exposure to a non-related pathogen (here COVID-19) exerts a more expeditious immune response due to hypervigilance of monocytes, NK cells, Th1 and Th17 cells post-initial vaccination.

Additional discussion points include:

- Similar studies using BCG instead of MMR are ongoing
- Researchers believe MMR is safer due to BCG resulting in elevated IL-6 levels

SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS-2: IMPLICATIONS FOR BLOOD SAFETY AND SUFFICIENCY

Kiely P, Hoad VC, Seed CR, Gosbell IB.. Vox Sang. 2020 Sep 23. doi: 10.1111/vox.13009. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

A literature review conducted by hematology experts associated with the Australian Red Cross assesses the potential risk of spreading SARS-CoV-2 during blood collection and transfusion. Although there are no reported instances of transfusion transmission, there is still potential for transfusion transmission since the virus exists in the blood in low levels. The authors recommend mitigation protocols against the possible risk of COVID-19's transfusion transmissibility at donation centers, such as donor deferral policies based on travel, diseased status, or potential risk of exposure.

ABSTRACT

BACKGROUND AND OBJECTIVE: Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is a novel coronavirus, first identified in China at the end of 2019 and has now caused a worldwide pandemic. In this review, we provide an overview of the implications of SARS-CoV-2 for blood safety and sufficiency. MATERIAL AND METHOD: We searched the PubMed database, the preprint sites bioRxiv and medRxiv, the websites of the World Health Organization, European Centre for Disease Prevention and Control, the US Communicable Diseases Center and monitored ProMed updates. RESULTS: An estimated 15%-46% of SARS-CoV-2 infections are asymptomatic. The reported mean incubation period is 3 to 7 days with a range of 1-14 days. The blood phase of SARS-CoV-2 appears to be brief and low level, with RNAaemia detectable in only a small proportion of patients, typically associated with more severe disease and not demonstrated to be infectious virus. An asymptomatic blood phase has not been demonstrated. Given these characteristics of SARS-CoV-2 infection and the absence of reported transfusion transmission (TT), the TT risk is currently theoretical. To mitigate any potential TT risk, but more importantly to prevent respiratory transmission in donor centres, blood centres can implement donor deferral policies based on travel, disease status or potential risk of exposure. CONCLUSION: The TT risk of SARS-CoV-2 appears to be low. The biggest risk to blood services in the current COVID-19 pandemic is to maintain the sufficiency of the blood supply while minimizing respiratory transmission of SARS-CoV-19 to donors and staff while donating blood.

SWITCHING HOST METABOLISM AS AN APPROACH TO DAMPEN SARS-COV-2 INFECTION

Soliman S, Faris ME, Ratemi Z, Halwani R.. Ann Nutr Metab. 2020 Sep 18:1-7. doi: 10.1159/000510508. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

Investigators of medicinal chemistry and nutrition at the University of Sharjah review the antiviral and cytokine-inhibitory mechanisms of lauric acid, enhanced phagocytic activity in high medium-chain triglyceride (MCT) diets, and suppression of several pro-inflammatory cytokines with intermittent fasting. They propose a ketogenic diet with intermittent fasting and supplemental MCT (diet regimen illustrated below) as a potential SARS-CoV-2 prophylaxis or adjuvant therapy for those with infection (Figure 1).

SUMMARY

The authors propose the following diet regimen to trigger metabolic switching for potential SARS-CoV-2 prophylaxis or adjuvant therapy:
- Breakfast: high content of ketogenic medium-chain triglycerides (MCT) from lauric acid/caprylic acid, monounsaturated long-chain fatty acid (MUFA) from olive oil.
- Following breakfast: 20g of supplemental ketogenic MCT drink
- 8-12 hour fast (can include lunch consisting of 20g supplemental ketogenic MCT drink without meal)
- Dinner: required amount of daily carbohydrates; fiber, vitamins, and minerals from fruit and vegetables

Some of the observations of this review include, but are not limited to, the following:
-Previous studies on Junin virus and Vesicular stomatitis virus revealed lauric acid's ability to inhibit late stage maturation during viral replication and prevent viral protein binding to host cell membrane.
- Lauric acid has also been shown to disrupt the viral envelope. In hosts, lauric acid is shown to downregulate IL-6, suggesting its role in inhibiting cytokine storm.
- Intermittent fasting has been associated with reduced expression of several pro-inflammatory cytokines that happen to be present in lung tissue during active SARS-CoV-2 infection.

