



International EPI Cell Daily Evidence Digest – 04/06/2020

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:

- Serology and immunology
- Genomics
- Epidemiology and clinical - children and pregnancy
- Epidemiology and clinical - risk factors
- Epidemiology and clinical - other
- Infection control
- Treatment
- Social sciences
- 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Please note that we are including preprints (**highlighted in red**), which are preliminary reports of work that have NOT been peer-reviewed.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.

Serology and immunology

Publication Date	Title/URL	Journal/ Article type	Digest
03.06.2020	Seroprevalence of SARS-CoV-2 in Hong Kong and in residents evacuated from Hubei province, China: a multicohort study	The Lancet Microbe / Article	<ul style="list-style-type: none">• Aimed to establish the sensitivity and specificity of their enzyme immunoassay and microneutralization assay, and the seroprevalence of SARS-CoV-2 in Hong Kong before and after the pandemic, as well as in Hong Kong residents evacuated from Hubei province, China.• The seropositivity rate in Hubei returnees indicates that RT-PCR-confirmed patients only represent a small proportion of the total number of cases.

- The low seroprevalence suggests that most of the Hong Kong and Hubei population remain susceptible to COVID-19.
- Future waves of the outbreak are inevitable without a vaccine or antiviral prophylaxis.

Genomics

Publication Date	Title/URL	Journal/ Article type	Digest
01.06.2020	Two linear epitopes on the SARS-CoV-2 spike protein that elicit neutralising antibodies in COVID-19 patients	Nat Commun / Letter	<ul style="list-style-type: none"> • In this study, using pools of overlapping linear B-cell peptides, the authors report two IgG immunodominant regions on SARS-CoV-2 spike glycoprotein that are recognised by sera from COVID-19 convalescent patients. • Notably, one is specific to SARS-CoV-2, which is located in close proximity to the receptor binding domain. The other region, which is localised at the fusion peptide, could potentially function as a pan-SARS target. Functionally, antibody depletion assays demonstrate that antibodies targeting these immunodominant regions significantly alter virus neutralisation capacities. • Taken together, identification and validation of these neutralising B-cell epitopes will provide insights towards the design of diagnostics and vaccine candidates against this high priority coronavirus.
01.06.2020	Ethnically diverse mutations in PIEZO1 associate with SARS-CoV-2 positivity	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Study of patient data in UK Biobank released on 16 April 2020 support the notion of genetic factors influencing SARS-CoV-2 infection and suggest a specific role for PIEZO1. • Single nucleotide polymorphisms (SNPs) in gene encoding PIEZO1 are more common in individuals testing positive for SARS-CoV-2 regardless of pre-existing hypertension, myocardial infarction, stroke, diabetes mellitus or arthritis. • Some SNPs more common in African and Caribbean populations. One SNP is a missense mutation that results in an amino acid change in an evolutionarily conserved and previously unexplored N-terminal region PIEZO1.
30.05.2020	The Role of Host Genetic Factors in Coronavirus Susceptibility: Review of Animal and Systematic Review of Human Literature	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • PubMed-based search and analysis for articles relevant to host genetic factors in coronavirus. 1,187 articles of potential relevance. • Authors outline key genes and loci from animal and human host genetic studies that may bear investigation in the nascent host genetic factor studies of COVID-19.

- Previous human studies to date limited, including relatively low numbers of eligible participants and limited availability of advanced genomic methods.

