



International EPI Cell Daily Evidence Digest – 31/07/2020

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 and genomics
- Epidemiology and clinical - children and pregnancy
- Epidemiology and clinical - risk factors
- Epidemiology and clinical - other
- Infection control
- Treatment
- 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Please note that we are including preprints (**highlighted in red**), which are preliminary reports of work that have NOT been peer-reviewed.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
29.07.2020	Rapid Screening Evaluation of SARS-CoV-2 IgG Assays Using Z-Scores to Standardize Results	Emerg Infect Dis / Research letter	<ul style="list-style-type: none">• Authors describe an approach to standardizing positivity thresholds and quantitative values for different assays that uses z-scores to enable rapid and efficient comparison of serologic test performance.
29.07.2020	Association of COVID-19 inflammation with activation of the C5a-C5aR1 axis	Nature / Article	<ul style="list-style-type: none">• Provide a longitudinal analysis of immune responses, including immune cell phenotyping and assessments of the soluble factors present in the blood and broncho-alveolar lavage fluid (BALF) of

			<p>patients at various stages of COVID-19 severity: paucisymptomatic, pneumonia and ARDS.</p> <ul style="list-style-type: none"> • Results suggest that C5a-C5aR1 axis blockade might be used as a means of limiting myeloid cell infiltration in damaged organs and preventing the excessive lung inflammation and endothelialitis associated with ARDS in COVID-19 patients.
29.07.2020	SARS-CoV-2-reactive T cells in healthy donors and patients with COVID-19	Nature / Article	<ul style="list-style-type: none"> • Investigated SARS-CoV-2 spike glycoprotein (S)-reactive CD4+ T cells in peripheral blood of patients with COVID-19 and SARS-CoV-2-unexposed healthy donors (HD). • Detected SARS-CoV-2 S-reactive CD4+ T cells in 83% of patients with COVID-19 but also in 35% of HD. S-reactive CD4+ T cells in HD reacted primarily to C-terminal S epitopes, which show a higher homology to spike glycoproteins of human endemic coronaviruses, compared to N-terminal epitopes. • The role of pre-existing SARS-CoV-2 cross-reactive T cells for clinical outcomes remains to be determined in larger cohorts. However, the presence of S-cross-reactive T cells in a sizable fraction of the general population may affect the dynamics of the current pandemic, and has important implications for the design and analysis of upcoming COVID-19 vaccine trials.
29.07.2020	A vaccine targeting the RBD of the S protein of SARS-CoV-2 induces protective immunity	Nature / Article	<ul style="list-style-type: none"> • Show that a recombinant vaccine comprising residues 319-545 of the S-RBD could induce a potent functional antibody response in the immunized mice, rabbits and non-human primates (Macaca mulatta) as early as 7 or 14 days after a single dose injection. • The sera from the immunized animals blocked RBD binding to ACE2 expressed on the cell surface and neutralized the infection by SARS-CoV-2 pseudovirus and live SARS-CoV-2 in vitro. • Importantly, the vaccination also provided protection in non-human primates from SARS-CoV-2 challenge in vivo.
29.07.2020	Papain-like protease regulates SARS-CoV-2 viral spread and innate immunity	Nature / Article	<ul style="list-style-type: none"> • Results highlight a dual therapeutic strategy in which targeting of SARS-CoV PLpro can suppress SARS-CoV-2 infection and promote anti-viral immunity.

Diagnostics and genomics

Publication Date	Title / URL	Journal / Article type	Digest
30.07.2020	Duration of SARS-CoV-2 RNA detection in COVID-19 patients in home isolation, Rhineland-Palatinate, Germany, 2020 – an interval-censored survival analysis	Eurosurveillance / Rapid communication	<ul style="list-style-type: none"> • Study analysing consecutive RT-qPCR results of 537 symptomatic COVID-19 patients in home quarantine from 28 Feb to 6 June 2020 in Germany. • Respectively 2, 3, and 4 weeks after symptom onset, 50%, 25% and 10% of patients had detectable RNA from SARS-CoV-2. • Suggest that in patients with mild COVID-19, RNA detection is likely to outlast currently known periods of infectiousness and fixed time periods may be more appropriate in determining the length of home isolation than laboratory-based approaches.
29.07.2020	Nationwide External Quality Assessment of SARS-CoV-2 Molecular Testing, South Korea	Emerg Infect Dis / Synopsis	<ul style="list-style-type: none"> • External quality assessment (EQA) essential for ensuring reliable test results, especially laboratories using assays authorized for emergency use for newly emerging pathogens. • EQA panel worked with 23 public health organization laboratories and 95 non-governmental laboratories: 110 (93.2%) laboratories reported correct results for all qualitative tests; potential weaknesses of currently available commercial reagent kits identified.
28.07.2020	Characterisation of the transcriptome and proteome of SARS-CoV-2 reveals a cell passage induced in-frame deletion of the furin-like cleavage site from the spike glycoprotein	Genome Med / Research	<ul style="list-style-type: none"> • Integrated analysis detected a 24 nt in-frame deletion in over half of the subgenomic mRNAs encoding the spike (S) glycoprotein. • Detection of an apparently viable deletion in the furin cleavage site of the S glycoprotein, a leading vaccine target, shows that this and other regions of SARS-CoV-2 proteins may readily mutate. • Data emphasises that the viral genome sequence should be carefully monitored during the growth of viral stocks for research, animal challenge models and, potentially, in clinical samples. Such variations may result in different levels of virulence, morbidity and mortality.

