



International EPI Cell Daily Evidence Digest – 09/06/2020

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:

- Diagnostics
- Genomics
- Epidemiology and clinical - children and pregnancy
- Epidemiology and clinical - risk factors
- Epidemiology and clinical - other
- Infection control
- Treatment
- Social sciences
- 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Please note that we are including preprints (**highlighted in red**), which are preliminary reports of work that have NOT been peer-reviewed.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
05.06.2020	CT Manifestations and Clinical Characteristics of 1115 Patients with Coronavirus Disease 2019 (COVID-19): A Systematic Review and Meta-analysis	Acad Radiol / Systematic review	<ul style="list-style-type: none">• A single-arm meta-analysis was conducted to obtain the pooled prevalence of significant computed tomographic(CT) manifestations of 14 articles (including 1115 patients).• In the lesion patterns on chest CTs, pure ground-glass opacities (GGO) (69%, 95% CI 58-80%), consolidation (47%, 35-60%) and "air bronchogram

sign" (46%, 25-66%) were more common than the atypical lesion of "crazy-paving pattern" (15%, 8-22%).

Genomics

Publication Date	Title/URL	Journal/ Article type	Digest
07.06.2020	Emerging viral mutants in Australia suggest RNA recombination event in the SARS-CoV-2 genome	Med J Aust/ Letter	<ul style="list-style-type: none"> • SARS-CoV-2 specimens independently isolated in Australia (in Sydney, the Gold Coast and Melbourne) exhibited very unusual mutations, which have not been identified in other countries. • The s2m sequence of coronaviruses is highly conserved, and spontaneous mutations in this motif were not expected to have occurred during the apparent short period when SARS-CoV-2 has been present; therefore, it is highly likely that the changes are due to recombination.

Epidemiology and clinical – children and pregnancy

Publication Date	Title/URL	Journal/ Article type	Digest
08.06.2020	Association Between Mode of Delivery Among Pregnant Women With COVID-19 and Maternal and Neonatal Outcomes in Spain	JAMA / Letter	<ul style="list-style-type: none"> • Assessed births to women with COVID-19 by mode of delivery. • In this cohort of pregnant women in Spain (n=82), severe adverse maternal outcomes occurred in 11% (9/82), 4 of whom presented with severe and 5 with mild COVID-19 symptoms. • Among patients with mild symptoms at presentation, all patients with a vaginal birth had excellent outcomes. In contrast, 13.5% of women undergoing caesarean delivery had severe maternal outcomes and 21.6% had clinical deterioration. • Women undergoing caesarean delivery may have been at higher risk of adverse outcomes, but after adjusting for confounding factors, caesarean birth remained independently associated with an increased risk of clinical deterioration. Caesarean delivery was also associated with an increased risk of NICU admission. • Limitations include a lack of sufficient information on new-borns to determine vertical transmission. Also, the 95% CIs around the odds ratios for caesarean birth were wide and the estimates fragile.

08.06.2020	Multisystem Inflammatory Syndrome Related to COVID-19 in Previously Healthy Children and Adolescents in New York City	JAMA / Letter	<ul style="list-style-type: none"> • This study describes 17 previously healthy children and adolescents who developed an inflammatory phenotype related to COVID-19. • Features overlapped with, but were distinct from, those of Kawasaki disease or toxic shock syndrome. • The observed pattern of cytokine expression suggests an interferon signalling component, along with IL-6 and IL-10 production, seen in KD5 and acute pulmonary COVID-19 infection. The lack of elevated TNF-α or IL-13 levels may differ from acute pulmonary COVID infections. The occurrence of abnormal cardiac findings suggests the need for long-term surveillance. • Limitations include the small number of patients, short follow-up period, and the inability to establish causality.
08.06.2020	Clinical Characteristics of 58 Children With a Pediatric Inflammatory Multisystem Syndrome Temporally Associated With SARS-CoV-2	JAMA / Original Investigation	<ul style="list-style-type: none"> • In this case series of hospitalized children who met criteria for paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (n=58), there was a wide spectrum of presenting signs and symptoms and disease severity, ranging from fever and inflammation to myocardial injury, shock, and development of coronary artery aneurysms. • The comparison with patients with Kawasaki disease (KD) and KD shock syndrome provides insights into this syndrome, and suggests this disorder differs from other paediatric inflammatory entities.