Epidemiology and clinical – children and pregnancy

Publication Date	Title/URL	Journal/ Article type	Digest
03.06.2020	Clinical and Immune Features of Hospitalized Pediatric Patients With Coronavirus Disease 2019 (COVID-19) in Wuhan, China	JAMA Network Open / Original investigation	<ul style="list-style-type: none"> • In this case series (n=157), systemic inflammation rarely occurred in paediatric patients with COVID-19, in contrast with the lymphopenia and aggravated inflammatory responses frequently observed in adults with COVID-19. • Gaining a deeper understanding of the role of neutrophils, CD4+ T cells, and B cells in the pathogenesis of SARS-CoV-2 infection could be important for the clinical management of COVID-19.
03.06.2020	Epidemiology, Clinical Features, and Disease Severity in Patients With Coronavirus Disease 2019 (COVID-19) in a Children's Hospital in New York City, New York	JAMA Pediatr / Article	<ul style="list-style-type: none"> • This retrospective review of electronic medical records from a tertiary care academically affiliated children's hospital in New York City, included hospitalized children and adolescents (≤ 21 years) who were tested based on suspicion for COVID-19 between March 1 to April 15, 2020, and had positive results for SARS-CoV-2. • In this case series study of children and adolescents (n=50) hospitalised with COVID-19, the disease had diverse manifestations. Infants and immunocompromised patients were not at increased risk of severe disease. Obesity was significantly associated with disease severity. Elevated inflammatory markers were seen in those with severe disease.
03.06.2020	Kawasaki-like multisystem inflammatory syndrome in children during the covid-19 pandemic in Paris, France: prospective observational study	British Medical Journal / Research	<ul style="list-style-type: none"> • Evaluated a potential temporal association with SARS-CoV-2 infection in a cluster of 21 children and adolescents with features of Kawasaki disease who were admitted to the general paediatric department of a university hospital in Paris, France between 27 April and 11 May 2020 and followed up until discharge by 15 May. • In this study an unusually high proportion of the affected children and adolescents had gastrointestinal symptoms, Kawasaki disease shock syndrome, and were of African ancestry.
03.06.2020	COVID-19 pandemic: Impact caused by school closure and national lockdown on pediatric visits and admissions for viral and non-viral infections, a time series analysis	Clin Infect Dis / Article	<ul style="list-style-type: none"> • A time series analysis of 871,543 paediatric emergency visits revealed that the COVID-19 lockdown and school closure in France were associated with a significant decrease in infectious diseases disseminated through airborne or

			faecal-oral transmissions: common cold, gastro-enteritis, bronchiolitis, acute otitis. No change was found for urinary tract infections.
02.06.2020	Lockdown: more domestic accidents than COVID-19 in children	Arch Dis Child	<ul style="list-style-type: none"> Assessed the frequency and severity of presentations for domestic accidents in children between 8 March, when lockdown measures were enforced in their region (Padove, Italy) and 20 April 2020 compared with the corresponding period during the previous year. Number and severity of paediatric emergency department (PED) presentations for domestic accidents has significantly increased during the lockdown period compared with the previous year. The authors acknowledge their results are limited by the single-centre design and the low absolute numbers of study outcomes, with the possibility that small variations in numbers in each period could affect the effect size of findings. However, they believe they are useful to raise awareness that domestic accidents are posing a higher threat to children's health than COVID-19.

Epidemiology and clinical - risk factors

Publication Date	Title/URL	Journal/ Article type	Digest
24.05.2020	Lymphopenia in severe coronavirus disease-2019 (COVID-19): systematic review and meta-analysis	J Intensive Care / Article	<ul style="list-style-type: none"> Review to investigate the association of lymphocyte count on admission and the severity of COVID-19. Total of 3099 patients from 24 studies. Meta-analysis showed patients with poor outcome have lower lymphocyte count (mean difference – 361.06 μL [– 439.18, – 282.95], $p < 0.001$; I² 84%) compared to good outcome. Lymphopenia associated with severe COVID-19 (OR 3.70 [2.44, 5.63], $p < 0.001$; I² 40%). Meta-regression showed association between lymphocyte count and composite poor outcome was affected by age ($p = 0.034$).
01.06.2020	Prevalence and mortality of Lung Comorbidities Among Patients with COVID-19: A systematic review and meta-analysis	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> Literature review on prevalence of underlying lung comorbidities among COVID-19 patients, associated mortality. Last search date 29th April 2020. 29 articles (26 from China, 3 U.S). Pooled prevalence of lung comorbidities including Asthma, COPD, and lung cancer was 3% (95% CI=0-14%), 2.2% (95% CI=0.02-0.03%) and 2.1% (95% CI=0.00-0.21%) respectively. Mortality rates associated with these comorbidities was 30% (41/137) for COPD and 19% (7/37) for lung cancer. No mortality rates were reported for patients with asthma.

