



International EPI Cell Daily Evidence Digest – 02/06/2020

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Please note that we are including preprints (**highlighted in red**), which are preliminary reports of work that have NOT been peer-reviewed.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

Serology and immunology

Publication Date	Title/URL	Journal/ Article type	Digest
28.05.2020	COVID-19 Patients with Recent Influenza A/B Infection: A Retrospective Study	J Infect / Letter	<ul style="list-style-type: none">• For this retrospective study, 1,386 COVID-19 patients were hospitalized between 18 Jan and 26 Apr 2020 at Tongji Hospital in Wuhan, China. All patients were pathogen-confirmed COVID-19 cases and accepted

			<p>serological influenza A/B IgM antibody tests upon admission.</p> <ul style="list-style-type: none"> • In summary, the results showed that recent influenza A/B infection in confirmed COVID-19 patients might be a common phenomenon. Moreover, they also observed that COVID-19 patients positive for influenza A IgM showed a lower risk of mortality and severe illness compared with those showing negative A/B IgM status. In contrast, this trend was not observed in influenza B IgM+ patients.
28.05.2020	Serum IgA, IgM, and IgG responses in COVID-19	Cell Mol Immunol / Correspondence	<ul style="list-style-type: none"> • Highly purified receptor-binding domain (RBD) of the SARS-CoV-2 spike protein was expressed in human 293F cells and used to make a set of chemical luminescence kits for detecting the presence of RBD-specific IgA, IgM, and IgG. • To evaluate the diagnostic power of the these kits, 216 sera from 87 SARS-CoV-2-infected patients and a total of 483 control sera including 330 healthy sera, 138 “interfering” sera of other-type patients and 15 sera from once-suspected pneumonia cases were tested. • This study provides valuable information regarding COVID-19 serological testing and seroconversion responses, especially for IgA antibodies.

Diagnostics

Publication Date	Title/URL	Journal/ Article type	Digest
28.05.2020	Improved sensitivity using a dual target, E and RdRp assay for the diagnosis of SARS-CoV-2 infection: Experience at a large NHS Foundation Trust in the UK	J Infect / Letter	<ul style="list-style-type: none"> • Explored the significance of E gene detection in relation to RdRp, and in the absence of RdRp detection in a retrospective evaluation of SARS-CoV-2 RT-PCR testing. • A total of 12,015 clinical samples (combined nose/throat swabs or lower respiratory tract samples) were tested for SARS-CoV-2 as part of routine clinical diagnostics between 2nd Mar 2020 and 5th Apr 2020 at Sheffield Teaching Hospitals NHS Foundation Trust. • By using the E gene target in addition to the RdRp gene target they observed a significantly increased diagnostic pick up (11.9%). The enhanced sensitivity seen for the E gene in their dual target E-RdRP assay is yet to be explained. • The authors believe dual target testing, using the E gene as a second target, will help improve both diagnostic sensitivity and the appropriate clinical response to this pandemic.

31.05.2020	Decreased B cells on admission was associated with prolonged viral RNA shedding from respiratory tract in Coronavirus Disease 2019: a case control study	J Infect Dis / Article	<ul style="list-style-type: none"> • Clinical data were collected and compared between patients with short and long viral RNA shedding (n=104). • The viral RNA shedding from respiratory tract in patients with normal B cell count was significantly shorter than patients with decreased B cell on admission (median [IQR], 11[9-13] vs 16[12-20] days, P=0.001).
30.05.2020	CT in coronavirus disease 2019 (COVID-19): a systematic review of chest CT findings in 4410 adult patients	Eur Radiol / Systematic review	<ul style="list-style-type: none"> • The objective of this systematic review was to evaluate the key imaging manifestations of COVID-19 on chest CT in adult patients by providing a comprehensive review of the published literature. • A total of 45 studies comprising 4410 patients were included. • The most common CT manifestations are bilateral, peripheral/subpleural, posterior GGOs with or without consolidations with a lower lobe predominance.
30.05.2020	SARS-CoV-2 PCR and antibody testing for an entire rural community: methods and feasibility of high-throughput testing procedures	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Describes high-volume, community-wide ascertainment of SARS-CoV-2 prevalence by PCR and antibody testing that was successfully performed using a community-led, drive-through model with strong operational support, well-trained testing units, and an effective technical platform.

