

International EPI Cell Daily Evidence Digest – 29/05/2020

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:

- 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
- Modelling
- 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Please note that we are including preprints (**highlighted in red**), which are preliminary reports of work that have NOT been peer-reviewed.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	Seroprevalence of SARS-CoV-2 among children visiting a hospital during the initial Seattle outbreak	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • In the US, children represent 22% of the population but only 1.7% of confirmed SARS-CoV-2 cases. One possibility is that symptom-based viral testing is less likely to identify infected children, since they often experience milder disease than adults. • Of 1,076 children seeking medical care during Mar and Apr of 2020, only one child was seropositive in March, but nine were seropositive in April

for a period seroprevalence of >1%. Most seropositive children (8/10) were not suspected of having had COVID-19.

Diagnostics

Publication Date	Title/URL	Journal/ Article type	Digest
28.05.2020	Implication of SARS-CoV-2 evolution in the sensitivity of RT-qPCR diagnostic assays	The Lancet Infectious Diseases / Correspondence	<ul style="list-style-type: none"> • Report analysis of all high-coverage SARS-CoV-2 genome sequences (n=1825) deposited in the GISAID database as of Mar 30, 2020. Aligned the sequences against the ref sequence Wuhan-Hu-1 (NC_045512). • Annotated in the alignments the binding sites of 33 oligonucleotides developed by different centres and shared by WHO for use in the RT-qPCR detection of SARS-CoV-2. • The observation that at least one of the previously designed primers (by the Chinese National Institute for Viral Disease Control and Prevention) is now likely to be ineffective at detecting up to 14% of the virus variants in circulation in 24 different countries strengthens the need to continue optimising the oligonucleotides in use in assays being developed.
28.05.2020	Letter to the editor: SARS-CoV-2 detection by real-time RT-PCR	Eurosurveillance / Letter	<ul style="list-style-type: none"> • The authors query the SAR-CoV-2 RT-PCR assay developed by Corman et al. (https://doi.org/10.2807/1560-7917.ES.2020.25.3.2000045). • The proposed RdRp reverse primer contained an incorrect degenerate base (S), that does not match with the SARS-CoV-2 RNA sequence, as shown in the alignment of Corman et al. • Authors reply: (https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.21.2001035) 'Based on experimental validation, it later turned out that the mismatched base pairs do not reduce RT-PCR sensitivity and are not to be seen as the reason for somewhat higher Ct values with the RdRp assay as compared to the E gene assay'.
28.05.2020	Clinical Evaluation and Utilization of Multiple Molecular In Vitro Diagnostic Assays for the Detection of SARS-CoV-2	Am J Clin Pathol / Article	<ul style="list-style-type: none"> • Study to evaluate the clinical performance of 3 molecular assays, Abbott ID NOW COVID-19 (Abbott ID NOW), DiaSorin Molecular Simplexa COVID-19 Direct (DiaSorin Simplexa), and Roche cobas 6800 SARS-CoV-2 (Roche cobas), for SARS-CoV-2 (n=182 samples). • The positive percent agreement was 91% (95% confidence interval [CI], 0.76-0.97) for Abbott ID NOW and 100% (95% CI, 0.90-1.00) for DiaSorin Simplexa and Roche cobas. The negative percent agreement was 100% (95% CI, 0.98-1.00) for all 3 assays. All swab types tested with the Abbott

			<p>assay produced concordant results.</p> <ul style="list-style-type: none"> • PCR assays had approximately 10 to 100 times lower limits of detection than Abbott ID NOW.
27.05.2020	Comparison of two commercial molecular tests and a laboratory-developed modification of the CDC 2019-nCoV RT-PCR assay for the detection of SARS-CoV-2	J Clin Microbiol / Article	<ul style="list-style-type: none"> • Comparison of the ability of 2 commercial molecular amplification assays [RealTime SARS-CoV-2 on the m2000 (Abbott) (ACOV) and ID NOW™ COVID-19 (Abbott) (IDNOW)] and a laboratory-developed test [modified CDC 2019-nCoV RT-PCR assay with RNA extraction by eMag® (bioMérieux) and amplification on QuantStudio™ 6 or ABI 7500 Real-Time PCR System (Life Technologies) (CDC COV)] to detect SARS-CoV-2 RNA in upper respiratory tract specimens (n=200). • The IDNOW test was the easiest to perform and provided a result in the shortest time, but detected fewer cases of COVID-19. The ACOV assay detected more cases of COVID-19 than CDC COV or IDNOW assays.