27.05.2020	Thrombosis risk associated with COVID-19 infection. A scoping review	Thrombosis Research / Article	<ul style="list-style-type: none"> • Scoping review identified 16 studies assessing thrombosis and coagulopathy in COVID-19 patients. Occurrence of venous thromboembolism and stroke in approximately 20% and 3% of patients, respectively. • A higher frequency seems to be present in severely ill patients, in particular those admitted to intensive care units.
02.06.2020	Thrombotic and hemorrhagic events in critically ill COVID-19 patients: a French monocenter retrospective study	Crit Care / Letter	<ul style="list-style-type: none"> • During the study period, 92 patients were admitted to their ICU for acute respiratory failure related to SARS-CoV-2 pneumonia. • At the time of analysis (May 6), 37 of them (40%) experienced a total of 39 thrombotic events (TE) including 31 venous (79%) and 8 arterial (21%) thrombosis, and 19 of them (21%) experienced a total of 22 haemorrhagic events (HE) during their ICU stay. • This study reports a high rate of TE and HE in ICU COVID-19 patients highlighting the necessity to adapt our thrombo-prophylaxis strategy as well as our TE screening strategy.
29.05.2020	Image-proven thromboembolism in patients with severe COVID-19 in a tertiary critical care unit in the United Kingdom	Thrombosis Research / Letter	<ul style="list-style-type: none"> • Assess prevalence and risk factors for image proven changes of immunothrombosis and venous thromboembolism (VTE) for 66 patients admitted to critical care with COVID-19. • 10 (15%) patients had at least one episode of image-proven thromboembolism (11 in total); there were six (9%) DVT and five (8%) patients with changes on CTPA. • Notably 11% patients also had major bleeding.

Epidemiology and clinical – other

Publication Date	Title/URL	Journal/ Article type	Digest
01.06.2020	Clinical characteristics of COVID-19 and active tuberculosis co-infection in an Italian reference hospital	Eur Respir J / Article	<ul style="list-style-type: none"> • This study describes clinical, radiological, and laboratory characteristics of a series of COVID-19 patients with concurrent active TB in a hospital in Sondrio province, Region Lombardy in northern Italy. • Among the 24 in-patients diagnosed with active TB, they identified 20 cases with COVID-19 co-infection. • Three patients reported having been vaccinated with Bacillus Calmette-Guérin (BCG). • Concluded that the impact of COVID-19 on active TB appears to be clinically manageable with proper care.