Genomics

Publication Date	Title/URL	Journal/ Article type	Digest
01.06.2020	Shared SARS-CoV-2 diversity suggests localised transmission of minority variants	bioRxiv (non-peer reviewed) / New results	<ul style="list-style-type: none"> • Analysis of minor allele frequencies in 413 clinical samples from two UK locations show that SARS-CoV-2 infections are characterised by extensive within-host diversity, which is frequently shared among infected individuals with patterns consistent with geographical structure. • The authors conclude that SARS-CoV-2 diversity is transmissible, and propose that geographic patterns are generated by co-circulation of distinct viral populations.
01.06.2020	The landscape of host genetic factors involved in infection to common viruses and SARS-CoV-2	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Comprehensive study linking germline genetic variation and gene expression with antibody response to 28 antigens for 16 viruses using serological data from 7924 participants in the UK Biobank cohort. • Analyses of SARS-CoV-2 revealed the first genome-wide significant infection susceptibility signal in EHF, an epithelial-specific transcriptional repressor implicated in airway disease. Targeted analyses of expression quantitative trait loci suggest a possible role for tissue-specific ACE2 expression in modifying SARS-CoV-2 susceptibility.

Epidemiology and clinical – children and pregnancy

Publication Date	Title/URL	Journal/ Article type	Digest
30.05.2020	Children's heart and COVID-19: Up-to-date evidence in the form of a systematic review	Eur J Pediatr / Systematic review	<ul style="list-style-type: none"> This systematic review is aimed at summarizing all COVID-19 cases with a cardiac involvement published in paediatric age and trying to explain the underlying mechanisms responsible for COVID-19-related myocardial damage.

Epidemiology and clinical - risk factors

Publication Date	Title/URL	Journal/ Article type	Digest
28.05.2020	COVID-19 mortality in patients with cancer on chemotherapy or other anticancer treatments: a prospective cohort study	Lancet / Article	<ul style="list-style-type: none"> In this prospective observational study, all patients with active cancer and presenting to the network of cancer centres were eligible for enrolment into the UK Coronavirus Cancer Monitoring Project (UKCCMP). Analysed 800 patients with a diagnosis of cancer and symptomatic COVID-19. Concluded that mortality from COVID-19 in cancer patients appears to be principally driven by age, gender, and comorbidities. They were not able to identify evidence that cancer patients on cytotoxic chemotherapy or other anticancer treatment are at an increased risk of mortality from COVID-19 disease compared with those not on active treatment.
29.05.2020	Clinical characteristics and risk factors associated with COVID-19 disease severity in patients with cancer in Wuhan, China: a multicentre, retrospective, cohort study	Lancet Oncol / Article	<ul style="list-style-type: none"> 13,077 patients with COVID-19 were admitted to the nine hospitals in Wuhan and 232 patients with cancer and 519 statistically matched patients without cancer were enrolled. Patients with cancer and COVID-19 were more likely to deteriorate into severe illness than those without cancer. The risk factors identified here could be helpful for early clinical surveillance of disease progression in patients with cancer who present with COVID-19.
27.05.2020	Ethnicity profiles of COVID-19 admissions and outcomes	J Infect / Letter	<ul style="list-style-type: none"> Analysed routinely collected data from adult patients at Sheffield Teaching Hospitals (STH) between 01/03/20 and 25/04/20. Ethnicities were categorised into BAME, White and Not Known. A total of 3018 patients were tested for COVID-19, of whom 1493 were female and 1499 male (26 gender-unknown). Overall data showed that of the 3018 patients tested, 806 (26.7%) were