Epidemiology and clinical - risk factors

Publication Date	Title/URL	Journal/ Article type	Digest
04.06.2020	Comparison of clinical characteristics and outcomes of patients with coronavirus disease 2019 at different ages	Aging (Albany NY) / Article	<ul style="list-style-type: none"> • 1,000 patients diagnosed with COVID-19 from Jan 1, 2020 to Feb 14, 2020 were enrolled. According to age, patients were divided into group 1 (<60 years old), group 2 (60-74 years old) and group 3 (\geq75 years old). • The symptoms of the elderly patients were more atypical, with more comorbidities, secondary infection, organ injuries, immune dysfunction and a higher risk of critical illness. Older age was an important risk factor for mortality.
05.06.2020	Acute myocardial injury in patients hospitalized with COVID-19 infection: A review	Prog Cardiovasc Dis / Review	<ul style="list-style-type: none"> • In this review of clinical studies, it was found that in 26 studies including 11,685 patients, the weighted pooled prevalence of acute myocardial injury was 20% (ranged from 5% to 38% depending on the criteria used). • The plausible mechanisms of myocardial injury are discussed and implications include the urgent need for randomized trials to investigate

			treatment modalities to reduce the incidence and mortality associated with COVID-19 related acute myocardial injury.
03.06.2020	Cardiovascular complications in COVID-19: A systematic review and meta-analysis	J Infect / Systematic review	<ul style="list-style-type: none"> • 17 retrospective cohort studies comprising of 5,815 patients with COVID-19 were included. • Across 15 studies, the pooled prevalence of pre-existing hypertension in COVID-19 patients was 29.3% and pre-existing CVD across 16 studies was 14.6%. • The current data based on up-to-date evidence suggests that the most common cardiovascular complications of COVID-19 are heart failure, myocardial injury and cardiac arrhythmias; however the mechanisms for cardiovascular complications are still yet to be elucidated.
04.06.2020	Risk of COVID-19 infection in MS and neuromyelitis optica spectrum disorders	Neurol Neuroimmunol Neuroinflamm / Article	<ul style="list-style-type: none"> • Survey conducted through the Chinese Medical Network for Neuroinflammation on the risk of COVID-19 in patients with MS and neuromyelitis optica spectrum disorders (NMOSD). • 882/1,804 (48.89%) patients with MS and 2,129/3,060 (69.58%) patients with NMOSD were receiving Disease-modifying drugs (DMDs) and there were no alterations in the patients' DMD regimen during Jan 15, 2020, to Mar 15, 2020, the 3-month period. • None of the patients with MS treated with DMDs had COVID-19. However, 2 patients with relapsing NMOSD were diagnosed with COVID-19-related pneumonia. After treatment, both patients recovered from pneumonia and neither patient experienced new attacks due to predisposing SARS-CoV-2 infection in the following 2 months.
03.06.2020	Increased Risk of COVID-19-Related Deaths among General Practitioners in Italy	Healthcare (Basel)	<ul style="list-style-type: none"> • In Italy, available data highlight that GPs are, apparently, the most heavily affected group. • They currently represent 44.1% of the total COVID-19 related death cases occurred among physicians, whereas they constitute about 15% of the total number of doctors. • This high proportion is most likely the consequence of a work-related contagion happening especially during the first weeks of the epidemic, and persisting also in the following weeks, after the national lockdown. • Especially at the beginning of the epidemic, GPs might have had scant information on the specific safety procedures for the prevention of SARS-CoV-2 transmission (e.g., there was limited knowledge on the possibility of contagions deriving from asymptomatic patients) and, moreover, the availability of personal protective equipment was insufficient.

