



International EPI Cell Daily Evidence Digest – 27/05/2020

This Daily Evidence Digest is produced by the PHE COVID-19 Literature Digest Team as a resource for professionals working in public health. We do not accept responsibility for the availability, reliability or content of the items included in this resource and do not necessarily endorse the views expressed within them. The papers are organised under the following themes:

- Diagnostics
- Serology and immunology
- Genomics
- Epidemiology and clinical - children and pregnancy
- Epidemiology and clinical - risk factors
- Epidemiology and clinical - other
- Infection control
- Treatment
- Modelling
- Guidance, consensus statements and hospital resources (no digest)
- Overviews, comments and editorials (no digest)

Please note that we are including preprints (**highlighted in red**), which are preliminary reports of work that have NOT been peer-reviewed. They should not be relied on to guide clinical practice or health-related behaviour and should NOT be reported in news media as established information.

Diagnostics

Publication Date	Title/URL	Journal/ Article type	Digest
25.05.2020	Role of biological Data Mining and Machine Learning Techniques in Detecting and Diagnosing the Novel Coronavirus (COVID-19): A Systematic Review	J Med Syst / Systematic review	<ul style="list-style-type: none">• This systematic review addresses automated AI applications based on data mining and machine learning (ML) algorithms for detecting and diagnosing COVID-19, aiming to address the limitations of utilising data mining and ML algorithms, and provide the health sector with the benefits of this technique.• The growing emphasis on data mining and ML techniques in

			medical fields can provide the right environment for change and improvement.
26.05.2020	Performance evaluation of the point-of-care SAMBA II SARS-CoV-2 Test for detection of SARS-CoV-2	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> Analytical and clinical sensitivity and specificity of the SAMBA II SARS-CoV-2 Test was evaluated on panels and residual clinical samples. The clinical performance was compared to the Public Health England reference tests. The clinical sensitivity was evaluated in 172 clinical samples provided by PHE, Cambridge, which showed a sensitivity of 98.9%, specificity of 100% , PPV of 100% and NPV of 98.78% compared to testing by PHE. SAMBA detected 3 positive samples that were initially negative by PHE. The data shows that the SAMBA II SARS-CoV-2 Test performs equivalently to the centralised testing methods with a much quicker turnaround time. Point of care testing, such as SAMBA, should enable rapid patient management and effective implementation of infection control measures.
26.05.2020	SARS-CoV-2 RNA detected in blood samples from patients with COVID-19 is not associated with infectious virus	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> Systematic literature review to assimilate the evidence for the frequency of vRNA in blood, and to identify associated clinical characteristics. Also performed RT-PCR in serum samples from a UK clinical cohort of acute and convalescent COVID-19 cases (n=212), together with convalescent plasma samples collected by NHS Blood and Transplant (n=212 additional samples). vRNA was detectable at low viral loads in a minority of serum samples collected in acute infection, but was not associated with infectious SARS-CoV-2 (within the limitations of the assays used).

Serology and immunology

Publication Date	Title/URL	Journal/ Article type	Digest
22.05.2020	Safety, tolerability, and immunogenicity of a recombinant adenovirus type-5 vectored COVID-19 vaccine: a dose-escalation, open-label, non-randomised, first-in-human trial	Lancet / Trial	<ul style="list-style-type: none"> Dose-escalation, single-centre, open-label, non-randomised, phase 1 trial of an Ad5 vectored COVID-19 vaccine to assess the safety, tolerability, and immunogenicity of a recombinant adenovirus type-5 (Ad5) vectored COVID-19 vaccine expressing the spike glycoprotein of a SARS-CoV-2 strain. 108 participants (51% male, 49% female; mean age 36.3 years)