ABSTRACT

BACKGROUND: COVID-19 pandemic, a global threat, adversely affects all daily lives, altered governmental plans around the world, and urges the development of therapeutics and prophylactics to avoid the expansion of the viral infection. With the recent gradual opening after long lockdown, several recommendations have been placed, with dietary modification as one of the most important approaches that have been appraised. SUMMARY: Here, we are reviewing how changing the host metabolism, particularly changing the host metabolic state from the carbohydrate-dependent glycolytic state to a fat-dependent ketogenic state, may affect viral replication. Furthermore, the impact of intermittent fasting (IF) in triggering metabolic switch along with the impact of supplementation with medium-chain triglycerides (MCTs) such as lauric acid in repressing the envelope formation and viral replication is also addressed. The amalgamation of IF and a ketogenic diet rich in MCTs is thought to work as a prophylactic measure for normal people and adjunct therapy for infected persons. Key Message: A diet regimen of ketogenic breakfast along with supplementation with two doses of lauric acid-rich MCTs at breakfast and lunch times, followed by 8-12-h IF and a dinner rich with fruits and vegetables, could be a potential prophylactic strategy and adjuvant therapy to combat SARS-CoV-2 infections.

FIGURES

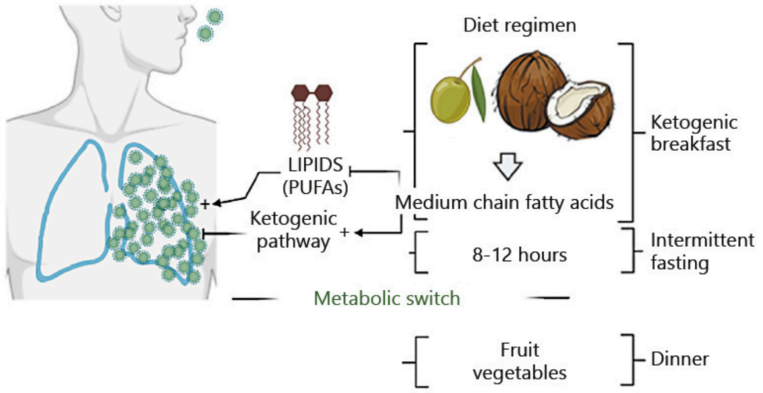

Fig 1. Schematic representation of a diet regimen proposed to dampen the SARS-CoV-2 infection by triggering metabolic switching. SARS-CoV-2, severe acute respiratory syndrome coronavirus-2; MCFAs, medium-chain fatty acids; IF, intermittent fasting.

PREVENTION IN THE HOSPITAL

OCCUPATIONAL HEAT STRESS AND PRACTICAL COOLING SOLUTIONS FOR HEALTHCARE AND INDUSTRY WORKERS DURING THE COVID-19 PANDEMIC

Foster J, Hodder SG, Goodwin J, Havenith G.. Ann Work Expo Health. 2020 Sep 21:wxaa082. doi: 10.1093/annweh/wxaa082. Online ahead of print.
Level of Evidence: Other - Guidelines and Recommendations

BLUF

Environmental researchers from Loughborough, UK penned a commentary to discuss the occupational hazards of over-heating (ie., hyperthermia, fatigue, and dehydration) associated with the use of impermeable, fluid resistant PPE when treating patients with COVID-19 (Summary). To combat these hazards, the authors recommend using several cooling methods and an environmental temperature range, Universal Thermal Climate Index (UTCI), to develop a heat action plan.

SUMMARY

The authors describe several hazards that are associated with the PPE health providers use when treating patients with COVID-19. In particular, the loss of effective evaporation of sweat from skin, the loss of convective flow of air along the skins surface, and the decreased ingestion of water all contribute to the physiological effects of overheating. The authors recommend using an environmental temperature range, Universal Thermal Climate Index (UTCI) to develop a heat action plan which would include worker training and enacting cooling methods. The cooling methods recommended include use of air conditioning with good ventilation, hydration - especially with cooler fluids or an ice slurry, use of cooling vests, use of regular breaks and forearm water immersion. The authors cite data from the HEAT-SHIELD project which receives EU funding and of which this writing is a part of.