04.06.2020	The impact of occupational risk from COVID on GP supply in England: A cross-sectional study	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Cross sectional study of 45,858 GPs and 6,771 GP practices in the English NHS, to identify the risk of general practitioner mortality from COVID. • A significant proportion of GPs working in England, particularly those serving patients in the most deprived neighbourhoods, are at high risk. Many of these GPs run single-handed practices. These GPs are particularly concentrated in London. • There is an opportunity to provide additional support to mitigate COVID risk for GPs, GP practices and their patients. Failure to do so will likely exacerbate existing health inequalities.
06.06.2020	Enforced inactivity in the elderly and diabetes risk: initial estimates of the burden of an unintended consequence of COVID-19 lockdown	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Health Survey for England data is used to estimate the prevalence of pre-diabetes and physical activity in adults aged 70 and older. • From 9 million older (≥ 70 yrs) people living in England, 2.1 million could be defined as pre-diabetic. The estimated population attributable fraction (0.281) would give rise to 392,948 new cases of diabetes which could be directly attributed to a prolonged period of lockdown. • The authors estimate that inactivity related to lockdown in previously active older adults may contribute up to GBP 1.17b in additional healthcare costs through a potential increase in diabetes.
07.06.2020	Relationship Between Blood Group and Risk of Infection and Death in COVID-19: a live Meta-Analysis	medRxiv (non-peer reviewed) / Meta-analysis	<ul style="list-style-type: none"> • Meta-analysis showing that individuals with blood group A are at higher risk for COVID-19 infection while those with blood group O are at lower risk. • Although the odds ratio of death for AB blood group was non-significant, it was considerable.
05.06.2020	The Role of Vitamin D in The Age of COVID-19: A Systematic Review and Meta-Analysis Along with an Ecological Approach	medRxiv (non-peer reviewed) / Systematic review	<ul style="list-style-type: none"> • Rapid systematic review of 9 studies and meta-analysis of six studies containing 3,822 participants, to investigate the role of vitamin D in the COVID-19. • The meta-analysis indicated that 46.5% of COVID-19 patients were suffering from vitamin D deficiency and in 43.3% of patients, levels of vitamin D were insufficient. • An ecological investigation resulted in substantial direct and reverse correlations between recovery and mortality rates of COVID-19 patients with vitamin D status in different countries. Considering latitudes, a small reverse correlation between vitamin D status and mortality rate was found globally. • It seems that populations with lower levels of vitamin D might be more susceptible to the novel coronavirus infection, but due to multiple limitations, this study does not allow to quantify a value of the Vitamin D with full confidence.

