



International EPI Cell Daily Evidence Digest – 15/06/2020

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
- 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Please note that we are including preprints (**highlighted in red**), which are preliminary reports of work that have NOT been peer-reviewed.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.

Serology and immunology

Publication Date	Title/URL	Journal/ Article type	Digest
12.06.2020	Assessment of spread of SARS-CoV-2 by RT-PCR and concomitant serology in children in a region heavily affected by COVID-19 pandemic	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none">• To examine spread of SARS-CoV-2, authors combined both RT-PCR testing and serology in 605 children in the most affected region in France during the epidemic.• 322 (53.2%) were asymptomatic and 283 (46.8%) symptomatic. RT-PCR testing and serology were positive for 11 (1.8%) and 65 (10.7%) of all children, respectively. Only 3 children were RT-PCR-positive without any antibody response detected.

		<ul style="list-style-type: none"> • Frequency of positivity on RT-PCR for SARS-CoV-2 was significantly higher in children with positive serology than those with a negative one. • Contact with a person with proven COVID-19 increased the odds of positivity on RT-PCR (OR 7.8, 95% confidence interval [1.5; 40.7]) and serology (15.1 [6.6; 34.6]). • Authors conclude rate of children with positive SARS-CoV-2 RT-PCR was very low (1.8%), but rate of positive on serology was higher (10.7%).
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Genomics

Publication Date	Title/URL	Journal/ Article type	Digest
12.06.2020	Genotyping SARS-CoV-2 through an interactive web application	The Lancet Digital Health / Comment	<ul style="list-style-type: none"> • Although platforms to survey epidemiological data are prevalent, tools that summarise publicly available viral genome data are scarce and those that are available do not offer users the ability to analyse inhouse sequencing data. • To address this gap, the authors have developed an accessible application, the COVID-19 Genotyping Tool (CGT).
12.06.2020	The D614G mutation in the SARS-CoV-2 spike protein reduces S1 shedding and increases infectivity	bioRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • SARS-CoV-2 isolates encoding a D614G mutation in the viral spike (S) protein predominate over time in locales where it is found, implying that this change enhances viral transmission. • Investigating this, the authors observed that retroviruses pseudotyped with SG614 infected ACE2-expressing cells markedly more efficiently than those with SD614, and this was correlated with less S1 shedding and greater incorporation of the S protein into the pseudovirion. • Similar results were obtained using the virus-like particles produced with SARS-CoV-2 M, N, E, and S proteins. However, SG614 did not bind ACE2 more efficiently than SD614, and the pseudoviruses containing these S proteins were neutralized with comparable efficiencies by convalescent plasma. • These results are consistent with epidemiological data suggesting that viruses with SG614 transmit more efficiently.
11.06.2020	SARS-CoV-2 mRNA Vaccine Development Enabled by Prototype Pathogen Preparedness	bioRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • The release of SARS-CoV-2 sequences triggered immediate rapid manufacturing of an mRNA vaccine expressing the prefusion-stabilized SARS-CoV-2 spike trimer (mRNA-1273). • Authors show that mRNA-1273 induces both potent neutralizing antibody and CD8 T cell responses and protects against SARS-CoV-2

			infection in lungs and nose of mice without evidence of immunopathology. <ul style="list-style-type: none"> • mRNA-1273 is currently in a Phase 2 clinical trial with a trajectory towards Phase 3 efficacy evaluation.
12.06.2020	Structural basis for the neutralization of SARS-CoV-2 by an antibody from a convalescent patient	bioRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • The authors report they have isolated an antibody, EY6A, from a late-stage COVID-19 patient and show it neutralises SARS-CoV-2 and cross-reacts with SARS-CoV-1. • EY6A Fab binds tightly (KD of 2 nM) the receptor binding domain (RBD) of the viral Spike glycoprotein and a 2.6Å crystal structure of an RBD/EY6A Fab complex identifies the highly conserved epitope, away from the ACE2 receptor binding site. Residues of this epitope are key to stabilising the pre-fusion Spike. • EY6A binds what is probably a major neutralising epitope, making it a candidate therapeutic for COVID-19.