Genomics

Publication Date	Title/URL	Journal/ Article type	Digest
28.05.2020	Insurgence and worldwide diffusion of genomic variants in SARS-CoV-2 genomes	bioRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • In this work the authors identified and traced over time 7 amino acid variants that are present with high frequency in Italy and Europe, but that were absent or present at very low frequencies during the first stages of the epidemic in China and the initial reports in Europe. • The analysis of these variants helps define 6 phylogenetic clades that are currently spreading throughout the world.

Epidemiology and clinical – children and pregnancy

Publication Date	Title/URL	Journal/ Article type	Digest
28.05.2020	No evidence of secondary transmission of COVID-19 from children attending school in Ireland, 2020	Eurosurveillance / Rapid communication	<ul style="list-style-type: none"> • As many countries begin to lift some of the restrictions to contain COVID-19 spread, lack of evidence of transmission in the school setting remains. • The authors examined Irish notifications of SARS-CoV2 in the school setting before school closures on 12 March 2020 and identified no paediatric transmission. • This adds to current evidence that children do not appear to be drivers

			of transmission, and we argue that reopening schools should be considered safe accompanied by certain measures.
28.05.2020	Ethnicity and COVID-19 in children with comorbidities	The Lancet Child & Adolescent Health / Correspondence	<ul style="list-style-type: none"> • Describe the effect of COVID-19 on paediatric patients with comorbidities and aim to facilitate rapid sharing of information in this dynamic and evolving situation. • Children (0-16 yo) with confirmed COVID-19 and comorbidities who required admission to hospital were prospectively identified from King's College Hospital, London, between Feb 25, 2020, and Apr 28, 2020. Demographic and clinical data were collected from electronic patient records or the clinical information system of the paediatric intensive care unit, or both. • Four of five patients with comorbidities were from BAME groups. In the wider group of paediatric patients admitted to hospital with COVID-19, nine (75%) of 12 patients were from a BAME group. This partly reflects the population of inner London, where ethnic minorities make up 39% of the population compared to just 13% in the rest of the UK. • Although hospitalisation for COVID-19 is rare in children, ethnicity and the presence of pre-existing comorbidities might be independent risk factors for severe disease.
28.05.2020	Multisystem Inflammatory Syndrome in Children during the COVID-19 pandemic: a case series	J Pediatric Infect Dis Soc / case series	<ul style="list-style-type: none"> • Case series of six critically ill children with Multisystem Inflammatory Syndrome in Children (MIS-C). • Key findings of this syndrome include fever, diarrhoea, shock, and variable presence of rash, conjunctivitis, extremity oedema, and mucous membrane changes.

Epidemiology and clinical - risk factors

Publication Date	Title/URL	Journal/ Article type	Digest
27.05.2020	Risk factors for death from COVID-19	Nat Rev Immunol/ In brief	<ul style="list-style-type: none"> • The authors used multivariable Cox proportional hazards model to identify the association of risk of death with older age, lower socio-economic status, being male, non-white ethnic background and certain clinical conditions. • Asthma was identified as a risk factor, despite prior suggestion of a potential protective role. • Higher risks due to ethnicity or lower socio-economic status could not be completely attributed to pre-existing health conditions.