			<p>were recruited and received the low dose (n=36), middle dose (n=36), or high dose (n=36) of the vaccine.</p> <ul style="list-style-type: none"> • The Ad5 vectored COVID-19 vaccine is tolerable and immunogenic at 28 days post-vaccination. Humoral responses against SARS-CoV-2 peaked at day 28 post-vaccination in healthy adults, and rapid specific T-cell responses were noted from day 14 post-vaccination. Findings suggest that the Ad5 vectored COVID-19 vaccine warrants further investigation.
26.05.2020	Human neutralizing antibodies elicited by SARS-CoV-2 infection	Nature / Article	<ul style="list-style-type: none"> • The authors report the isolation and characterization of 206 RBD-specific monoclonal antibodies derived from single B cells of eight SARS-CoV-2 infected individuals. • Crystal structure analysis of RBD-bound antibody revealed steric hindrance that inhibits viral engagement with ACE2 and thereby blocks viral entry. • Findings suggest that anti-RBD antibodies are viral species-specific inhibitors.
26.05.2020	A human neutralizing antibody targets the receptor binding site of SARS-CoV-2	Nature / Article	<ul style="list-style-type: none"> • Study reporting the isolation of 2 specific human monoclonal antibodies (MAbs) from a convalescent COVID-19 patient. • CA1 and CB6 demonstrated potent SARS-CoV-2-specific neutralization activity in vitro against SARS-CoV-2. In addition, CB6 inhibited SARS-CoV-2 infection in rhesus monkeys at both prophylactic and treatment settings. • Further structural studies revealed that CB6 recognizes an epitope that overlaps with angiotensin converting enzyme 2 (ACE2)-binding sites in SARS-CoV-2 receptor binding domain (RBD), thereby interfering with the virus/receptor interactions by both steric hindrance and direct interface-residue competition.
30.04.2020	Association of viral load with serum biomarkers among COVID-19 cases	Virology / Article	<ul style="list-style-type: none"> • This study measured and compared viral loads of SARS-CoV-2 from pharyngeal swab, IgM anti-SARS-CoV-2, CRP and SAA from serum of 114 COVID-19 patients on admission. • Positive rates of IgM anti-SARS-CoV-2, CRP and SAA were 80.7%, 36% and 75.4% respectively. Among IgM-positive patients, viral loads showed different trends among cases with different severity, While viral loads of IgM-negative patients tended to increase along with the time after onset. • As the worsening of severity, the positive rates of CRP and SAA also showed trends of increase. Different CRP/SAA type showed

			associations with viral loads in patients in different severity and different time after onset.
26.05.2020	SARS-CoV-2 IgG Antibody Responses in New York City	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> Describe SARS-CoV-2 IgG antibody responses in 11,092 patients from the New York City metropolitan area and report a SARS-CoV-2 IgG positivity rate of nearly 50%, indicating the widespread nature of the pandemic in the city and state of New York. Additionally, they report on the correlation between SARS-CoV-2 patient symptom severity and level of SARS-CoV-2 IgG antibody found in the patient sample.
26.05.2020	Study on the expression levels of antibodies against SARS-CoV-2 at different period of disease and its related factors in 192 cases of COVID-19 patients	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> Depict the kinetics profile of antibodies against SARS-CoV-2 in COVID-19 patients (n=192) and found that the levels of antibodies were related to the disease severity, age, gender and virus clearance.
23.05.2020	Deep immune profiling of COVID-19 patients reveals patient heterogeneity and distinct immunotypes with implications for therapeutic interventions	bioRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> Analysed 71 COVID-19 patients compared to recovered and healthy subjects using high dimensional cytometry. Integrated analysis of ~200 immune and >30 clinical features revealed activation of T cell and B cell subsets, but only in some patients. These analyses identified three “immunotypes” associated with poor clinical trajectories versus improving health. These immunotypes may have implications for therapeutics and vaccines.
26.05.2020	Multi-site Validation of a SARS-CoV-2 IgG/IgM Rapid Antibody Detection Kit	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> Data provided in this study supports the utility of a newly-designed lateral flow immunoassay (LFA) for detecting SARS-CoV-2 IgM and IgG antibodies. Employed a clinical cohort of 1,892 SARS-CoV-2 patients and controls, including individuals diagnosed by RT-qPCR at Yale New Haven Hospital, The First Affiliated Hospital of Anhui Medical University, the Chinese Center for Disease Control and Prevention of Hefei City (Hefei CDC), Anhui Province (Anhui Province CDC), and Fuyang City (Fuyang CDC). Detected SARS-CoV-2 IgM and IgG antibodies with a specificity of 97.9-100% for IgM, 99.7-100% for IgG, and sensitivities ranging from 94.1-100% for patients >14-days post symptom onset.
26.05.2020	Convalescent plasma therapy for the treatment of patients with COVID-19: Assessment of methods available for antibody detection and their correlation with neutralising antibody levels	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> Assessed whether neutralising antibody titres correlated with reactivity in a range of ELISA assays targeting the spike (S) protein, the main target for human immune response. Blood samples were collected from 52 individuals with a previous laboratory confirmed SARS-CoV-2 infection at least 28 days after