Epidemiology and clinical – children and pregnancy

Publication Date	Title / URL	Journal / Article type	Digest
30.07.2020	Age-Related Differences in Nasopharyngeal Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Levels in Patients With Mild to Moderate Coronavirus Disease 2019 (COVID-19)	JAMA Pediatrics / Research letter	<ul style="list-style-type: none"> • A single-centre cohort study of 145 patients with mild to moderate COVID-19 suggests children younger than 5 years (n = 46) have high amounts of SARS-CoV-2 viral RNA in their nasopharynx compared with older children (n = 51) and adults (n = 48). • The study was limited to detection of viral nucleic acid, although SARS-CoV-2 paediatric studies report a correlation between higher nucleic acid levels and the ability to culture infectious virus. Thus, young children could potentially be important drivers of SARS-CoV-2 spread. • Authors express concern for SARS-CoV-2 amplification in school or day care, and suggest targeting immunization efforts in this population.

Epidemiology and clinical - risk factors

Publication Date	Title / URL	Journal / Article type	Digest
29.07.2020	Characteristics and Quality of US Nursing Homes Reporting Cases of Coronavirus Disease 2019 (COVID-19)	JAMA Network Open / Research letter	<ul style="list-style-type: none"> • Study describing the characteristics and quality of nursing homes with COVID-19 cases (n=3021) in 23 US states and the District of Columbia. • Rates of deficiencies and complaints, defined as failures to meet or allegations of noncompliance with federal requirements, were higher in nursing homes that reported COVID-19 cases. • The largest difference between nursing homes with and without COVID-19 cases was observed in county-level rates of COVID-19, suggesting that when the surrounding population case rate is high, area nursing homes are at a high risk of infections.
28.07.2020	Cardiac injury associated with severe disease or ICU admission and death in hospitalized patients with COVID-19: a meta-analysis and systematic review	Crit Care / Systematic review and meta- analysis	<ul style="list-style-type: none"> • The analysis included 23 studies with 4631 total individuals. • Concluded that COVID-19 patients with elevated TnI levels are at significantly higher risk of severe disease, ICU admission, and death. Elevated CK, CK-MB, LDH, and IL-6 levels and emerging arrhythmia are associated with the development of severe disease