28.05.2020	Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study	The Lancet / Article	<ul style="list-style-type: none"> • Characterise the outcomes of a cohort of patients with cancer and COVID-19 and identify potential prognostic factors for mortality and severe illness. • Of 1035 records entered into the COVID-19 and Cancer Consortium (CCC19) database during the study period, 928 patients met inclusion criteria for analysis. • Among patients with cancer and COVID-19, 30-day all-cause mortality was high and associated with general risk factors and risk factors unique to patients with cancer. Longer follow-up is needed to better understand the effect of COVID-19 on outcomes in patients with cancer, including the ability to continue specific cancer treatments.
28.05.2020	Description of COVID-19 in HIV-infected individuals: a single-centre, prospective cohort	The Lancet HIV / Article	<ul style="list-style-type: none"> • Included all consecutive HIV-infected individuals (aged ≥ 18 years) who had suspected or confirmed COVID-19 as of April 30, 2020, at the Hospital Universitario Ramón y Cajal (Madrid, Spain). • 51 HIV-infected individuals were diagnosed with COVID-19. • Concluded that HIV-infected individuals should not be considered to be protected from SARS-CoV-2 infection or to have lower risk of severe disease. Generally, they should receive the same treatment approach applied to the general population.
28.05.2020	Associations of hypertension with the severity and fatality of SARS-CoV-2 infection: A meta-analysis	Epidemiol Infect / review	<ul style="list-style-type: none"> • Twelve publications with 2389 COVID-19 patients (674 severe cases) were included for the analysis of disease severity. • The severity rate of COVID-19 in hypertensive patients was much higher than in non-hypertensive cases (37.58% vs 19.73%, pooled OR: 2.27; 95% CI: 1.80-2.86). • The pooled ORs of COVID-19 severity for hypertension versus non-hypertension was 2.21 (95%CI: 1.58-3.10) and 2.32 (95% CI: 1.70-3.17) in age < 50 years and ≥ 50 years patients, respectively.
27.05.2020	Impact of cardiovascular disease and cardiac injury on in-hospital mortality in patients with COVID-19: a systematic review and meta-analysis	Heart / review	<ul style="list-style-type: none"> • A total of 10 studies were enrolled in this meta-analysis, including eight studies for CVD, seven for hypertension and eight for acute cardiac injury. • The presence of CVD and hypertension was associated with higher odds of in-hospital mortality and acute cardiac injury was also associated with a higher unadjusted odds of 21.15 (95% CI 10.19 to 43.94; $I(2)=71\%$). • COVID-19 patients with underlying cardiovascular comorbidities, including CVD and hypertension, may face a greater risk of fatal outcomes. Acute cardiac injury may act as a marker of mortality risk.
26.05.2020	Diabetes is associated with increased risk for in-hospital mortality in patients with COVID-19: a systematic	medRxiv (non-peer reviewed) / Systematic review	<ul style="list-style-type: none"> • Systematic review and meta-analysis of the available observational studies reporting the effect of diabetes in mortality among hospitalized patients with COVID-19. 18,506 patients were included in this meta-

	review and meta-analysis comprising 18,506 patients	<p>analysis (3,713 diabetics and 14,793 non-diabetics).</p> <ul style="list-style-type: none"> • Patients with diabetes were associated with a higher risk of death compared to patients without diabetes. The heterogeneity was high. A study level meta-regression analysis was performed for all the important covariates and no significant interactions were found between the covariates and the outcome of mortality. • This meta-analysis shows that the likelihood of death is 65% higher in diabetic hospitalized patients with COVID-19 compared to non-diabetics. Further studies are needed to assess whether this association is independent or not, as well as to investigate the role of glucose control prior or during the disease.
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Epidemiology and clinical – other