			<p>symptom resolution.</p> <ul style="list-style-type: none"> • All samples contained SARS-CoV-2 antibodies, whereas neutralising antibody titres of greater than 1:20 were detected in 43 samples (83% of those tested) and >1:100 in 22 samples (42%). • Robust associations between virus neutralising antibody titres and reactivity in several ELISA-based antibody tests demonstrate their possible utility for scaled-up production of convalescent plasma containing potentially therapeutic levels of anti-SARS-CoV-2 neutralising antibodies.
26.05.2020	COVID-19 serology at population scale: SARS-CoV-2-specific antibody responses in saliva	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Developed a multiplex SARS-CoV-2 antibody immunoassay based on Luminex technology and tested 167 saliva and 324 serum samples, including 134 and 118 negative saliva and serum samples, respectively, collected before the COVID-19 pandemic, and 33 saliva and 206 serum samples from participants with RT-PCR-confirmed SARS-CoV-2 infection. • Among individuals with SARS-CoV-2 infection confirmed with RT-PCR, the temporal kinetics of IgG, IgA, and IgM in saliva were consistent with those observed in serum. • SARS-CoV-2 antibody testing in saliva can play a critically important role in large-scale 'sero'-surveillance to address key public health priorities and guide policy and decision-making for COVID-19.

Genomics

Publication Date	Title/URL	Journal/ Article type	Digest
26.05.2020	A Unique Clade of SARS-CoV-2 Viruses is Associated with Lower Viral Loads in Patient Upper Airways	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Examined the genome sequences of 88 SARS-CoV-2 viruses from COVID-19 patients in Chicago, USA and identified three distinct phylogenetic clades. • Clade 1 was most closely related to clades centered in New York, and showed evidence of rapid expansion across the USA, while Clade 3 was most closely related to those in Washington. Clade 2 was localized primarily to the Chicago area with limited evidence of expansion elsewhere. • Average viral loads in the airways of patients infected with the rapidly spreading Clade 1 viruses were significantly higher than those of the poorly spreading Clade 2. These results show that multiple

			variants of SARS-CoV-2 are circulating in the USA that differ in their relative airway viral loads and potential for expansion.
23.05.2020	Comprehensive genome analysis of 6,000 USA SARS-CoV-2 isolates reveals haplotype signatures and localized transmission patterns by state and by country	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • By haplotype analysis of 6,356 US isolates, authors identified a pattern of strongly localized outbreaks at the city, state, and country-levels, and temporal transmissions. This points to the effectiveness of existing travel restriction policies and public health measures in controlling the transmission of SARS-CoV-2.
22.05.2020	Full genome viral sequences inform patterns of SARS-CoV-2 spread into and within Israel	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Here, with a focus on Israel, the authors sequenced 212 SARS-CoV-2 sequences and used them to perform a comprehensive analysis to trace the origins and spread of the virus. • A phylogenetic analysis including thousands of globally sampled sequences allowed them to infer multiple independent introductions into Israel, followed by local transmission. • Returning travellers from the U.S. contributed dramatically more to viral spread relative to their proportion in incoming infected travellers. • Overall, the findings underscore the ability of this virus to efficiently transmit between and within countries, as well as demonstrate the effectiveness of social distancing measures for reducing its spread.