ABSTRACT

Treatment and management of severe acute respiratory syndrome coronavirus-2, which causes coronavirus disease (COVID-19), requires increased adoption of personal protective equipment (PPE) to be worn by workers in healthcare and industry. In warm occupational settings, the added burden of PPE threatens worker health and productivity, a major lesson learned during the West-African Ebola outbreak which ultimately constrained disease control. In this paper, we comment on the link between COVID-19 PPE and occupational heat strain, cooling solutions available to mitigate occupational heat stress, and practical considerations surrounding their effectiveness and feasibility. While the choice of cooling solution depends on the context of the work and what is practical, mitigating occupational heat stress benefits workers in the healthcare and industrial sectors during the COVID-19 disease outbreak.

MANAGEMENT

THE NEED FOR IMPROVED DISCHARGE CRITERIA FOR HOSPITALISED PATIENTS WITH COVID-19-IMPLICATIONS FOR PATIENTS IN LONG TERM CARE FACILITIES

Sze S, Pan D, Williams CML, Barker J, Minhas JS, Miller C, Tang JW, Squire IB, Pareek M.. Age Ageing. 2020 Sep 19:afaa206. doi: 10.1093/ageing/afaa206. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

Researchers from the University of Leicester in England reviewed broad heterogeneity in hospital discharge criteria among the ten countries with the highest incidence of COVID-19 as of July 26, 2020 and found RT-PCR tests may not accurately correlate to a patient's infectivity, most transmission occurred during the pre-symptomatic phase, and there was a lack of discharge guidelines specific for release to long term care facilities (LTCF). Authors propose universal discharge criteria to include patient release 10 days after symptom onset or 10 days after the date of first positive RT-PCR test, arguing that these criteria would support patient safety and effective use of hospital resources.

ABSTRACT

In the COVID-19 pandemic, patients who are older and residents of long term care facilities (LTCF) are at greatest risk of worse clinical outcomes. We reviewed discharge criteria for hospitalised COVID-19 patients from ten countries with the highest incidence of COVID-19 cases as of 26th July 2020. Five countries (Brazil, Mexico, Peru, Chile and Iran) had no discharge criteria; the remaining five (United States of America, India, Russia, South Africa and the United Kingdom) had discharge guidelines with large inter-country variability. India and Russia recommend discharge for a clinically recovered patient with two negative reverse transcription polymerase chain reaction (RT-PCR) tests 24 hours apart; the USA offers either a symptom based strategy-clinical recovery and ten days after symptom onset, or the same test-based strategy. The UK suggests that patients can be discharged when patients have clinically recovered; South Africa recommends discharge 14 days after symptom onset if clinically stable. We recommend a unified, simpler discharge criteria, based on current studies which suggest that most SARS-CoV-2 loses its infectivity by 10 days post-symptom onset. In asymptomatic cases, this can be taken as 10 days after the first positive PCR result. Additional days of isolation beyond this should be left to the discretion of individual clinician. This represents a practical compromise between unnecessarily prolonged admissions and returning highly infectious patients back to their care facilities, and is of particular importance in older patients discharged to LTCFs, residents of which may be at greatest risk of transmission and worse clinical outcomes.

PSYCHIATRY AND COVID-19

Öngür D, Perlis R, Goff D.. JAMA. 2020 Sep 22;324(12):1149-1150. doi: 10.1001/jama.2020.14294.
Level of Evidence: Other - Expert Opinion

BLUF

McLean Hospital (U.S.) psychiatrists describe how the COVID-19 pandemic led to several challenges for psychiatric patients, including delays in delivery of care for established patients and the emerging psychotic disorders of untreated patients. Although the emergence of telemedicine in the field has helped to decrease these concerns, the increased rates of anxiety from COVID-19 and mitigation strategies have created the need for more psychiatrists. The authors propose increasing the capacity for mental health care by:

1) adequately funding current psychiatric care facilities,
2) enhancing collaboration between psychiatrists and other physicians,
3) increasing access to internet self-help, and
4) expanding psychiatrist availability.