Publication Date	Title/URL	Journal/ Article type	Digest
28.05.2020	Sharing patient-level real-time COVID-19 data	The Lancet Digital Health / Correspondence	<ul style="list-style-type: none"> • The paper highlights a dataset, containing international patient-level deidentified real-time data, released and curated by the Open COVID-19 Data Curation Group. • As of May, 2020, the dataset contains data of over 540 000 patients from 131 countries. All data are geocoded and include, where available, simple demographics, presence of comorbidity, symptoms, key dates, travel history, and outcomes. • A live version of the data record is available online and being continually updated. • This record has already yielded important results, such as a real-time visualisation tool (https://www.healthmap.org/covid-19/) and scientific publications, for example, on factors contributing to mortality or on the effect of human mobility on the pandemic.
29.05.2020	Report 24 - Anonymised & aggregated crowd level mobility data from mobile phones suggests initial compliance with COVID19 social distancing interventions was high & geographically consistent across UK	Imperial College / Report	<ul style="list-style-type: none"> • Used two mobile phone-based datasets to assess changes in average mobility, both overall and broken down into high and low population density areas, and changes in the distribution of journey lengths. • Show that there was a substantial overall reduction in mobility with the most rapid decline on the 24th Mar 2020, the day after the Prime Minister's announcement of an enforced lockdown. • Although mobility has remained low since 26th Mar 2020, they detected a gradual increase since that time.

			<ul style="list-style-type: none"> • These analyses form a baseline with which to monitor changes in behaviour in the UK as social distancing is eased.
29.05.2020	Report 25: Response to COVID-19 in South Korea and implications for lifting stringent interventions	Imperial College / Report	<ul style="list-style-type: none"> • Caution is needed in attempting to duplicate the South Korean response in settings with larger more generalized epidemics. • Finding, testing and isolating cases that are linked to clusters may be more difficult in such settings.
27.05.2020	Co-infections in people with COVID-19: a systematic review and meta-analysis	Journal of Infection / Systematic review	<ul style="list-style-type: none"> • SR and meta-analysis evaluating the burden of co-infections in patients with COVID-19. • Thirty studies including 3834 patients were included. Overall, 7% of hospitalised COVID-19 patients had a bacterial co-infection (95% CI 3-12%, n=2183, I²=92.2%). A higher proportion of ICU patients had bacterial co-infections than patients in mixed ward/ICU settings (14%, 95% CI 5-26, I²=74.7% versus 4%, 95% CI 1-9, I²=91.7%). • The most common bacteria were Mycoplasma pneumonia, Pseudomonas aeruginosa and Haemophilus influenzae. The pooled proportion with a viral co-infection was 3% (95% CI 1-6, n=1014, I²=62.3%), with Respiratory Syncytial Virus and influenza A being the most common. Three studies reported fungal co-infections. • A low proportion of COVID-19 patients have a bacterial co-infection; less than in previous influenza pandemics. These findings do not support the routine use of antibiotics in the management of confirmed COVID-19 infection.
28.05.2020	Coinfection with SARS-CoV-2 and other respiratory pathogens in COVID-19 patients in Guangzhou, China	J Med Virol / Letter	<ul style="list-style-type: none"> • Report of 14 cases of COVID-19 coinfecting with other respiratory pathogens and compare the clinical characteristics and laboratory results of COVID-19 patients with or without coinfection.
28.05.2020	Alterations in smell or taste - Classic COVID-19?	Clin Infect Dis / Letter	<ul style="list-style-type: none"> • To address deficiencies of current data the authors utilized a prospectively collected dataset from 1788 patients assessed for COVID-19 to determine if anosmia and/or ageusia were more frequent in patients with confirmed SARS-CoV-2 infection. • Their data highlights a significantly lower prevalence of symptoms in a comparative outpatient COVID-19 population (39.3% [AUS] versus 64.4% [US] versus 68% [Germany]) when prospective data is used. • They also demonstrate similar olfactory symptoms in the control group (SARS-CoV-2 negative) and conclude that from data available, anosmia and/or ageusia whilst associated with COVID-19 should not yet be considered pathognomonic for the disease.