Epidemiology and clinical – children and pregnancy

Publication Date	Title/URL	Journal/ Article type	Digest
26.05.2020	Erythema multiforme and Kawasaki disease associated with COVID-19 infection in children	J Eur Acad Dermatol Venereol / Letter	<ul style="list-style-type: none"> • Report of two life-threatening cases of children presenting with fever and eruptions with mucous membrane involvement - erythema multiforme and Kawasaki disease - associated with COVID-19.
23.05.2020	Delivery For Respiratory Compromise Among Pregnant Women With COVID-19	Am J Obstet Gynecol / Research article	<ul style="list-style-type: none"> • Retrospective observational study to evaluate the safety and utility of delivery of COVID-19 infected pregnant women needing respiratory support. • Delivery did not worsen the respiratory status of women with persistent oxygen desaturation and the need for increasing respiratory support. • Among women not needing a ventilator, return of normal respiratory status after delivery occurred within hours to days. • The one patient intubated intraoperatively took longer to recover.

Epidemiology and clinical - risk factors

Publication Date	Title/URL	Journal/ Article type	Digest
23.05.2020	Lifestyle Risk Factors, Inflammatory Mechanisms, and COVID-19 Hospitalization: A Community-Based Cohort Study of 387,109 Adults in UK	Brain Behav Immun / Cohort study	<ul style="list-style-type: none"> • Large-scale UK general population study on lifestyle risk factors for COVID-19 using prospective cohort data for 387,109 men and women residing in England from UK Biobank study. • After adjustment for age, sex and mutually for each lifestyle factor, physical inactivity, smoking but not heavy alcohol consumption were all related to COVID-19. • There was also a dose-dependent increase in risk of COVID-19 with less favourable lifestyle scores, such that participants in the most adverse category had 4-fold higher risk compared to people with the most optimal lifestyle. • Based on UK risk factor prevalence estimates, unhealthy behaviours in combination accounted for up to 51% of the population attributable fraction of severe COVID-19.
25.05.2020	Predictive symptoms and comorbidities for severe COVID-19 and intensive care unit admission: a systematic review and meta-analysis	Int J Public Health / Systematic review	<ul style="list-style-type: none"> • This systematic review identifies specific symptoms and comorbidities predicting severe COVID-19 and intensive care unit (ICU) admission. Seven studies (including 1813 COVID-19 patients) were included. • ICU patients were older (62.4 years) than non-ICU (46 years), with a greater proportion of males. • Dyspnoea was the only symptom predictive for severe disease (pOR 3.70, 95% CI 1.83-7.46) and ICU admission (pOR 6.55, 95% CI 4.28-10.0). • COPD was the strongest predictive comorbidity for severe disease (pOR 6.42, 95% CI 2.44-16.9) and ICU admission (pOR 17.8, 95% CI 6.56-48.2), followed by cardiovascular disease and hypertension.
25.05.2020	Do underlying cardiovascular diseases have any impact on hospitalised patients with COVID-19?	Heart / Research article	<ul style="list-style-type: none"> • Retrospective analysis to explore the early clinical characteristics of COVID-19 patients with cardiovascular disease (CVD). • The study included 541 patients with COVID-19. A total of 144 (26.6%) patients had a history of CVD. The mortality of patients with CVD reached 22.2%, which was higher than that of the overall population of this study (9.8%). • Patients with CVD were also more likely to develop liver function abnormality, elevated blood creatinine and lactic dehydrogenase ($p < 0.05$). Symptoms of sputum production were more common in

			<p>patients with CVD ($p=0.026$). Lymphocytes, haemoglobin and albumin below the normal range were pervasive in the CVD group ($p<0.05$).</p> <ul style="list-style-type: none"> • The proportion of critically ill patients in the CVD group (27.8%) was significantly higher than that in the non-CVD group (8.8%).
26.05.2020	Delayed-Phase Thrombocytopenia in Patients of Coronavirus Disease 2019 (COVID-19)	Br J Haematol / Short report	<ul style="list-style-type: none"> • Retrospective single-centre study which screened 450 COVID-19 patients and enrolled 271 patients. • COVID-19 associated delayed-phase thrombocytopenia occurred in 11.8% percent of enrolling patients. The delayed-phase thrombocytopenia in COVID-19 is prone to develop in elderly patients or patients with low lymphocyte count on admission, and is significantly associated with increased length of hospital stay and higher mortality rate. • The authors speculate that immune mediated platelet destruction might account for the delayed-phase thrombocytopenia in a group of patients.
25.05.2020	Systematic assessment of venous thromboembolism in COVID-19 patients receiving thromboprophylaxis: incidence and role of D-dimer as predictive factors	J Thromb Thrombolysis / Research article	<ul style="list-style-type: none"> • Retrospective French cohort study to determine incidence and risk factors of venous thromboembolism (VTE) in COVID-19 in patients receiving thromboprophylaxis. • Of 71 patients, 16 developed VTE (22.5%) and 7 PE (10%) despite adequate thromboprophylaxis. D-dimers at baseline were significantly higher in patients with DVT ($p < 0.001$). Demographics, comorbidities, disease manifestations, severity score, and other biological parameters, including inflammatory markers, were similar in patients with and without VTE. • Despite thromboprophylaxis, the risk of VTE is high in COVID-19 non-ICU inpatients. Increased D-dimer concentrations of more than 1.0 $\mu\text{g/ml}$ predict the risk of venous thromboembolism. D-dimer level-guided aggressive thromboprophylaxis regimens using higher doses of heparin should be evaluated in prospective studies.