			and need for ICU admission, and the mortality is significantly higher in patients with elevated LDH and IL-6 levels.
27.07.2020	Outcomes of Cardiovascular Magnetic Resonance Imaging in Patients Recently Recovered From Coronavirus Disease 2019 (COVID-19)	JAMA Cardiol / Original investigation	<ul style="list-style-type: none"> • Prospective observational cohort study evaluating presence of myocardial injury in 100 patients recently recovered from COVID-19. • CMR revealed cardiac involvement in 78 patients (78%) / ongoing myocardial inflammation in 60 patients (60%), independent of pre-existing conditions, severity and overall course of the acute illness, and time from the original diagnosis. • Findings indicate the need for ongoing investigation of the long-term cardiovascular consequences of COVID-19.
27.07.2020	Association of Cardiac Infection With SARS-CoV-2 in Confirmed COVID-19 Autopsy Cases	JAMA Cardiol / Brief report	<ul style="list-style-type: none"> • Cardiac tissue from 39 consecutive autopsy cases: SARS-CoV-2 positivity in cardiac tissue as well as CD3+, CD45+, and CD68+ cells in the myocardium and gene expression of tumour necrosis growth factor α, interferon γ, chemokine ligand 5, as well as interleukin-6, -8, and -18. • A cytokine response panel consisting of 6 proinflammatory genes was increased in 16 patients compared with 15 patients without any SARS-CoV-2 in the heart. • Viral load above 1000 copies per μg RNA could be documented in 16 of 39 patients (41.0%).
29.07.2020	Cardiac Endotheliitis and Multisystem Inflammatory Syndrome After COVID-19	Ann Intern Med / Letter	<ul style="list-style-type: none"> • Case study on pathologic findings of vasculitis of the small vessels of the heart, which likely represents MIS, leading to death in a young adult after presumed resolution of COVID-19.
29.07.2020	Body Mass Index and Risk for Intubation or Death in SARS-CoV-2 Infection: A Retrospective Cohort Study	Ann Intern Med / Original research	<ul style="list-style-type: none"> • Retrospective cohort study of 2466 COVID-19 hospitalized adults • Compared with overweight patients, patients with obesity had higher risk for intubation or death, with the highest risk among those with class 3 obesity (hazard ratio, 1.6 [95% CI, 1.1 to 2.1]). • Obesity is associated with increased risk for intubation or death from COVID-19 in adults younger than 65 years, but not in adults aged 65 years or older.
29.07.2020	Abnormal Liver Tests in COVID-19: A Retrospective Observational Cohort Study of 1827 Patients in a Major U.S. Hospital Network	Hepatology / Rapid communication	<ul style="list-style-type: none"> • Retrospective cohort study of 1827 hospitalized patients with COVID-19: abnormal liver tests commonly observed both at admission (AST 66.9%, ALT 41.6%, ALP 13.5%, TBIL 4.3%) and peak hospitalization (AST 83.4%, ALT 61.6%, ALP 22.7%, TBIL 16.1%). • Association between abnormal liver tests and severe COVID-19, including ICU admission, mechanical ventilation, and death; associations with age, male gender, BMI, and diabetes mellitus

			also observed.
30.07.2020	Legionella pneumonia: increased risk after COVID-19 lockdown? Italy, May to June 2020	Eurosurveillance / Rapid communication	<ul style="list-style-type: none"> Abnormal liver tests occur in most hospitalized patients with COVID-19 and may be associated with poorer clinical outcomes. A case report of <i>Legionella pneumonia</i> in the dishwasher of a restaurant in Rome, Italy, just after the end of the lockdown that was in place to control the COVID-19 epidemic. Highlights the importance of strict monitoring of water and air systems immediately before reopening business or public sector buildings, and the need to consider Legionella infections among the differential diagnosis of respiratory infections after lockdown due to the ongoing COVID-19 pandemic.

Epidemiology and clinical – other

Publication Date	Title / URL	Journal / Article type	Digest
29.07.2020	Estimates of the rate of infection and asymptomatic COVID-19 disease in a population sample from SE England	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> The authors undertook enzyme linked immunosorbent assay characterisation of IgM and IgG responses against SARS-CoV-2 spike glycoprotein and nucleocapsid protein of 431 unselected general-population participants of the TwinsUK cohort from South-East England, aged 19-86 (median age 48; 85% female). A seroprevalence of 12% (51 participants of 431) was observed. Of 48 seropositive individuals with full symptom data, nine (19%) were fully asymptomatic, and 16 (27%) were asymptomatic for core COVID-19 symptoms: fever, cough or anosmia. Specificity of anosmia for seropositivity was 95%, compared to 88% for fever cough and anosmia combined.
31.07.2020	Symptom Duration and Risk Factors for Delayed Return to Usual Health Among Outpatients with COVID-19 in a Multistate Health Care Systems Network - United States, March-June 2020	MMWR Morb Mortal Wkly Rep / Article	<ul style="list-style-type: none"> In a US multistate telephone survey of symptomatic adults who had a positive outpatient test result for COVID-19 infection, 35% had not returned to their usual state of health when interviewed 2–3 weeks after testing. Among persons aged 18–34 years with no chronic medical conditions, one in five had not returned to their usual state of health. Suggests COVID-19 can result in prolonged illness, even among young adults without underlying chronic medical conditions.