Epidemiology and clinical – other

Publication Date	Title/URL	Journal/ Article type	Digest
08.06.2020	Low rate of bacterial co-infection in patients with COVID-19	The Lancet Microbe / Correspondence	<ul style="list-style-type: none"> Reviewed all microbiology results for patients admitted to Whiston hospital (Prescot, UK) with PCR-confirmed COVID-19 between Mar 6, and Apr 7, 2020. Identified 195 patients. Five (3% of 195, or 4% of 137 patients specifically tested), had pneumococcal co-infection and all survived to hospital discharge. One of 31 patients tested was positive for the Legionella antigen without lower respiratory tract samples to confirm legionellosis. Bacteria grew from four of 26 sputum samples. All bacteria were Gram-negative bacilli more typically associated with oropharyngeal colonisation than community-acquired pneumonia. Findings suggest that bacterial co-infection is uncommon in patients with COVID-19 who are newly admitted to hospital. The main limitation is the variability of microbiological sampling. Results might not be generalisable to other geographical settings.
08.06.2020	Pulmonary post-mortem findings in a series of COVID-19 cases from northern Italy: a two-centre descriptive study	The Lancet Infectious Diseases / Article	<ul style="list-style-type: none"> Systematically analysed lung tissue samples from 38 patients who died from COVID-19 in two hospitals in northern Italy between Feb 29 and Mar 24, 2020. The predominant pattern of lung lesions in patients with COVID-19 patients is diffuse alveolar damage, as described in patients infected with SARS and MERS coronaviruses. Hyaline membrane formation and pneumocyte atypical hyperplasia are frequent. Importantly, the presence of platelet–fibrin thrombi in small arterial vessels is consistent with coagulopathy, which appears to be common in patients with COVID-19 and should be one of the main targets of therapy.
04.06.2020	Early evidence of pronounced brain involvement in fatal COVID-19 outcomes	Lancet / Correspondence	<ul style="list-style-type: none"> Reports the findings of autopsies of six patients (four men and two women, aged 58–82 years) who died from COVID-19 in April, 2020. In addition to pneumonia, a pronounced CNS involvement with pan-encephalitis, meningitis, and brainstem neuronal cell damage were key events in all cases. In patients younger than 65 years, CNS haemorrhage was a fatal complication of COVID-19.
01.06.2020	Analysis of Gastrointestinal and Hepatic Manifestations of SARS-CoV-2 Infection in 892 patients in Queens, NY	Clin Gastroenterol Hepatol / Article	<ul style="list-style-type: none"> Retrospective review of 892 consecutive adult, non-pregnant patients admitted to a New York hospital for SARS-CoV-2 between Mar 14, 2020 and Apr 1, 2020.

			<ul style="list-style-type: none"> • There was no difference between patients with or without GI symptoms on presentation with regard to rate of intubation (p=0.3), ICU admission (p=0.4), length of stay (p=0.8), or mortality (p=0.067). • An abnormal initial AST as compared to a normal initial AST was associated with higher rates of intubation (18% vs. 12%; p=0.01), ICU admission (18% vs. 11%; p=0.005), and mortality (28% vs. 20%; p=0.009).
05.06.2020	Associations between COVID-19 infection, tobacco smoking and nicotine use, common respiratory conditions and inhaled corticosteroids: a prospective QResearch-Case Mix Programme data linkage study January-May 2020	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Prospective cohort study linking English general practice records from the QResearch database to Public Health England's database of SARS-CoV-2 positive tests, Hospital Episode Statistics, admission to intensive care units, and death from COVID-19. • Analysis of data from this representative population sample will present a comprehensive examination of the association between smoking, nicotine use without smoking, respiratory disease, and severity of COVID-19. • The authors will undertake several sensitivity analyses to examine the potential for bias in these associations.
08.06.2020	First Reported Cases of SARS-CoV-2 Infection in Companion Animals — New York, March–April 2020	CDC / MMWR Morbidity and Mortality Weekly Report	<ul style="list-style-type: none"> • Two domestic cats with respiratory illnesses lasting 8 and 10 days are the first reported companion animals with SARS-CoV-2 infection in the United States. • Both cats were owned by persons with suspected or confirmed COVID-19, and both cats fully recovered.
08.06.2020	Analysis of hospital traffic and search engine data in Wuhan China indicates early disease activity in the Fall of 2019	DASH.Harvard.edu / Article	<ul style="list-style-type: none"> • Origin of COVID-19 is believed to be linked to Wuhan's Huanan Seafood Market in Nov/Dec 2019. Evidence suggests the virus may have already been circulating at the time of the outbreak. • Used previously validated data streams - satellite imagery of hospital parking lots and Baidu search queries of disease related terms - to investigate this possibility. • Observed an upward trend in hospital traffic and search volume beginning in late Summer and early Fall 2019. While queries of the respiratory symptom "cough" show seasonal fluctuations coinciding with yearly influenza seasons, "diarrhoea" is a more COVID-19 specific symptom and only shows an association with the current epidemic. • The increase of both signals precede the documented start of the COVID-19 pandemic in Dec, highlighting the value of novel digital sources for surveillance of emerging pathogens. <p><i>(This paper was included due to significant media pick-up)</i></p>