Epidemiology and clinical – other

Publication Date	Title/URL	Journal/ Article type	Digest
26.05.2020	Projected baselines of COVID-19 in the EU/EEA and the UK for assessing the impact of de-escalation of measures	European Centre for Disease Control and Prevention / Technical report	<ul style="list-style-type: none"> • This report aims to provide a short-term 30-day forecast of the expected number of COVID-19 cases, deaths and hospitalised cases (including general hospital ward and intensive care unit) under a set

			<p>of assumptions.</p> <ul style="list-style-type: none"> • After widespread transmission of SARS-CoV-2 in EU/EEA countries and the UK over several weeks, the COVID-19 epidemic reached its peak in most countries in April or early May 2020. • Some countries have since experienced a sustained decrease in the number of reported cases, progressively reaching the level of transmission reported during the first week of the outbreak. • Due to this decrease in transmission and improvements in epidemiological surveillance and healthcare capacity, a number of countries have decided to discontinue several non-pharmaceutical interventions and now plan to gradually phase out their 'stay-at-home' policies.
27.05.2020	What explains the high rate of SARS-CoV-2 transmission in meat and poultry facilities?	Oxford COVID-19 Evidence Service / COVID-19	<ul style="list-style-type: none"> • Numerous COVID-19 outbreaks have been described in relation to meat and poultry processing facilities in different countries. • The working environment in these facilities is favourable to SARS-CoV-2 persistence (metallic surfaces, low temperatures and relative humidity). • The working environment may help SARS-CoV-2 transmission (crowded working places, shared transportation, production of aerosols, droplets, fomites). • A vulnerable, low-paid workforce may be under pressure to keep working despite having symptoms of COVID-19
24.05.2020	Clinical characteristics of patients hospitalized with COVID-19 in Spain: results from the SEMI-COVID-19 Network	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Up to April 30, 6,424 patients from 109 hospitals included in study. Those hospitalized in Spain mostly severe cases; one in three developed respiratory distress, one in five died. • Prevalence of hypertension, dyslipidaemia, and diabetes mellitus were 50.2%, 39.7%, and 18.7%, respectively. • High values of ferritin (72.4%), lactate dehydrogenase (70.2%), and D-dimer (61.5%), as well as lymphopenia (52.6%), were frequent. • Most used antiviral drugs: hydroxychloroquine (85.7%) and lopinavir/ritonavir (62.4%). 31.5% developed respiratory distress. • Overall mortality rate 21.1%, marked increase with age (50-59 years: 4.2%, 60-69 years: 9.1%, 70-79 years: 21.4%, 80-89 years: 42.5%, ≥ 90 years: 51.1%).
24.05.2020	Characteristics and predictors of hospitalization and death in the first 9,519 cases with a positive RT-PCR test for SARS-CoV-2 in Denmark: A nationwide cohort	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Nationwide population-based cohort of all 228,677 consecutive Danish individuals tested (positive or negative) for COVID-19. • Number of comorbidities strongly associated with fatal disease (OR 5.2, for cases with ≥4 comorbidities versus no comorbidities); 82% of