R&D: DIAGNOSIS & TREATMENTS

IS NASO-PHARYNGEAL SWAB ALWAYS SAFE FOR SARS-COV-2 TESTING? AN UNUSUAL, ACCIDENTAL FOREIGN BODY SWALLOWING

De Luca L, Maltoni S.. Clin J Gastroenterol. 2020 Sep 20. doi: 10.1007/s12328-020-01236-y. Online ahead of print.
Level of Evidence: Other - Case Report

BLUF

Gastroenterologists from Pesaro, Italy describe a case of a 47 year old man undergoing a nasopharyngeal swab (NPS) test for SARS-CoV-2 during which a 7.5 cm segment of the swab broke off during the procedure and was swallowed by the patient. This resulted in the patient needing intubation and endoscopic extraction of the broken segment that was lodged in the stomach. Although the man had no long term effects the authors stress the importance of correct procedure during NPS testing especially when clinical sites are being overly burdened due to the COVID-19 pandemic.

ABSTRACT

Long and sharp objects can be foreign body intentionally or accidentally ingested. Timing of endoscopy relies on foreign body shape and size, localization in gastrointestinal tract, patient's clinical conditions, occurrence of symptoms, or onset of complications. We present a case of a 47-year-old male with no known comorbidity, who accidentally swallowed a portion of a naso-pharyngeal swab half-broken during the second diagnostic test for SARS-CoV-2. The intact swab had a total length of 15 cm and was made of wood. The patient was asymptomatic, laboratory tests were normal, and neck-chest-abdominal X-ray and CT scan were negative for major complications. Upper gastrointestinal endoscopy was promptly performed to prevent the long sharp swab from crossing the pylorus leading to serious complications and, therefore, risk surgical intervention. The patient was intubated and the procedure was carried out under general anesthesia. In the gastric body, broken naso-pharyngeal swab was detected among the food debris, and using a latex rubber hood, the 7.5 cm foreign body was removed with a retrieval alligator-tooth forceps. Our hospital is located in a high-risk area of COVID-19 outbreak where many naso-pharyngeal swabs are performed, and to our knowledge, this is the first report of swab ingestion during SARS-CoV-2 test.

CURRENT DIAGNOSTICS

COMPARATIVE ASSESSMENT OF MULTIPLE COVID-19 SEROLOGICAL TECHNOLOGIES SUPPORTS CONTINUED EVALUATION OF POINT-OF-CARE LATERAL FLOW ASSAYS IN HOSPITAL AND COMMUNITY HEALTHCARE SETTINGS

Pickering S, Betancor G, Galão RP, Merrick B, Signell AW, Wilson HD, Kia Ik MT, Seow J, Graham C, Acors S, Kouphou N, Steel KJA, Hemmings O, Patel A, Nebbia G, Douthwaite S, O'Connell L, Luptak J, McCoy LE, Brouwer P, van Gils MJ, Sanders RW, Martinez Nunez R, Bisnauthsing K, O'Hara G, MacMahon E, Batra R, Malim MH, Neil SJD, Doores KJ, Edgeworth JD.. PLoS Pathog. 2020 Sep 24;16(9):e1008817. doi: 10.1371/journal.ppat.1008817. eCollection 2020 Sep.
Level of Evidence: 5 - Mechanism-based reasoning

BLUF

Infectious disease experts and immunologists examine the sensitivity and specificity of anti-SARS-CoV-2 antibody tests using five ELISAs, seven colloidal gold lateral flow immunoassays, and ten commercial serological assays on 110 serum samples collected from 87 individuals with known COVID-19 infections between 4 March and 21 April 2020. Tests varied from 60.9% to 87.3% in sensitivity and 82% to 100% in specificity (Figures 2 and 3), but it was clear that all tests achieved the highest performance on samples taken at or greater than 20 days after onset of symptoms (Figure 5). The authors suggest there are a range of viable antibody tests for SARS-CoV-2 available, and that antibody tests are best used 20-days post-onset of symptoms as earlier tests will likely be negative due to lack of antibody formation.