03.06.2020	Prevalence of Asymptomatic SARS-CoV-2 Infection	Annals of Internal Medicine / Review	<ul style="list-style-type: none"> • The authors sought to review and synthesize the available evidence on asymptomatic SARS-CoV-2 infection. • Asymptomatic persons seem to account for approximately 40% to 45% of SARS-CoV-2 infections, and they can transmit the virus to others for an extended period, perhaps longer than 14 days.
03.06.2020	Parotitis-Like Symptoms Associated with COVID-19, France, March-April 2020	Emerg Infect Dis / Letter	<ul style="list-style-type: none"> • Report the clinical features of 3 patients in France who had parotitis (inflammation of the parotid salivary glands) as a clinical manifestation of confirmed coronavirus disease. Results from magnetic resonance imaging support the occurrence of intraparotid lymphadenitis, leading to a parotitis-like clinical picture.
02.06.2020	Characteristics of U.S. Nursing Homes with COVID-19 Cases	J Am Geriatr Soc / Brief report	<ul style="list-style-type: none"> • Examined the characteristics of nursing homes with documented COVID-19 cases in 30 US states reporting individual facilities affected. • Of 9,395 nursing homes in their sample, 2,949 (31.4%) had a documented COVID-19 case. • Larger facility size, urban location, greater percentage of African American residents, non-chain status, and state were significantly ($p < 0.05$) related to increased probability of having a COVID-19 case. • Five-star rating, prior infection violation, Medicaid dependency, and ownership were not significantly related.
31.05.2020	Hospital readmissions of discharged patients with COVID-19	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Out of 1368 COVID-19 patients discharged from hospital during the study period, 61 patients (4.4%) were readmitted. • Rate of readmission after discharge was low. Immunocompromised patients and those presenting with fever during 48 hours prior to discharge at greater risk of readmission.
01.06.2020	Oxford Royal College of General Practitioners Clinical Informatics Digital Hub: Rapid innovation to deliver extended COVID-19 surveillance and trial platforms	JMIR Public Health Surveill / Article	<ul style="list-style-type: none"> • This paper describes the rapid design and development of the Oxford Royal College of General Practitioners Clinical Informatics Digital (ORCHID) Hub, and its first two platforms. • The Surveillance Platform will provide extended primary care surveillance, while the Trials Platform will be a streamlined clinical trials platform integrated into routine primary care practice.

Infection control

Publication Date	Title/URL	Journal/ Article type	Digest
04.06.2020	Social network-based distancing strategies to flatten the COVID-19 curve in a post-lockdown world	Nature Human Behaviour / Article	<ul style="list-style-type: none"> • Adopting a social network approach, they evaluate the effectiveness of three distancing strategies designed to keep the curve flat and aid compliance in a post-lockdown world. • Demonstrate that a strategic social network-based reduction of contact strongly enhances the effectiveness of social distancing measures while keeping risks lower. • Provide scientific evidence for effective social distancing that can be applied in public health messaging and that can mitigate negative consequences of social isolation.
01.06.2020	Test, track, and trace: How is the NHSX Covid app performing in a hospital setting?	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Survey of 462 (~15%) NHS staff members employed by Isle of Wight NHS Trust, to assess uptake and use of trial contact tracing app. 421 had no problem installing it. • 35 people either had to report symptoms or received an alert of contact with a suspected covid case. Of these over 20% were not clear what to do in such a situation. • Recommend: wording of alerts and guidance are clearer and more accessible; developments to facilitate use by healthcare workers in a clinical setting. Plus "app instructors" made available in hospitals to ensure that patients and staff can access help and advice on use of the app.
03.06.2020	SARS-CoV-2 RNA Detection on Disposable Wooden Chopsticks, Hong Kong	Emerg Infect Dis / Letter	<ul style="list-style-type: none"> • Detected SARS-CoV-2 RNA on disposable wooden chopsticks used by 5 consecutive asymptomatic and post symptomatic patients admitted for isolation and care at their hospital. • Although they did not assess virus viability, the findings may suggest potential for transmission through shared eating utensils.
28.05.2020	SARS-CoV-2 in environmental samples of quarantined households	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • 21 households under quarantine conditions randomly selected. Throat swabs from all adults and most children. Air, wastewater samples and surface swabs (commodities) analysed by RT-PCR. Positive swabs were cultivated to analyse for viral infectivity. • 26 of all 43 tested adults (60.47 %) positive. All 15 air samples PCR-negative. 10 of 66 wastewater samples were positive (15.15 %) and 4 of 119 object samples (3.36 %). • No infectious virus could be isolated under cell culture conditions. • Role of domestic environment, in particular the wastewater load in

washbasins and showers, in transmission of SARS CoV-2 should be further clarified.