			<p>fatal cases had at least 2 comorbidities.</p> <ul style="list-style-type: none"> • Wide range of major chronic diseases associated with: hospitalization with ORs ranging from 1.3-1.4 (e.g. stroke, ischemic heart disease) to 2.2-2.7 (e.g. heart failure, hospital-diagnosed kidney disease, chronic liver disease); mortality with ORs ranging from 1.2-1.3 (e.g. ischemic heart disease, hypertension) to 2.4-2.7 (e.g. major psychiatric disorder, organ transplantation). • In absence of comorbidities, mortality was relatively low (5% or less) in persons aged up to 80 years.
26.05.2020	SARS-CoV-2 infection, clinical features and outcome of COVID-19 in United Kingdom nursing homes	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Investigated COVID-19 infection and transmission in UK nursing homes - included 394 residents and 70 staff in 4 nursing homes affected by COVID-19 outbreaks in central London. • Two point-prevalence surveys one week apart where residents underwent SARS-CoV-2 testing and had relevant symptoms documented. Asymptomatic staff from three of the four homes were also offered SARS-CoV-2 testing. • The SARS-CoV-2 outbreak was associated with a very high mortality rate in residents of nursing homes. Systematic testing of all residents and a representative sample of staff identified high rates of SARS-CoV-2 positivity across the four nursing homes, highlighting a potential for regular screening to prevent future outbreaks.
27.05.2020	Suspected COVID-19 in primary care: how GP records contribute to understanding differences in prevalence by ethnicity	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Quantified the prevalence and time-course of suspected COVID-19 presenting to general practices during the London epidemic. Report disease prevalence by ethnic group, and explore how far differences by ethnicity can be explained by data in the electronic health record (EHR). • Cross-sectional study using anonymised data from the primary care records of 1.3 million people registered with 157 practices in four adjacent east London CCGs. The study area includes 48% of people from ethnic minorities and is in the top decile of social deprivation in England. • Using data in GP records Black and south Asian ethnicity remain as predictors of community cases of COVID-19, with levels of risk similar to hospital admission cases. Further understanding of these differences requires social and occupational data.
26.05.2020	Ethnic Disparities in Hospitalization for COVID-19: a Community-Based Cohort Study in the UK	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Aimed to explain any ethnic differentials in COVID-19 hospitalization based on socioeconomic, lifestyle, mental and physical health factors.

			<ul style="list-style-type: none"> • Included 340,966 men and women (mean age 56.2 (SD=8.1) years; 54.3% women) residing in England from the UK Biobank study. • Findings show clear ethnic differences in risk of hospitalization for COVID-19 which do not appear to be fully explained by known explanatory factors. If replicated, the results have implications for health policy, including the targeting of prevention advice and vaccination coverage.
26.05.2020	Excess mortality in England and Wales during the first wave of the COVID-19 pandemic	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Quantified excess mortality in regions of England and Wales during the pandemic, for all causes and for non-COVID-19 associated deaths. • Between 7 Mar and 8 May 2020, there were 47,243 excess deaths in England and Wales, of which 9,948 were not associated with COVID-19. • Overall excess mortality rates varied from 49 per 100,000 in the South West to 102 per 100,000 in London. Non-COVID-19 associated excess mortality rates ranged from -1 per 100,000 in Wales (i.e. mortality rates were no higher than expected) to 26 per 100,000 in the West Midlands. • The COVID-19 pandemic has had markedly different impacts on the regions of England and Wales, both for deaths directly attributable to COVID-19 infection and for deaths resulting from the national public health response.
26.05.2020	Molecular Detection of SARS-CoV-2 Infection in FFPE Samples and Histopathologic Findings in Fatal SARS-CoV-2 Cases	Am J Clin Pathol / Article	<ul style="list-style-type: none"> • Report of findings of 2 autopsies with molecular evaluation of severe SARS-CoV-2 positive individuals using formalin-fixed paraffin-embedded (FFPE) tissue types. • Post-mortem examinations revealed diffuse alveolar damage, while no viral-associated hepatic, cardiac, or renal damage was observed. Viral RNA was detected in lungs, bronchi, lymph nodes, and spleen in both cases using qRT-PCR method. • RNA sequencing using NGS in case 1 revealed mutations most consistent with Western European Clade A2a with ORF1a L3606F mutation.
26.05.2020	Clinical Significance of Blue-Green Neutrophil and Monocyte Cytoplasmic Inclusions in SARS-CoV-2 Positive Critically Ill Patients	Br J Haematol / Letter	<ul style="list-style-type: none"> • Identification of blue-green cytoplasmic inclusions in neutrophils and/or monocytes on peripheral blood smears is a rare, and likely underreported, finding described in few case reports and small case series studies in critically ill patients with acute liver dysfunction and lactic acidosis. • This letter describes six critically ill patients diagnosed with SARS-