Infection control

Publication Date	Title/URL	Journal/ Article type	Digest
08.06.2020	Options for the decontamination and reuse of respirators in the context of the COVID-19 pandemic	European Centre for Disease Control and Prevention / Technical report	<ul style="list-style-type: none"> • This document provides an overview of the evidence on the available methods for decontaminating respirators or filtering face pieces (FFP), in the event of shortages, used in healthcare settings providing care to possible, probable or confirmed COVID-19 patients. • Guiding principles for reuse are: <ul style="list-style-type: none"> - Respirators which have been visibly contaminated (e.g. during procedure at intubated patients, such as suction cleaning of airways, taking probes, extubation attempts, etc.) or are damaged or not fitting, should be discarded and cannot be taken for re-use or decontamination procedures. - Respirators may be protected by a medical face mask in order to prevent soiling. - Use of new 'expired respirators' (manufacturers expiry date) is possible if they were properly stored until use.

Treatment

Publication Date	Title/URL	Journal/ Article type	Digest
08.06.2020	Stability and neutralising capacity of SARS-CoV-2-specific antibodies in convalescent plasma	The Lancet Microbe / Correspondence	<ul style="list-style-type: none"> • Analysed the effect of psoralen and ultraviolet light pathogen inactivation on the total SARS-CoV-2 IgG titre and neutralising capacity (live virus assay) in convalescent plasma obtained from patients who have recovered from COVID-19. • Data suggest that pathogen inactivation of convalescent plasma from patients who have recovered from COVID-19 does not alter the potential therapeutic potency and should be recommended to mitigate the risk for transfusion associated viral transmission. • Considering the currently unproven clinical benefit of convalescent plasma obtained from patients who have had COVID-19, a shift in the risk–benefit ratio towards benefit by means of pathogen inactivation should be employed in all cases, in settings where the use of pathogen inactivation methods are available and established.
04.06.2020	Drug-Drug interactions between COVID-19 treatments and antipsychotics drugs:	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Evidence review and systematic review of drug-drug interactions between COVID-19 treatments and antipsychotics.

	integrated evidence from 4 databases and a systematic review	<ul style="list-style-type: none"> • The main interaction between COVID-19 drugs and antipsychotics are the risk of QT prolongation and TdP, and CYP interactions. • Remdesivir, favipiravir, baricitinib, and anakinra can be used concomitantly with antipsychotics with no risk of drug-drug interaction (except for haematological risk with clozapine and baricitinib). • Tocilizumab is rather safe to use in combination with antipsychotics, although it can restore the activity of CYP3A4 and therefore its substrate metabolism may increase. • The most demanding COVID-19 treatments for co-administration with antipsychotics are chloroquine, hydroxychloroquine, azithromycin (all prolong QT interval) and lopinavir / ritonavir (CYP interaction and risk of QT prolongation).
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Social sciences

Publication Date	Title/URL	Journal/ Article type	Digest
13.05.2020	The online competition between pro- and anti-vaccination views	Nature / Article	<ul style="list-style-type: none"> • The authors describe a theoretical framework that reproduces the recent explosive growth in anti-vaccination views, and predicts that these views will dominate in a decade. • Insights provided by this framework can inform new policies and approaches to interrupt this shift to negative views. • The results challenge the conventional thinking about undecided individuals in issues of contention surrounding health, shed light on other issues of contention such as climate change, and highlight the key role of network cluster dynamics in multi-species ecologies.
06.06.2020	Predictors of Mental Health during the early Covid-19 Pandemic in the US: role of economic concerns, health worries and social distancing	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Online survey data from the Understanding America Study (UAS) showed that ~ 29% (CI:27.4-.30.4%) of the US adult population reported some depression/anxiety symptoms over the study period, with symptoms deteriorating over the month of March. • Worsening mental health was most strongly associated with concerns about the economic consequences of the pandemic, while concerns about the potential impact of the virus on respondents' own health and the practice of social distancing also predicted the presence of depression and anxiety symptoms, albeit less strongly. • These findings point towards a major mental health crisis unfolding simultaneously with the pandemic in the US.