Treatment

Publication Date	Title/URL	Journal/ Article type	Digest
03.06.2020	A Randomized Trial of Hydroxychloroquine as Postexposure Prophylaxis for Covid-19	New England Journal of Medicine / Article	<ul style="list-style-type: none"> • Conducted a randomized, double-blind, placebo-controlled trial across the United States and parts of Canada testing hydroxychloroquine as postexposure prophylaxis. • After high-risk or moderate-risk exposure to Covid-19, hydroxychloroquine did not prevent illness compatible with Covid-19 or confirmed infection when used as postexposure prophylaxis within 4 days after exposure.
03.06.2020	Lopinavir/ritonavir and interferon combination therapy may help shorten the duration of viral shedding in patients with COVID-19: a retrospective study in two designated hospitals in Anhui, China	J Med Virol / Article	<ul style="list-style-type: none"> • Factors associated with prolonged viral shedding were analysed with the Cox proportional hazards model. • Among 181 patients, the mean age was 44.3±13.2 years, and 55.2% were male. The median duration of viral shedding from illness onset was 18.0 days (IQR 15.0-24.0). • The severity of COVID-19 had nothing to do with prolonged shedding. Moreover, the median time from onset to antiviral treatment initiation was 5.0 days (IQR 3.0-7.0). Delayed antiviral treatment and lopinavir/ritonavir + IFN-α combination therapy as the initial antiviral treatment were independent factors associated with prolonged SARS-CoV-2 RNA shedding. • Early initiation of lopinavir/ritonavir + IFN-α combination therapy may help shorten the duration of SARS-CoV-2 shedding.
03.06.2020	COVID-19 patients benefit from early antiviral treatment: a comparative, retrospective study	J Med Virol / Article	<ul style="list-style-type: none"> • Enrolled 129 confirmed COVID-19 mild to moderate patients who had been treated with antiviral drugs during their hospitalization in Wuhan Union Hospital China. The patients were divided into early antiviral treatment group and late antiviral treatment group. • Data showed that the median time from illness onset to initiation of antiviral treatment was 6 days in all patients. The group with early antiviral treatment demonstrated 7 days shorter in the virus clearance time when compared to the group with late antiviral treatment. After virus clearance, the group with early antiviral treatment showed milder illness than the group with late antiviral treatment.

			<ul style="list-style-type: none"> • Early antiviral treatment could effectively shorten the virus clearance time, and prevent the rapid progression of COVID-19.
03.06.2020	Effect of Convalescent Plasma Therapy on Time to Clinical Improvement in Patients With Severe and Life-threatening COVID-19: A Randomized Clinical Trial	JAMA / Original Investigation	<ul style="list-style-type: none"> • Among patients with severe or life-threatening COVID-19, convalescent plasma therapy added to standard treatment (n=52), compared with standard treatment alone (n=51), did not result in a statistically significant improvement in time to clinical improvement within 28 days. • Interpretation is limited by early termination of the trial, which may have been underpowered to detect a clinically important difference.
30.05.2020	Therapeutic Anticoagulation Is Associated with Decreased Mortality in Mechanically Ventilated COVID-19 Patients	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Retrospective review of 245 COVID-19 patients admitted to ICU requiring mechanical ventilation: either received therapeutic anticoagulation for minimum of 5 days or prophylactic dose anticoagulation. • Propensity score (PS) weighted Kaplan-Meier plot demonstrated a survival advantage (57% vs. 25%) at 35 days from admission to ICU in patients who received therapeutic anticoagulation for a minimum of 5 days • A multivariate Cox proportional hazard regression model with PS weights to adjust for baseline differences found a 79% reduction in death in patients who were therapeutically anticoagulated HR 0.209, [95% CI (0.10, 0.46), p <0.001].
30.05.2020	Missing clinical trial data: the knowledge gap in the safety of potential COVID-19 drugs	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Review identifies important evidence gap for safety of drugs being repurposed for COVID-19. Clinical trial sponsors urged to report missing results retrospectively. • Of 3754 completed trials, 1516 (40.4%) did not post results on ClinicalTrials.gov or in academic literature. 1172 (31.2%) completed trials had tabular results on ClinicalTrials.gov. A further 1066 (28.4%) completed trials had results from the literature search, but did not report results on ClinicalTrials.gov. • Key drugs missing clinical trial results include hydroxychloroquine (37.0% completed trials unreported), favipiravir (77.8%) and lopinavir (40.5%).