			<p>positive for COVID-19, including 95 from a BAME and 631 from a White background.</p> <ul style="list-style-type: none"> • Found that BAME men were significantly more likely to test positive compared to white men and BAME women in their cohort, and were at highest risk of ITU admission. The reasons for this are likely to be multifactorial, but they postulate that these may include a genetic predisposition to COVID-19 or because underlying co-morbidities make BAME groups more prone to becoming infected
01.06.2020	COVID-19 in Multiple Sclerosis Patients and Risk Factors for Severe Infection	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Prospective multicentre cohort study with 40 consecutive multiple sclerosis patients with COVID-19 between Mar 1st and May 18th, 2020. • Multiple sclerosis patients with more severe COVID-19 courses tended to be older, were more likely to suffer from progressive staging, and had a higher degree of disability. However, disease-modifying therapy use was not different among courses.
01.06.2020	Smoking and the risk of COVID-19 in a large observational population study	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • A case-control study among patients who underwent SARS-CoV-2 testing, to assess the impact of smoking on infection incidence and severity. • 114,545 distinct CHS members underwent RT-PCR tests for SARS-Cov-2, 4,537 (4.0%) of whom tested positive. Among them, they found that 9.8% were current smokers and 11.7% past smokers, while their corresponding rates within the adult population of CHS were 19.4% and 13.9% respectively (P<0.001). • Individuals with positive tests were matched in a 1:5 ratio to individuals who tested negative, of the same sex, age, and ethnicity/religion. • Current smoking was associated with significantly reduced odds ratio (OR) for testing positive OR=0.457 (95% confidence interval (CI) 0.407-0.514). Among patients that tested positive, there was no evidence of significantly increased risk of developing severe or fatal disease.
01.06.2020	The Association Between Angiotensin-Converting Enzyme Inhibitors and Angiotensin Receptor Blockers and the Number of Covid-19 Confirmed Cases and Deaths in the United States: Geospatial Study	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Geospatial study using publicly available county-level data, including Medicare ACE inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) prescription rates and confirmed cases and deaths from COVID-19. • The ACEI use had no effect on Covid-19 confirmed case rate and ARBs use (compared to no-use) was associated with a higher Covid-19 confirmed case rate and death rate. • Each percent increase in ARBs use was associated with an increase in confirmed case rate by 0.2(0.03-0.4)% and death rate by 0.14(0.08-0.21)%.

Epidemiology and clinical – other

Publication Date	Title/URL	Journal/ Article type	Digest
30.05.2020	Clinical features of 1487 COVID-19 patients with outpatient management in the Greater Paris: the COVID-call study	Intern Emerg Med / Article	<ul style="list-style-type: none"> • Investigated clinical features and classified symptoms as general, digestive, ear–nose–throat, thoracic symptoms, and eye disease. • 1487 patients included: 700 (47%) males and 752 (51%) females, with a median age of 44 (32–57) years. • The main difference between male and female patients was an increased prevalence of ear–nose–throat symptoms as well as diarrhoea, chest pains, and headaches in female patients. • General symptoms and ear–nose–throat symptoms were predominant in COVID-19 patients presenting mild-to-moderate symptoms. Shortness of breath and chest pain were remarkably frequent.
15.05.2020	Report into a nosocomial outbreak of coronavirus disease 2019 (COVID-19) at Netcare St. Augustine’s Hospital	Krisp / Report	<ul style="list-style-type: none"> • This report presents the findings and recommendations in an investigation into a nosocomial outbreak of COVID-19 at St. Augustin’s Hospital in Durban, South Africa. • Between 9 Mar and 30 Apr 2020, 119 confirmed cases were identified at St. Augustin’s Hospital (39 patients and 80 staff). • Overall they estimated that up to 135 infections may have been nosocomially acquired as a result of a single introduction of the virus to the hospital. • Phylogenetic analyses supports the main hypothesis of a unique introduction followed by widespread transmission in the hospital.
01.06.2020	Delirium Incidence, Duration and Severity in Critically Ill Patients with COVID-19	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Observational study at two large urban academic Level 1 trauma centres looking at delirium incidence, duration and severity in patients admitted to the intensive care unit (ICU) due to COVID-19 . • 73.6% (106/144) of patients admitted to the ICU with COVID-19 experience delirium that persists for approximately 1 week. Invasive mechanical ventilation is significantly associated with odds of delirium. • Clinical attention to prevent and manage delirium and reduce delirium duration and severity is urgently needed for patients with COVID-19.
25.05.2020	COVID-19-associated hyperviscosity: a link between inflammation and thrombophilia?	Lancet / Correspondence	<ul style="list-style-type: none"> • Describe COVID-19 associated hyperviscosity, a potentially severe consequence of infection with SARS-CoV-2, in 15 patients tested to date.

Infection control

Publication Date	Title/URL	Journal/ Article type	Digest
01.06.2020	Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis	The Lancet / Article	<ul style="list-style-type: none"> • Investigated the effects of physical distance, face masks, and eye protection on virus transmission in health-care and non-health-care (e.g., community) settings. • The findings of this systematic review and meta-analysis support physical distancing of 1 m or more and provide quantitative estimates for models and contact tracing to inform policy. • Optimum use of face masks, respirators, and eye protection in public and health-care settings should be informed by these findings and contextual factors.