			CoV-2 infection in New York City who all died within days of these peculiar blood smear findings.
26.05.2020	Age, gender and COVID-19 infections	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Data for ten European countries which provide detailed distribution of COVID-19 cases by sex and age show that among people of working age, women diagnosed with COVID-19 substantially outnumber infected men. This pattern reverses around retirement: infection rates among women fall at age 60-69, resulting in a cross-over with infection rates among men. • The relative disadvantage of women peaks at ages 20-29, whereas the male disadvantage in infection rates peaks at ages 70-79. The elevated infection rates among women of working age are likely tied to their higher share in health- and care-related occupations.
25.05.2020	The fate of SARS-CoV-2 in wastewater treatment plants points out the sludge line as a suitable spot for incidence monitoring	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Sampling several spots in primary, secondary and sludge treatment at the Ourense (Spain) WWTP showed that, in effect, most of SARS-CoV-2 particles cannot be detected in the water effluent as they are retained by the sludge line. • The sludge thickener was identified as a suitable spot for detecting SARS-CoV-2 particles thanks to its higher solids concentration (more virus particles) and longer residence time (less sensitive to dilution caused by precipitation). • Although more studies will be needed for confirmation, these results contribute to clarify the role of WWTPs in COVID-19 mitigation.

Infection control

Publication Date	Title/URL	Journal/ Article type	Digest
26.05.2020	Investigating SARS-CoV-2 surface and air contamination in an acute healthcare setting during the peak of the COVID-19 pandemic in London	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Evaluated SARS-CoV-2 surface and air contamination during the peak of the COVID-19 pandemic in London. • Air and surface samples were collected from a range of clinical areas and a public area of the hospital. • Viral RNA was detected on 114/218 (52.3%) of surface and 14/31 (38.7%) air samples but no virus was cultured. • Findings of extensive viral RNA contamination of surfaces and air across a range of acute healthcare settings in the absence of cultured virus underlines the potential risk from surface and air contamination

			in managing COVID-19, and the need for effective use of PPE, social distancing, and hand/surface hygiene.
26.05.2020	Using HoloLens™ to reduce staff exposure to aerosol generating procedures during a global pandemic	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • In a tertiary centre in London the authors implemented HoloLens technology, allowing other medical staff to remotely join the consulting clinician when in a high-risk patient area delivering oxygen therapy. The study primary outcome was to reduce the exposure to staff and demonstrate non-inferiority staff satisfaction when compared to not using the device. The secondary outcome was to reduce extrapolated PPE costs when using the device. • Demonstrated HoloLens can reduce the number of staff exposed to aerosol generating areas in a novel infectious disease. The results show it did not impair communication, medical staff availability or end of life care. HoloLens technology may also reduce the use of PPE, which has equipment availability and cost benefits.

Treatment

Publication Date	Title/URL	Journal/ Article type	Digest
26.05.2020	The role of nicotine in COVID-19 infection	Oxford COVID-19 Evidence Service / Treatments for COVID	<ul style="list-style-type: none"> • There are biologically plausible pathways through which nicotine may impact SARS-CoV-2, but the clinical significance of these is entirely unclear. • Early studies are underway regarding the role of nicotine replacement therapy as a therapeutic aid for COVID-19. • Evidence so far is too limited to inform any decisions about use of nicotine replacement therapy in COVID-19. • When used for smoking cessation, there is high certainty evidence that nicotine replacement therapy is safe and effective.
26.05.2020	Remdesivir use in patients with coronavirus COVID-19 disease: a systematic review and meta-analysis	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • In this rapid systematic review, the authors present pooled evidence from the 2 included RCT studies that reveal that remdesivir has a modest yet significant reduction in mortality and significantly improves the time to recovery, as well as significantly reduced risk in adverse events and serious adverse events. • It is more than likely that as an antiviral, remdesivir is not sufficient on its own and may be suitable in combination with other antivirals or treatments such as convalescent plasma. Research is ongoing to clarify and contextual these promising findings.