27.05.2020	A systematic review on COVID-19: urological manifestations, viral RNA detection and special considerations in urological conditions	World J Urol / review	<ul style="list-style-type: none"> • Of 21 studies with 3714 COVID-19 patients, urinary symptoms were absent in all of them and 7.58% (95% CI 3.30-13.54%) developed acute kidney injury with a mortality rate of 93.27% (95% CI 81.46-100%) amongst them. • 5.74% (95% CI 2.88-9.44%) of COVID-19 patients had positive viral RNA in urine samples, but the duration of viral shedding in urine was unknown. • 31.6% of renal transplant recipients with COVID-19 required non-invasive ventilation, and the overall mortality rate was 15.4%.
28.05.2020	Continuous Electroencephalography (cEEG) Characteristics and Acute Symptomatic Seizures in COVID-19 Patients	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Retrospective cohort study of 22 critically-ill COVID-19 patients above the age of 18 years who underwent EEG (electroencephalography) monitoring. • 17 patients underwent EEG monitoring for unexplained altered mental status changes and 5 patients underwent monitoring for a seizure-like event. 5 patients had epileptiform abnormalities on EEG (4 patients on cEEG, 1 on routine EEG); and only 2 of 5 epileptic EEG patients had a prior history of epilepsy. • A higher proportion of patients in this series had electrographic seizures than previous literature suggests. This may be influenced by the duration of monitoring with cEEG and the use of a 21 channel electrode system.
28.05.2020	Acute Symptomatic Seizures in Critically Ill Patients with COVID-19: Is There an Association?	Neurocrit Care / Article	<ul style="list-style-type: none"> • Report two cases of acute symptomatic seizures, in non-epileptic patients, associated with severe COVID-19 disease.
27.05.2020	Unspecific post-mortem findings despite multiorgan viral spread in COVID-19 patients	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Study to evaluate whether some specific post-mortem features are observed in COVID-19 non-survivors and if these changes are related to the presence of the virus in different organs (in n=17 non-survivors). • Concluded that the autopsies revealed great heterogeneity of COVID-19-related organ injury and the remarkable absence of any specific viral lesions, even when RT-PCR identified the presence of the virus in many organs.

Infection control

Publication Date	Title/URL	Journal/ Article type	Digest
27.05.2020	Automated and partially-automated contact tracing: a rapid systematic	medRxiv (non-peer reviewed) / Rapid systematic review	<ul style="list-style-type: none"> • Rapid systematic review of automated or partially-automated contact tracing, registered with PROSPERO (CRD42020179822). • 4,033 citations were identified and 15 were included. No empirical

	review to inform the control of COVID-19	<p>evidence of automated contact tracing's effectiveness was identified. 4/7 included modelling studies suggested that controlling COVID-19 requires high population uptake of automated contact-tracing apps (estimates from 56% to 95%), typically alongside other control measures.</p> <ul style="list-style-type: none"> • Studies of partially-automated contact tracing generally reported more complete contact identification and follow-up, and greater intervention timeliness (0.5-5 hours faster), than previous systems. • Automated contact tracing has potential to reduce transmission with sufficient population uptake and usage. However, there is an urgent need for well-designed prospective evaluations as no studies provided empirical evidence of its effectiveness
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Treatment

Publication Date	Title/URL	Journal/ Article type	Digest
22.05.2020	Efficacy and safety of convalescent plasma for severe COVID-19 based on evidence in other severe respiratory viral infections: a systematic review and meta-analysis	Cmaj / Systematic review	<ul style="list-style-type: none"> • To support a guideline on COVID-19 management, the authors conducted a systematic review and meta-analysis of convalescent plasma in COVID-19 and other severe respiratory viral infections. • Of 1099 unique records, 6 studies were eligible, and none of these included patients with COVID-19. • Studies of non-COVID-19 severe respiratory viral infections provide indirect, very low-quality evidence that raises the possibility that convalescent plasma has minimal or no benefit in the treatment of COVID-19 and low-quality evidence that it does not cause serious adverse events.
28.05.2020	Experience with Hydroxychloroquine and Azithromycin in the COVID-19 Pandemic: Implications for QT Interval Monitoring	J Am Heart Assoc / Research article	<ul style="list-style-type: none"> • Case series of COVID-19 positive/suspected patients who were treated with azithromycin, hydroxychloroquine, or a combination. • Of 98 eligible participants, Azithromycin was prescribed in 28%, hydroxychloroquine in 10%, and both in 62%. • Overall 12% of patients manifested critical QTc prolongation, and the combination caused greater prolongation than either drug alone.
28.05.2020	Mechanistic insights into ventricular arrhythmogenesis of hydroxychloroquine and azithromycin for the treatment of COVID-19	bioRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Using comprehensive In Vitro ProArrhythmia Assay (CiPA) Schema IC50 paradigms, this study examined the cardiac electrophysiological effects of HCQ and HCQ/AZM. Molecular modelling explored HCQ and AZM binding properties to hERG. • Results provide an electrophysiological basis for recent FDA guidelines cautioning against combined HCQ/AZM administration for the treatment