Epidemiology and clinical – children and pregnancy

Publication Date	Title/URL	Journal/ Article type	Digest
12.06.2020	Paediatric Inflammatory Multisystem Syndrome: Temporally Associated with SARS-CoV-2 (PIMS-TS): Cardiac Features, Management and Short-Term Outcomes at a UK Tertiary Paediatric Hospital	Pediatr Cardiol / Article	<ul style="list-style-type: none"> • Describe cardiac findings and short-term outcomes in children with Paediatric Inflammatory Multisystem Syndrome-temporally associated with SARS-CoV-2 (PIMS-TS) at a tertiary children's hospital.

Epidemiology and clinical - risk factors

Publication Date	Title/URL	Journal/ Article type	Digest
09.06.2020	Clinical characteristics and outcomes of COVID-19 hospitalized patients with diabetes in UK: A retrospective single centre study	Diabetes Res Clin Pract / Article	<ul style="list-style-type: none"> • A retrospective cross-sectional study was conducted among patients admitted to the William Harvey Hospital in England between Mar 10 and May 10, 2020 with a laboratory-confirmed SARS-CoV-2 (n= 232). • Variation in characteristics, length of stay in hospital, diabetes status, duration of diabetes, control of diabetes, comorbidities and outcomes were examined. • Males were more likely to be admitted to hospital with COVID-19 illness

			<p>than females.</p> <ul style="list-style-type: none"> • Hospitalized COVID-19 patients with diabetes had a longer LOS in hospital than patients without diabetes. • Older age COVID-19 patients with diabetes and patients without diabetic ketoacidosis (DKA) were less likely to survive compared to younger patients and patients with DKA, respectively.
12.06.2020	Factors Associated With Surgical Mortality and Complications Among Patients With and Without Coronavirus Disease 2019 (COVID-19) in Italy	JAMA Surg / Original investigation	<ul style="list-style-type: none"> • Evaluated early surgical outcomes of patients with COVID-19 in different subspecialties. • Of the 123 patients of the combined cohorts (78 women [63.4%]; mean [SD] age, 76.6 [14.4] years), 30-day mortality was significantly higher for those with COVID-19 compared with control patients without COVID-19 (odds ratio [OR], 9.5; 95% CI, 1.77-96.53). • Complications were also significantly higher (OR, 4.98; 95% CI, 1.81-16.07); pulmonary complications were the most common (OR, 35.62; 95% CI, 9.34-205.55), but thrombotic complications were also significantly associated with COVID-19 (OR, 13.2; 95% CI, 1.48). • In this matched cohort study, surgical mortality and complications were higher in patients with COVID-19 compared with patients without COVID-19. These data suggest that, whenever possible, surgery should be postponed in patients with COVID-19.
10.06.2020	Value of leukocytosis and elevated C-reactive protein in predicting severe coronavirus 2019 (COVID-19): A systematic review and meta-analysis	Clin Chim Acta / Article	<ul style="list-style-type: none"> • Investigated the association between severe COVID-19 and a change in white blood cell (WBC) count, an elevation of C-reactive protein (CRP), and fever. • In patients with COVID-19, fever, leucocytosis, and an elevated CRP were associated with severe outcomes. Leucocytosis and CRP on arrival may predict poor outcomes.
10.06.2020	Ethnicity and outcomes in patients hospitalised with COVID-19 infection in East London: an observational cohort study	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Prospective analysis of registry data describing patients admitted to five acute NHS Hospitals in east London, UK for COVID-19. • 1737 patients included in analysis of whom 511 had died by day 30 (29%). 538 (31%) were from Asian, 340 (20%) Black and 707 (40%) white backgrounds. • Patients from BAME backgrounds were younger, with differing co-morbidity profiles and less frailty. Asian and black patients more likely to be admitted to intensive care and to receive invasive ventilation (OR 1.54, [1.06-2.23]; p=0.023 and 1.80 [1.20-2.71]; p=0.005, respectively). • After adjustment for age and sex, patients from Asian (HR 1.49 [1.19-1.86]; p<0.001) and black (HR 1.30 [1.02-1.65]; p=0.036) backgrounds were more likely to die.