Modelling

Publication Date	Title/URL	Journal/ Article type	Digest
08.06.2020	The effect of large-scale anti-contagion policies on the COVID-19 pandemic	Nature / Article	<ul style="list-style-type: none"> • Analysis of data on 1,717 local, regional, and national non-pharmaceutical interventions deployed in China, South Korea, Italy, Iran, France, and the US to evaluate the effect that anti-contagion policies have had on the growth rate of infections. • They estimate that across these six countries, interventions prevented or delayed on the order of 62 million confirmed cases, corresponding to averting roughly 530 million total infections. • These findings may help inform whether or when these policies should be deployed, intensified, or lifted, and they can support decision-making in the other 180+ countries where COVID-19 has been reported.
08.06.2020	Estimating the effects of non-pharmaceutical interventions on COVID-19 in Europe	Nature / Article	<ul style="list-style-type: none"> • Modelling study of the impact of major interventions across 11 European countries for the period from the start of COVID-19 until the 4 May 2020 when lockdowns started to be lifted. • Current interventions have been sufficient to drive the reproduction number and achieve epidemic control. • It is estimated that across all 11 countries, between 12 and 15 million individuals have been infected with SARS- CoV-2 up to 4 May, representing between 3.2% and 4.0% of the population. • The results show that major non-pharmaceutical interventions and lockdown in particular have had a large effect on reducing transmission.
08.06.2020	Report 26 Reduction in mobility and COVID-19 transmission	Imperial College / Report 26	<ul style="list-style-type: none"> • Developed a framework to infer the relationship between mobility and the key measure of population-level disease transmission, the reproduction number (R). The framework was applied to 53 countries with sustained SARS-CoV-2 transmission based on two distinct country-specific automated measures of human mobility, Apple and Google mobility data. • For both datasets, the relationship between mobility and transmission was consistent within and across countries and explained more than 85% of the variance in the observed variation in transmissibility. • While social contacts were sufficiently reduced in France, Spain and the UK to control COVID-19 as of the 10th of May, they find that enhanced control measures are still warranted for the majority of countries. • Easing social-distancing restrictions should be considered very carefully, as small increases in contact rates are likely to risk resurgence even where COVID-19 is apparently under control.

03.06.2020	Discrete SIRIR modelling using empirical infection data shows that SARS-CoV-2 infection provides short-term immunity	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> Modelling study predicting that cases of reinfection should have been observed by now if primary SARS-CoV-2 infection did not protect from subsequent exposure in the short term, however, no such cases have been documented.
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Guidance, consensus statements

Publication Date	Title/URL	Journal/ Article type
25.05.2020	Consensus summary report for CEPI/BC March 12-13, 2020 meeting: Assessment of risk of disease enhancement with COVID-19 vaccines	Vaccine / Conference report

Overviews, comments and editorials

Publication Date	Title/URL	Journal/ Article type
04.06.2020	Autoimmune and inflammatory diseases following COVID-19	Nat Rev Rheumatol / news & views
08.06.2020	SARS-CoV-2–Related Inflammatory Multisystem Syndrome in Children: Different or Shared Etiology and Pathophysiology as Kawasaki Disease?	Jama / Editorial
08.06.2020	Monitoring investments in coronavirus research and development	The Lancet Microbe / Correspondence
05.06.2020	The "virtual wards" supporting patients with covid-19 in the community	Bmj / Feature
08.06.2020	We risk letting a new threat expose us to old enemies	The Lancet Microbe / Editorial

Produced by the PHE COVID-19 Literature Digest Team