ABSTRACT

There is a clear requirement for an accurate SARS-CoV-2 antibody test, both as a complement to existing diagnostic capabilities and for determining community seroprevalence. We therefore evaluated the performance of a variety of antibody testing technologies and their potential use as diagnostic tools. Highly specific in-house ELISAs were developed for the detection of anti-spike (S), -receptor binding domain (RBD) and -nucleocapsid (N) antibodies and used for the cross-comparison of ten commercial serological assays-a chemiluminescence-based platform, two ELISAs and seven colloidal gold lateral flow immunoassays (LFIAs)-on an identical panel of 110 SARS-CoV-2-positive samples and 50 pre-pandemic negatives. There was a wide variation in the performance of the different platforms, with specificity ranging from 82% to 100%, and overall sensitivity from 60.9% to 87.3%. However, the head-to-head comparison of multiple sero-diagnostic assays on identical sample sets revealed that performance is highly dependent on the time of sampling, with sensitivities of over 95% seen in several tests when assessing samples from more than 20 days post onset of symptoms. Furthermore, these analyses identified clear outlying samples that were negative in all tests, but were later shown to be from individuals with mildest disease presentation. Rigorous comparison of antibody testing platforms will inform the deployment of point-of-care technologies in healthcare settings and their use in the monitoring of SARS-CoV-2 infections.