			<ul style="list-style-type: none"> Analyses suggest that patients of Asian and Black backgrounds suffered disproportionate rates of premature death from COVID-19.
10.06.2020	Multimorbidity, Polypharmacy, and COVID-19 infection within the UK Biobank cohort	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> Using data from the UK Biobank, the authors examine the relationships between multimorbidity, polypharmacy (a proxy of multimorbidity), and COVID-19; and how these differ by sociodemographic, lifestyle, and physiological prognostic factors. Increasing multimorbidity, especially cardiometabolic multimorbidity, and polypharmacy were found to be associated with a higher risk of developing COVID-19. Those with multimorbidity and additional factors, such as non-white ethnicity, are at heightened risk of COVID-19.
11.06.2020	Renin-angiotensin system blockers and susceptibility to COVID-19: a multinational open science cohort study	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> Systematic cohort study with prevalent ACE, ARB, calcium channel blocker (CCB) and thiazide diuretic (THZ) use to determine relative risk of COVID-19 diagnosis and related hospitalization outcomes. Over 1.1 million antihypertensive users identified between November 2019 and January 2020 followed. No clinically significant increased risk of COVID-19 diagnosis or hospitalization with ACE or ARB use. Users should not discontinue or change their treatment to avoid COVID-19.
11.06.2020	Comorbidity and Sociodemographic determinants in COVID-19 Mortality in an US Urban Healthcare System	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> Evaluation of 7,592 confirmed COVID-19 patients in New York City, to determine to what degree medical comorbidity and sociodemographic determinants impact COVID-19 mortality in the US. Of common comorbid conditions (hypertension, chronic kidney disease, chronic obstructive pulmonary disease, asthma, obesity, diabetes, HIV, cancer), when adjusted for covariates, chronic kidney disease remained significantly associated with increased odds of mortality. Patients who had more than one comorbidities, former smokers, treated with Azithromycin without Hydroxychloroquine, reside within the boroughs of Brooklyn and Queens Higher had higher odds of death.
11.06.2020	SARS-CoV-2 Viral Load Predicts COVID-19 Mortality	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> The authors report that SARS-CoV-2 viral load at the time of presentation is an independent predictor of COVID-19 mortality in a large patient cohort (n=1,145). Viral loads should be used to identify higher-risk patients that may require more aggressive care and should be included as a key biomarker in the development of predictive algorithms.

Epidemiology and clinical – other

Publication Date	Title/URL	Journal/ Article type	Digest
12.06.2020	Considerations relating to passenger locator data, entry and exit screening and health declarations in the context of COVID-19 in the EU/EEA and the UK	European Centre for Disease Control and Prevention / Technical Report	<ul style="list-style-type: none"> • In order for contact tracing to be successful and efficient, passenger locator data should become available to public health authorities as soon as possible after the identification of a confirmed case among airline passengers. • Current evidence indicates that entry and/or exit screening at ports of entry, such as airports, is ineffective in preventing the spread of SARS-CoV-2 virus. • A health declaration form or health screening questionnaire is part of the exit or entry screening process targeting a specific disease and this needs to be assessed by a health professional with the objective of detecting cases in incoming passengers. • ECDC advises against combining passenger locator data and health declarations or health screening questionnaires in the same form, as this will delay the transfer of data and the contact tracing procedures.
15.06.2020	Report 27 - Adapting hospital capacity to meet changing demands during the COVID-19 pandemic	Imperial College / Report 27	<ul style="list-style-type: none"> • In this report, the authors calculated hospital capacity for emergency treatment of COVID-19 and other patients during the pandemic surge in April and May 2020; to evaluate the increase in capacity achieved via five interventions (cancellation of elective surgery, field hospitals, use of private hospitals, and deployment of former and newly qualified medical staff); and to determine how to reintroduce elective surgery considering continued demand from COVID-19 patients.
12.06.2020	Neuropathological Features of Covid-19	N Engl J Med / Correspondence	<ul style="list-style-type: none"> • Report the neuropathological findings from autopsies of 18 consecutive patients with SARS-CoV-2 infection who died in a single teaching hospital between April 14 and April 29, 2020. • Histopathological examination of brain specimens obtained from 18 patients who died 0 to 32 days after the onset of symptoms of Covid-19 showed only hypoxic changes and did not show encephalitis or other specific brain changes referable to the virus. • There was no cytoplasmic viral staining on immunohistochemical analysis. The virus was detected at low levels in 6 brain sections obtained from 5 patients; these levels were not consistently related to the interval from the onset of symptoms to death. Positive tests may have been due to in situ virions or viral RNA from blood.