Social sciences

Publication Date	Title/URL	Journal/ Article type	Digest
30.05.2020	COVID-19 pandemic and mental health consequences: systematic review of the current evidence	Brain Behav Immun / Systematic review	<ul style="list-style-type: none"> • A total of 43 studies were included. Out of these, only two studies evaluated patients with confirmed COVID-19 infection, whereas 41 evaluated the indirect effect of the pandemic (2 on patients with pre-existing psychiatric disorders, 20 on medical health care workers, and 19 on

			<p>the general public).</p> <ul style="list-style-type: none"> • The two studies investigating COVID-19 patients found a high level of post-traumatic stress symptoms (PTSS) (96.2%) and significantly higher level of depressive symptoms. • Patients with pre-existing psychiatric disorders reported worsening of psychiatric symptoms. • Studies investigating health care workers found increased depression/depressive symptoms, anxiety, psychological distress and poor sleep quality. • Studies of the general public revealed lower psychological well-being and higher scores of anxiety and depression compared to before COVID-19, while no difference when comparing these symptoms in the initial phase of the outbreak to four weeks later.
03.06.2020	Racial disparities in knowledge, attitudes and practices related to COVID-19 in the USA	J Public Health (Oxf) / Article	<ul style="list-style-type: none"> • The aim of this study was to determine whether disparities exist in the levels of knowledge, attitudes and practices (KAPs) related to COVID-19. • Analysed data from 1216 adults in the March 2020 Kaiser Family Foundation 'Coronavirus Poll', to determine levels of KAPs across different groups. Univariate and multivariate regression analysis was used to identify predictors of KAPs. • Racial and socioeconomic disparity exists in the levels of KAPs related to COVID-19. More work is needed to identify educational tools that tailor to specific racial and socioeconomic groups.
08.05.2020	Adolescents' Motivations to Engage in Social Distancing During the COVID-19 Pandemic: Associations With Mental and Social Health	J Adolesc Health / Article	<ul style="list-style-type: none"> • Using a large sample of adolescents from across the United States, this study examined adolescents' motivations for social distancing, their engagement in social distancing, and their mental and social health. • Data were collected on March 29th and 30th, 2020, two weeks after COVID-19 was declared a national emergency in the US. The sample consisted of 683 adolescents. • The most commonly reported motivations for social distancing concerned social responsibility and not wanting others to get sick. • Specific motivations for social distancing were differentially associated with adolescents' anxiety symptoms, depressive symptoms, burdensomeness, and belongingness.

Guidance, consensus statements

Publication Date	Title/URL	Journal/ Article type
04.06.2020	Conducting in-action and after-action reviews of the public health response to COVID-19	European Centre for Disease Control and Prevention / Technical report

Overviews, comments and editorials

Publication Date	Title/URL	Journal/ Article type
02.06.2020	Covid-19: 146 researchers raise concerns over chloroquine study that halted WHO trial	Bmj / News
03.06.2020	A Randomized Trial of Convalescent Plasma for COVID-19—Potentially Hopeful Signals	JAMA / Editorial
03.06.2020	Swabs Collected by Patients or Health Care Workers for SARS-CoV-2 Testing	New England Journal of Medicine / Correspondence
03.06.2020	Population serology for SARS-CoV-2 is essential to regional and global preparedness	The Lancet Microbe / Comment
23.05.2020	Co-infections among patients with COVID-19: The need for combination therapy with non-anti-SARS-CoV-2 agents?	J Microbiol Immunol Infect / Review
02.06.2020	Antimicrobial use, drug-resistant infections and COVID-19	Nat Rev Microbiol / Comment

Produced by the PHE COVID-19 Literature Digest Team

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