FIGURES

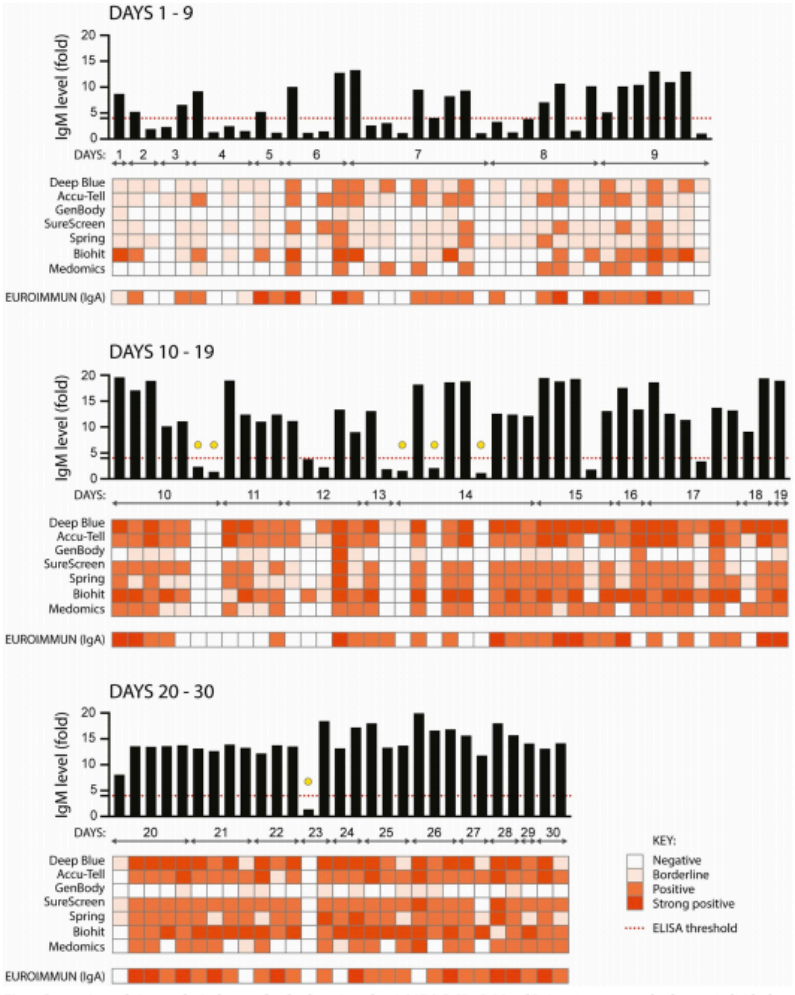

Fig 2. Comparison of nine serological assays for the detection of anti-SARS CoV-2 IgM and IgA. 110 serum samples from 87 individuals with confirmed SARS-CoV-2 infection (RNA+ by RT-PCR) were assayed for anti-SARS CoV-2 IgM using an in-house anti-S ELISA (shown in the graph across the top of each panel, black bars), seven colloidal gold lateral flow tests (Deep Blue, Accu-Tell, GenBody, SureScreen, Spring, Biohit and Medomics), and for anti-S1 IgA using a commercial ELISA (EUROIMMUN). The threshold for a positive result in the in-house ELISA is set at 4-fold above background, as indicated by the red dashed line. Results for the other tests are represented as heatmaps, with colour intensity corresponding to strength of signal for each test. For EUROIMMUN, scores of <0.8 are negative, ≥0.8 to <1.1 are borderline, ≥1.2 to <4 are positive, and ≥4 are strong positive. Samples are grouped according to days post onset of COVID-19 symptoms, and squares aligned in columns under each bar of the graph show results for a single serum sample. Yellow circles indicate samples from 10 days or more POS that were negative by ELISA and in at least 6 other tests, as detailed in the text.

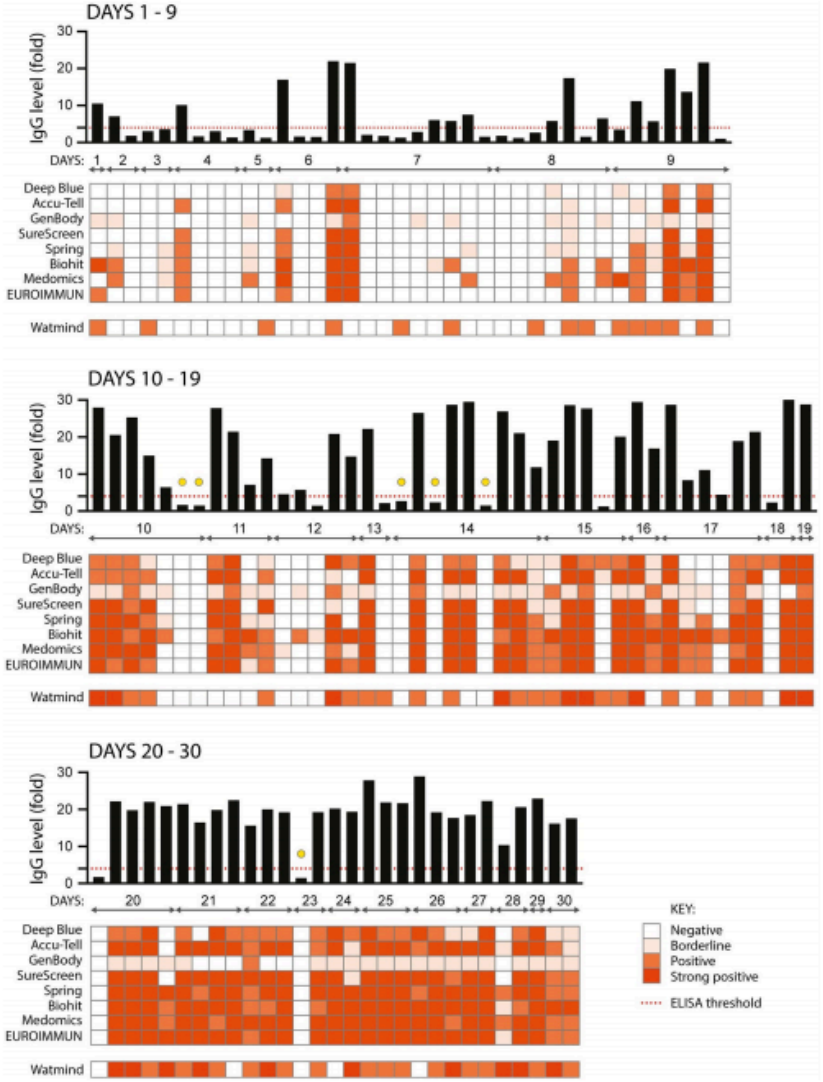

Fig 3. Comparison of ten serological assays for the detection of anti-SARS CoV-2 IgG. As for in Fig 2, the same 110 serum samples were assessed for the presence of anti-SARS CoV-2 IgG. Each sample was assayed using an in-house anti-S ELISA (shown in the graph