Treatment

Publication Date	Title/URL	Journal/ Article type	Digest
01.06.2020	Mortality reduction in 46 severe Covid-19 patients treated with hyperimmune plasma. A proof of concept single arm multicenter interventional trial	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Multicentre one arm proof of concept interventional study. • 46 patients with Covid-19 disease with moderate-to-severe Acute Respiratory Distress Syndrome, elevated C-reactive Protein and need for mechanical ventilation and/or CPAP were enrolled. • Hyperimmune plasma showed promising benefits on mortality that need to be confirmed in a randomized controlled trial.

Modelling

Publication Date	Title/URL	Journal/ Article type	Digest
01.06.2020	Determining the optimal strategy for reopening schools, work and society in the UK: balancing earlier opening and the impact of test and trace strategies with the risk of occurrence of a secondary COVID-19 pandemic wave	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • This work uses an individual-based model to predict the impact of a suite of possible strategies to reopen schools in the UK, including that currently proposed by the UK government. • If UK schools reopen in phases from June 2020, prevention of a second wave would require testing 51% of symptomatic infections, tracing of 40% of their contacts, and isolation of symptomatic and diagnosed cases. • However, without such measures, reopening of schools together with

			gradual relaxing of the lockdown measures are likely to induce a secondary pandemic wave, as are other scenarios for reopening. <ul style="list-style-type: none"> To prevent a secondary COVID-19 wave, relaxation of social distancing including reopening schools in the UK must be implemented alongside an active large-scale population-wide testing of symptomatic individuals and effective tracing of their contacts, followed by isolation of symptomatic and diagnosed individuals.
01.06.2020	Estimating excess mortality in people with cancer and multimorbidity in the COVID-19 emergency	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> Weekly data until April 2020 demonstrate significant falls in admissions for chemotherapy (45-66% reduction) and urgent referrals for early cancer diagnosis (70-89% reduction), compared to pre-emergency levels. Under conservative assumptions of the emergency affecting only people with newly diagnosed cancer (incident cases) at COVID-19 PAE of 40%, and an RIE of 1.5, the model estimated 6,270 excess deaths at 1 year in England and 33,890 excess deaths in the US. Across a range of model assumptions, and across incident and prevalent cancer cases, 78% of excess deaths occur in cancer patients with ≥ 1 comorbidity.
01.06.2020	Effects of voluntary event cancellation and school closure as countermeasures against COVID-19 outbreak in Japan	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> Modelling the effects of voluntary event cancellation and school closure (VECSC) in Japan during January 14 through March 25, on the reproduction number before VECSC (R), during VECSC (Re), and after VECSC (Ra). Results suggest R before VECSC as 1.987 [1.908, 2.055], Re during VECSC as 1.122 [0.980, 1.260], and Ra after VECSC as 3.086 [2.529, 3.739]. Results demonstrated that VECSC can reduce COVID-19 infectiousness considerably, but the value of R rose to exceed 2.5 after VECSC.

Overviews, comments and editorials

Publication Date	Title/URL	Journal/ Article type
01.06.2020	Acute myocardial injury: a novel clinical pattern in children with COVID-19	The Lancet Child & Adolescent Health / Correspondence
28.05.2020	Shielding from covid-19 should be stratified by risk	British Medical Journal / Editorial
01.06.2020	Airborne Spread of SARS-CoV-2 and a Potential Role for Air Disinfection	JAMA / Viewpoint
01.06.2020	The COVID-19 Pandemic—Can open access modeling give us better answers more quickly?	Journal of Applied Clinical Medical Physics / Editorial
01.06.2020	Physical distancing, face masks, and eye protection for prevention of COVID-19	The Lancet / Comment
27.05.2020	Increased cardiovascular mortality in African Americans with COVID-19	Lancet Respir Med / Comment

29.05.2020	Poor clinical outcomes for patients with cancer during the COVID-19 pandemic	Lancet Oncol / Comment
29.05.2020	Cancer and COVID-19: what do we really know?	Lancet / Comment

Produced by the PHE COVID-19 Literature Digest Team

Bláthnaid Mahon, Caroline De Brún, Nicola Pearce-Smith, Ruth Muscat, Rachel Gledhill, Emma Farrow, Cath Hayes, Paul Rudd