30.07.2020	Post-discharge symptoms and rehabilitation needs in survivors of COVID-19 infection: a cross-sectional evaluation	J Med Virol / Research article	<ul style="list-style-type: none"> • The post-discharge symptoms of COVID-19 survivors discharged from a large UK University hospital (n=100) were assessed by telephone 4-8 weeks after discharge. • Thirty-two participants required treatment in intensive care (ICU group) and 68 were managed in hospital wards without needing ICU care (ward group). • New illness-related fatigue was the most common reported symptom by 72% participants in ICU group and 60.3% in ward group. • Next most common symptoms were breathlessness (65.6% in ICU group; 42.6% in ward group) and psychological distress (46.9% in ICU group; 23.5% in ward group).
29.07.2020	Observations of the global epidemiology of COVID-19 from the prepandemic period using web-based surveillance: a cross-sectional analysis	The Lancet Infectious Diseases / Article	<ul style="list-style-type: none"> • Describes the global spread of COVID-19 and characteristics of COVID-19 cases and clusters before the characterisation of COVID-19 as a pandemic. • Cases with travel links to China, Italy, or Iran accounted for almost two-thirds of the first reported COVID-19 cases from affected countries. • Among cases with age information available, most were among adults aged 18 years and older. • Although there were many clusters of household transmission among early cases, clusters in occupational or community settings tended to be larger, supporting a possible role for physical distancing to slow the progression of SARS-CoV-2 spread.

Infection control

Publication Date	Title / URL	Journal / Article type	Digest
29.07.2020	Comparison of Face-Touching Behaviors Before and During the Coronavirus Disease 2019 Pandemic	JAMA Network Open / Original investigation	<ul style="list-style-type: none"> • Study analysed mask-wearing and face-touching behaviour of individuals in public areas before the COVID-19 pandemic (n=4699), and during the pandemic (n=2887), using videos recorded in public places in China, Japan, South Korea, Western Europe (England, France, Germany, Spain, and Italy), and the US. • Logistic regression found that mask wearing was associated with a reduction in face touching in China and South Korea, and of touching the nose, mouth, and eyes.

29.07.2020	Association Between Statewide School Closure and COVID-19 Incidence and Mortality in the US	JAMA / Original Investigation	<ul style="list-style-type: none"> • US population–based observational study suggests that between 9 Mar and 7 May 2020, school closure in the US was temporally associated with decreased COVID-19 incidence and mortality. • States that closed schools earlier, when cumulative incidence of COVID-19 was low, had the largest relative reduction in incidence and mortality. • It remains possible some of the reduction is related to other concurrent nonpharmaceutical interventions.
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Treatment

Publication Date	Title / URL	Journal / Article type	Digest
29.07.2020	The potential health and economic impact of dexamethasone treatment for patients with COVID-19	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Authors state dexamethasone has been shown to reduce mortality in hospitalised COVID-19 patients needing oxygen and ventilation by 18% and 36%, respectively. • This study estimates potential number of lives saved and life years gained if dexamethasone treatment is rolled out in the UK and globally. • Suggests in the UK, approximately 12,000 [4,250 - 27,000] lives could be saved by Jan 2021. • If dexamethasone has a similar effect size in settings where access to oxygen therapies is limited, this would translate into approximately 650,000 [240,000 - 1,400,000] lives saved globally. If dexamethasone acts differently in these settings, the impact could be less than half of this value. • Further clinical research is needed in settings with limited access to oxygen and/or ventilators, e.g. low and middle-income countries.

Modelling

Publication Date	Title / URL	Journal / Article type	Digest
29.07.2020	The risk of COVID-19 transmission in train passengers: an epidemiological and modelling study	Clin Infect Dis / Article	<ul style="list-style-type: none">• A model to quantify the transmission risk of COVID-19 on high-speed train passengers using data from 2,334 index patients and 72,093 close contacts who had co-travel times of 0-8 hours from 19 Dec 2019 through 6 March 2020 in China.• Suggests COVID-19 has a high transmission risk among train passengers, but this risk shows significant differences with co-travel time and seat location.

Overviews, comments and editorials

Publication Date	Title / URL	Journal / Article type
29.07.2020	Reopening Primary Schools during the Pandemic	NEJM / Article
29.07.2020	COVID-19 and School Closures	Jama / Editorial
30.07.2020	Letter to the editor: COVID-19: how accurate are seroprevalence studies?	Eurosurveillance / Letter
30.07.2020	Authors' response: COVID-19: how accurate are seroprevalence studies?	Eurosurveillance / Letter
29.07.2020	COVID-19 and Dexamethasone: A Potential Strategy to Avoid Steroid-Related Strongyloides Hyperinfection	JAMA / Viewpoint
30.07.2020	Inhaled corticosteroids in virus pandemics: a treatment for COVID-19?	The Lancet Respiratory Medicine / Comment
30.07.2020	SARS-CoV-2-related atypical thyroiditis	The Lancet Diabetes & Endocrinology / Correspondence
28.07.2020	Lung fibrosis: an undervalued finding in COVID-19 pathological series	The Lancet Infectious Diseases / Correspondence
28.07.2020	Mortality in COVID-19 is not merely a question of resource availability	The Lancet Respiratory Medicine / Comment

Produced by the PHE COVID-19 Literature Digest Team

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