Public Health England

International EPI Cell Daily Evidence Digest – 20/07/2020

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
- Genomics
- Epidemiology and clinical - children and pregnancy
- Epidemiology and clinical - risk factors
- Treatment
- 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Please note that we are including preprints (highlighted in red), which are preliminary reports of work that have NOT been peer-reviewed.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
20.07.2020	Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2: a preliminary report of a phase 1/2, single-blind, randomised controlled trial	The Lancet / Article	• Did a phase 1/2, single-blind, randomised controlled trial in five trial sites in the UK of a chimpanzee adenovirus-vectored vaccine (ChAdOx1 nCoV-19) expressing the SARS-CoV-2 spike protein compared with a meningococcal conjugate vaccine (MenACWY) as control. • Between Apr 23 and May 21, 2020, 1077 participants were enrolled and assigned to receive either ChAdOx1 nCoV-19 (n=543) or MenACWY (n=534), ten of whom were enrolled in the non-randomised ChAdOx1 nCoV-19 prime-boost group. • ChAdOx1 nCoV-19 showed an acceptable safety profile, and homologous boosting increased antibody responses. These results, together with the induction of both humoral and cellular immune

			responses, support large-scale evaluation of this candidate vaccine in an ongoing phase 3 programme.
20.07.2020	Immunogenicity and safety of a recombinant adenovirus type-5-vectored COVID-19 vaccine in healthy adults aged 18 years or older: a randomised, double-blind, placebo-controlled, phase 2 trial	The Lancet / Article	• A randomised controlled trial with 508 healthy adults in Wuhan, China, assessed the immunogenicity and safety of a candidate non-replicating adenovirus type-5 (Ad5)-vectored COVID-19 vaccine. • It was found that Ad5-vectored COVID-19 vaccine at 5×10^{10} viral particles is safe, and induced significant immune responses in the majority of recipients after a single immunisation.
13.07.2020	Longitudinal Isolation of Potent Near-Germline SARS-CoV-2-Neutralizing Antibodies from COVID-19 Patients	Cell / Article	• Analysed the antibody response of 12 COVID-19 patients from 8 to 69 days after diagnosis. • By screening 4,313 SARS-CoV-2-reactive B cells, they isolated 255 antibodies from different time points as early as 8 days after diagnosis. Of these, 28 potently neutralized authentic SARS-CoV-2 with IC(100) as low as 0.04 µg/mL, showing a broad spectrum of variable (V) genes and low levels of somatic mutations. • Results demonstrate that SARS-CoV-2-neutralizing antibodies are readily generated from a diverse pool of precursors, fostering hope for rapid induction of a protective immune response upon vaccination.
08.07.2020	Human B cell clonal expansion and convergent antibody responses to SARS-CoV-2	bioRxiv (non-peer reviewed) / Article	• The human B cell compartment in patients with COVID-19 is rapidly altered with the early recruitment of B cells expressing a limited subset of IGHV genes, progressing to a highly polyclonal response of B cells with broader IGHV gene usage and extensive class switching to IgG and IgA subclasses with limited somatic hypermutation in the initial weeks of infection. • Sequence-based detection in COVID-19 patients of convergent B cell clonotypes previously reported in SARS-CoV infection predicts the presence of SARS-CoV / SARS-CoV-2 cross-reactive antibody titres specific for the receptor-binding domain. • These findings offer molecular insights into shared features of human B cell responses to SARS-CoV-2 and other zoonotic spill over coronaviruses.
18.07.2020	Lower prevalence of antibodies neutralizing SARS-CoV-2 in group O French blood donors	Antiviral Res / Short communication	• Investigated the distribution of antibodies neutralizing SARS-CoV-2 according to age, sex or blood group in French blood donors. • 998 samples collected from blood donors during the last week of Mar or the first week of Apr 2020 were tested. As expected at this stage of the outbreak, the prevalence was low (2.7%) and, importantly, criteria for blood donation imply that the vast majority of seropositives had asymptomatic or pauci-symptomatic SARS-CoV-2 infections.