of Covid-19 on the grounds of potential cardiac safety.

- The authors strongly recommend monitoring of electrocardiographic QT interval with the use of this combination of medications.

Social sciences

Publication Date	Title/URL	Journal/ Article type	Digest
28.05.2020	Mental Health Outcomes Among Frontline and Second-Line Health Care Workers During the Coronavirus Disease 2019 (COVID-19) Pandemic in Italy	JAMA Netw Open/Research letter	<ul style="list-style-type: none"> • Cross-sectional, web-based study reporting on mental health outcomes among HCWs in Italy. • These results are in line with previous reports from China, confirming a substantial proportion of mental health issues, particularly among young women and frontline HCWs.
26.05.2020	Mental health outcomes and associations during the coronavirus disease 2019 pandemic: A cross-sectional survey of the US general population	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Internet-based cross-sectional survey to determine the presence of and magnitude of associations between baseline associations and anxiety and depression in the US general population. • 232 subjects (23.6%) met criteria for clinical depression. On multivariable analysis, male sex, increased time outdoors, and living in a larger home, were associated with decreased odds of meeting depression criteria. Having lost a job, loneliness, and history of hospitalization, were associated with an increased odds of meeting depression criteria. • Income, media consumption, and religiosity were not associated with mental health outcomes.

Modelling

Publication Date	Title/URL	Journal/ Article type	Digest
24.05.2020	Modelling SARS-COV2 Spread in London: Approaches to Lift the Lockdown	J Infect / article	<ul style="list-style-type: none"> • A mathematical model for the transmission of SARS-CoV2 in London. • A combination of NPIs such as universal testing, contact tracing and mask use while under lockdown would be associated with least deaths and infections. • This approach would require high uptake and sustained local effort but it is potentially feasible as may lead to elimination in a relatively short time scale.

27.05.2020	Risk for COVID-19 Resurgence Related to Duration and Effectiveness of Physical Distancing in Ontario, Canada	Ann Intern Med / Letter	<ul style="list-style-type: none"> • Modelling study to explore the effect of physical distancing measures on COVID-19 transmission in the population of Ontario, Canada. • Without intervention, they projected that Ontario would have rapidly exceeded ICU capacity and observed substantially higher mortality. • The modelling also shows the challenges associated with relaxation of physical distancing measures without a concomitant increase in other public health measures. Specifically, when the number of contacts between persons returns to more than 50% of normal, they expect disease activity to resurge rapidly and ICUs to quickly reach capacity. • The model results suggest that in the absence of improved capacity for testing and contact tracing as a means of controlling COVID-19 spread, policymakers could consider staged relaxation of physical distancing and monitor changes in contacts as an early warning signal.
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Overviews, comments and editorials

Publication Date	Title/URL	Journal/ Article type
28.05.2020	COVID-19 and the difficulty of inferring epidemiological parameters from clinical data	The Lancet Infectious Diseases / Correspondence
28.05.2020	How might the NHS protect the mental health of health-care workers after the COVID-19 crisis?	The Lancet Psychiatry / Comment
27.05.2020	Digital contact tracing for COVID-19	Cmaj
28.05.2020	COVID-19 in people with HIV	The Lancet HIV / Comment

Produced by the PHE COVID-19 Literature Digest Team

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