11.06.2020	Clinical manifestations and evidence of neurological involvement in 2019 novel coronavirus SARS-CoV-2: a systematic review and meta-analysis	J Neurol / Review	<ul style="list-style-type: none"> • Systematically collected and investigated the clinical manifestations and evidence of neurological involvement in COVID-19. • A total of 41 articles were eligible and included in this review, showing a wide spectrum of neurological manifestations in COVID-19. • Most common manifestations were fatigue (33.2% [23.1-43.3]), anorexia (30.0% [23.2-36.9]), dyspnoea/shortness of breath (26.9% [19.2-34.6]), and malaise (26.7% [13.3-40.1]). The common specific neurological symptoms included olfactory (35.7-85.6%) and gustatory (33.3-88.8%) disorders, especially in mild cases. Guillain-Barré syndrome and acute inflammation of the brain, spinal cord, and meninges were repeatedly reported after COVID-19. • The underlying mechanisms can include both direct invasion and maladaptive inflammatory responses.
11.06.2020	Asymptomatic and presymptomatic transmission of SARS-CoV-2: A systematic review	medRxiv (non-peer reviewed) / Systematic review	<ul style="list-style-type: none"> • Systemic review to discuss the literature of asymptomatic and pre-symptomatic transmission, highlight limitations of recent studies, and propose experiments that, if conducted, would provide a more definitive analysis of the relative role of pre-symptomatic and asymptomatic transmission in the ongoing SARS-CoV-2 pandemic.
12.06.2020	Asymptomatic carriage rates and case-fatality of SARS-CoV-2 infection in residents and staff in Irish nursing homes	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Examined characteristics of nursing homes (NH)s across three Community Health Organisations (CHOs) in Ireland, proportions with COVID-19 outbreaks, staff and resident, symptom-profile and resident case-fatality. • Surveys were returned from (62.2%, 28/45) of NHs (2043 residents, 2303 beds). Three-quarters (21/28) had COVID-19 outbreaks (1741 residents, 1972 beds). • Resident COVID-19 incidence was (43.9%, 764/1741): laboratory-confirmed (40.1%, 710/1741) with (27.2%, 193/710 asymptomatic), and clinically-suspected (3.1%, 54/1741). Resident case-fatality was (27.6%, 211/764) for combined laboratory-confirmed/clinically-suspected COVID-19. • Among 675 NH staff across 24 sites who had confirmed/suspected COVID-19 (23.6%, 159/675) were asymptomatic. There was a significant correlation between the proportion of staff with symptomatic COVID-19 and resident numbers with confirmed/suspected COVID-19 (Spearman's rho=0.81, p<0.001).
14.06.2020	Healthcare Worker COVID-19 Cases in Ontario, Canada: A Cross-sectional Study	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Describe and compare healthcare worker (HCW) and non-HCW COVID-19 cases in Ontario, as well as the frequency of COVID-19 among HCWs household members.

		<ul style="list-style-type: none"> • There were 4,230 (17.5%) HCW COVID-19 cases in Ontario, of whom 20.2% were nurses, 2.3% were physicians, and the remaining 77.4% other specialties. HCWs were more likely to be between 30-60 years of age and female. • The mortality among HCWs was 0.2% compared to 10.5% of non-HCWs. The rate of new infections was 5.5 times higher in HCWs than non-HCWs, but mirrored the epidemic curve. • Identified 391 (9.8%) probable secondary household transmissions. • HCWs represent a disproportionate number of COVID-19 cases in Ontario but with low confirmed numbers of nosocomial transmission.
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Infection control