26.05.2020	Determinants of cardiac adverse events of chloroquine and hydroxychloroquine in 20 years of drug safety surveillance reports	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • In this study the authors analysed over thirteen million adverse event reports from the United States FDA Adverse Event Reporting System to confirm and quantify the association of cardiac side effects of Chloroquine and hydroxychloroquine. • Additionally, they identified several confounding factors, including male sex, NSAID coadministration, advanced age, and prior diagnoses contributing to the risk of drug related cardiotoxicity. These findings may help guide therapeutic decision making and ethical trial design for COVID-19 treatment.
26.05.2020	IMPACT OF GLUCOCORTICOID TREATMENT IN SARS-COV-2 INFECTION MORTALITY: A RETROSPECTIVE CONTROLLED COHORT STUDY	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Single-centre retrospective cohort study on impact of steroid use in COVID-19 pneumonia in-hospital mortality: 396 (46.7%) consecutive patients treated with steroids; 67 in control. • In-hospital mortality lower in steroid treated patients (13.9% [55/396] versus 23.9% [16/67], OR 0.51 [0.27 to 0.96], p= 0.044). Steroid treatment reduced mortality by 41.8% (RRR 0,42 [0.048 to 0.65]). • Patient survival with SARS-CoV2 pneumonia higher when treated with glucocorticoids. In-hospital mortality not different between initial regimens of 1 mg/kg/day of methylprednisolone or equivalent and glucocorticoid pulses.

Modelling

Publication Date	Title/URL	Journal/ Article type	Digest
26.05.2020	Visualizing the invisible: The effect of asymptomatic transmission on the outbreak dynamics of COVID-19	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • The authors used reported symptomatic case data in conjunction with antibody seroprevalence studies, a mathematical epidemiology model, and a Bayesian framework to infer the epidemiological characteristics of COVID-19. • Study reveals that the outbreak dynamics of COVID-19 are sensitive to three parameters: the effective reproduction number, the ratio between the symptomatic and asymptomatic populations, and the infectious periods of both groups. • For three distinct locations, Santa Clara County (CA, USA), New York City (NY, USA), and Heinsberg (NRW, Germany), their model estimates the fraction of the population that has been infected and recovered by May 13, 2020 to 6.2%, 22.7%, and 20.5%.

			<ul style="list-style-type: none"> Managing community transmission through increasing population awareness, promoting physical distancing, and encouraging behavioural changes could become more relevant.
22.05.2020	The effectiveness of full and partial travel bans against COVID-19 spread in Australia for travellers from China during and after the epidemic peak in China	J Travel Med / Research article	<ul style="list-style-type: none"> Modelling study of three scenarios to test the impact of travel bans on epidemic control. Scenario one was no ban, scenario two and three were the current ban followed by a full or partial lifting (allow over 100 000 university students to enter Australia, but not tourists) from the 8th of March 2020. Travel restrictions were highly effective for containing the COVID-19 epidemic in Australia during the epidemic peak in China and averted a much larger epidemic at a time when COVID-19 was largely localised to China.

Guidance, consensus statements

Publication Date	Title/URL	Journal/ Article type
26.05.2020	Considerations for travel-related measures to reduce spread of COVID-19 in the EU/EEA	European Centre for Disease Control and Prevention / Technical report
26.05.2020	Scope, quality, and inclusivity of clinical guidelines produced early in the covid-19 pandemic: rapid review	British medical Journal / Research

Overviews, comments and editorials

Publication Date	Title/URL	Journal/ Article type
26.05.2020	SARS-CoV-2, bacterial co-infections, and AMR: the deadly trio in COVID-19?	EMBO Mol Med / Opinion
26.05.2020	Face coverings for the public: Laying straw men to rest	J Eval Clin Pract / Review

Produced by the PHE COVID-19 Literature Digest Team

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