across the top of each panel, black bars), seven colloidal gold lateral flow tests (Deep Blue, Accu-Tell, GenBody, SureScreen, Spring, Biohit and Medomics), and a commercial ELISA (EUROIMMUN). A chemiluminescent assay for total anti-SARS CoV-2 IgM, IgG and IgA (Watmind) was also included. The threshold for a positive result in the in-house ELISA is set at 4-fold above background, as indicated by the red dashed line. Results for the other tests are represented as heatmaps, with colour intensity corresponding to strength of signal for each test. For EUROIMMUN, scores of <0.8 are negative, ≥0.8 to <1.1 are borderline, ≥1.2 to <4 are positive, and ≥4 are strong positive. For Watmind, scores <1 are negative, >1 to <10 are positive, and >10 to 100 are strong positive. Yellow circles indicate samples from 10 days or more POS that were negative by ELISA and in all commercial tests

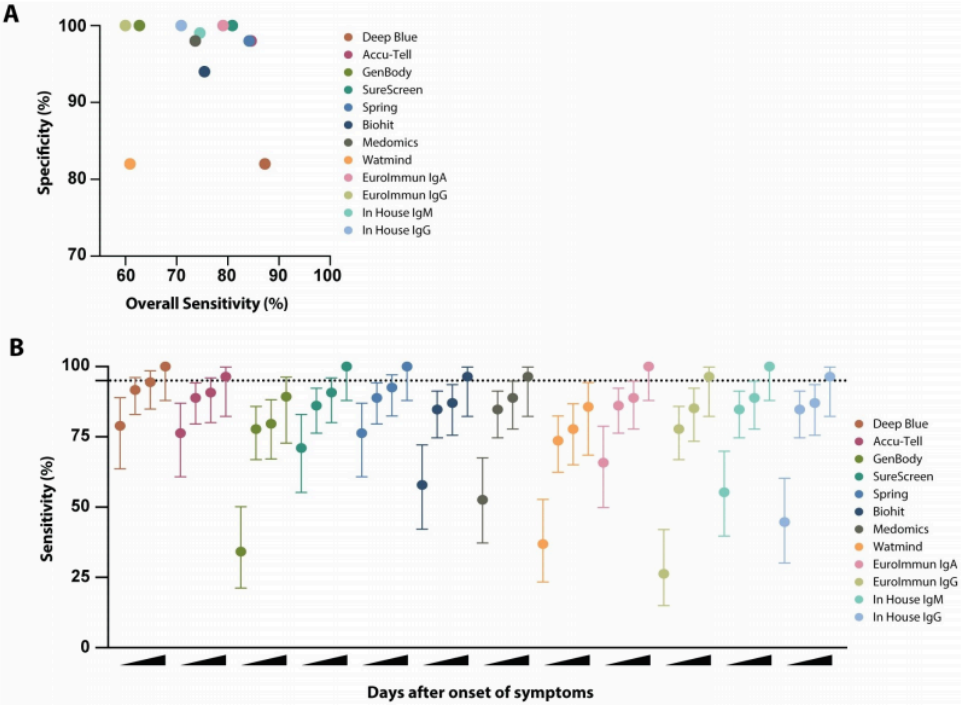

Fig 5. Sensitivity and specificity comparison of serological assays. (A) Specificity was determined for each serological assay using a panel of 50 pre-pandemic serum samples the St Thomas' emergency admissions cohort (STH Healthy, March 2019). Overall sensitivity was
determined for each serological assay, based on results for 110 serum samples from known SARS-CoV-2-positive individuals (shown in Figs 3 and 4). For the lateral flow assays, a positive result for IgM, IgG or both is considered positive. For the EUROIMMUN and in-house
ELISAs, sensitivities for IgA, IgM and IgG are calculated separately. (B) Sensitivity and 95% confidence intervals (vertical lines) were determined for each serological assay at increasing days POS. 95% sensitivity is indicated by the horizontal dashed line. Results for each test
were categorised according to whether the serum sample was from <10, ≥10, ≥14, or ≥20 days POS.

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