Publication Date	Title/URL	Journal/ Article type	Digest
11.06.2020	Stability of SARS-CoV-2 on Critical Personal Protective Equipment	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • This study provides the first comprehensive assessment of SARS-CoV-2 stability on experimentally contaminated personal protective equipment (PPE). • Persistence of viable virus was monitored over 21 days on eight different materials, including nitrile medical examination gloves, reinforced chemical resistant gloves, N-95 and N-100 particulate respirator masks, Tyvek, plastic, cotton, and stainless steel. • Viable SARS-CoV-2 in the presence of a soil load persisted for up to 21 days on experimentally inoculated PPE, including materials from filtering facepiece respirators (N-95 and N-100 masks) and a plastic visor. • Conversely, when applied to 100% cotton fabric, the virus underwent rapid degradation and became undetectable in less than 24 hours.

Social sciences

Publication Date	Title/URL	Journal/ Article type	Digest
15.06.2020	The mental health effects of the first two months of lockdown and social distancing during the Covid-19 pandemic in the UK	Institute for Fiscal Studies / Working paper	<ul style="list-style-type: none"> • Using longitudinal microdata for the UK over the period 2009-2020 they controlled for pre-existing previous trends in mental health in order to isolate and quantify the effects of the Covid-19 pandemic. • Mental health in the UK worsened by 8.1% on average as a result of the

pandemic and by much more for young adults and for women, which are groups that already had lower levels of mental health before Covid-19.

- Hence inequalities in mental health have been increased by the pandemic.

Modelling

Publication Date	Title/URL	Journal/ Article type	Digest
09.06.2020	An imperfect tool: COVID-19 'test & trace' success relies on minimising the impact of false negatives and continuation of physical distancing	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Modelling study which shows that incorporating poor sensitivity testing into tracing protocols could reduce efficacy, due to false negative results impacting isolation duration. • It is imperative that test results are interpreted with caution due to high false-negative rates and that contact tracing is used in combination with physical distancing measures. • If the risks associated with imperfect test sensitivity are mitigated, the authors find that contact tracing can facilitate control when the reproduction number with physical distancing, R_s, is less than 1.5.
05.06.2020	The effectiveness of social bubbles as part of a Covid-19 lockdown exit strategy, a modelling study	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Modelling study to estimate the impact of contact clustering in social bubbles on epidemic and mortality risk using the UK as a case study. • Results show that clustering contacts outside the household into exclusive social bubbles is an effective strategy of increasing contacts while limiting some of the associated increase in epidemic risk. Different scenarios and associated risks are explored.
10.06.2020	On the sensitivity of non-pharmaceutical intervention models for SARS-CoV-2 spread estimation	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Input-sensitivity analysis to investigate the method used by the Imperial College COVID-19 Research Team (ICCRT) for estimation of NPI effects from the system theoretical viewpoint of model identifiability. • Despite being simplistic with few free parameters, the system model was found to suffer from severe input sensitivities. This analysis indicated that the model lacks practical parameter identifiability from data. • The analysis also showed that this limitation is fundamental, and not something readily resolved should the model be driven with data of higher reliability.

Guidelines, consensus statements

Publication Date	Title/URL	Journal/ Article type
15.06.2020	Guidance on infection prevention and control of COVID-19 in migrant and refugee reception and detention centres in the EU/EEA and the UK	European Centre for Disease Control and Prevention / Technical report

Overviews, comments and editorials

Publication Date	Title/URL	Journal/ Article type
11.06.2020	Covid-19: Children with conditions managed in primary care may not need to shield	Bmj / News
11.06.2020	Covid-19 communication aids	Bmj / Practice
12.06.2020	Natural History of Asymptomatic SARS-CoV-2 Infection	N Engl J Med / Correspondence
11.06.2020	Keeping governments accountable: the COVID-19 Assessment Scorecard (COVID-SCORE)	Nat Med / Comment
12.06.2020	COVID-19 and ethnicity: who will research results apply to?	The Lancet / Comment
12.06.2020	The effects of physical distancing on population mobility during the COVID-19 pandemic in the UK	The Lancet Digital Health / Comment
12.06.2020	Asymptomatic SARS-CoV-2 infection	The Lancet Infectious Diseases / Comment

Produced by the PHE COVID-19 Literature Digest Team