			• Authors conclude that virus infection occurs with a similar incidence in men and women among French blood donors, but that blood group O persons are less at risk of being infected and not only of suffering from severe clinical presentations, as previously suggested.
17.07.2020	ABO polymorphism and SARS-CoV-2 infection - a meta-analysis	medRxiv (non-peer reviewed) / Meta-analysis	• Meta-analysis investigating the association between SARS-CoV-2 infection and ABO blood group polymorphism and determining the odds of SARS-CoV-2 positive individuals having a specific blood group compared to controls. • Results indicate SARS-CoV-2 positive individuals are more likely to have blood group A (pooled OR 1.21; 95%CI: 1.08-1.37) and less likely to have blood group O (pooled OR 0.76, 95%CI: 0.66-0.87). • Further studies needed to investigate mechanisms at the basis of this association.

Genomics

Publication Date	Title/URL	Journal/ Article type	Digest
16.07.2020	Rapid SARS-CoV-2 whole-genome sequencing and analysis for informed public health decision-making in the Netherlands	Nat Med / Letter	• The combination of near to real-time whole-genome sequence analysis and epidemiology resulted in reliable assessments of the extent of SARS-CoV-2 transmission in the community, facilitating early decision-making to control local transmission of SARS-CoV-2 in the Netherlands. • This paper demonstrates how these data were generated and analysed, and how SARS-CoV-2 WGS, in combination with epidemiological data, was used to inform public health decision-making in the Netherlands.
15.07.2020	A dynamic nomenclature proposal for SARS-CoV-2 lineages to assist genomic epidemiology	Nat Microbiol / Article	• The authors present a rational and dynamic virus nomenclature that uses a phylogenetic framework to identify lineages that contribute most to active spread of SARS-CoV-2. • The system is made tractable by constraining the number and depth of hierarchical lineage labels and by flagging and de-labelling virus lineages that become unobserved and hence are probably inactive. • By focusing on active virus lineages and those spreading to new locations, this nomenclature will assist in tracking and understanding the patterns and determinants of the global spread of SARS-CoV-2. *This paper was previously included as a preprint.*

Epidemiology and clinical - children and pregnancy

Publication Date	Title/URL	Journal/ Article type	Digest
14.07.2020	Clinical characteristics of children and young people hospitalised with covid-19 in the United Kingdom: prospective multicentre observational cohort study	medRxiv (non-peer reviewed) / Article	• Observational cohort study to characterise clinical features of children and young people (n=451) less than 19 years admitted to hospital with COVID-19 infection in the UK between 17th Jan and 5th June 2020. Explored factors associated with admission to critical care, mortality, and development of multisystem inflammatory syndrome temporarily related to covid-19 (MIS-C). • Median age was 3.9 years, 36% (162/451) were under 12 months old, and 57% (256/450) were male. 56% (224/401) were White, 12% (49/401) South Asian and 10% (40/401) Black. 43% (195/451) had at least one recorded comorbidity. • Data confirmed less severe COVID-19 in children and young people than in adults. • The authors provide additional evidence for refining the MIS-C case definition. • The identification of a muco-enteric symptom cluster suggests that MIS-C is the severe end of a spectrum of disease.
15.07.2020	Clinical Manifestations and Outcomes of Critically Ill Children and Adolescents with COVID-19 in New York City	J Pediatr / Article	• Retrospective observational study of children 1 month to 21 years admitted Mar 14 to May 2, 2020 to 9 NY City paediatric intensive care units (PICUs) with SARS-CoV-2 infection. • Of 70 children admitted to PICUs: median age 15 [IQR 9, 19] years; 61.4% male; 38.6% Hispanic; 32.9% Black; 74.3% with comorbidities. Fever (72.9%) and cough (71.4%) were the common presenting symptoms. • Critically ill children with COVID-19 predominantly are adolescents, have comorbidities, and require some form of respiratory support. The presence of ARDS is significantly associated with prolonged PICU and hospital stay.

Epidemiology and clinical - risk factors

Publication Date	Title/URL	Journal/ Article type	Digest
10.07.2020	Pulmonary embolism in hospitalised patients with COVID-19	Thromb Res / Article	• Determined the incidence of pulmonary embolism (PE) in hospitalised patients with COVID-19 and the diagnostic yield of Computer Tomography Pulmonary Angiography (CTPA) for PE. • Retrospective review of single-centre data of all CTPA studies in patients with suspected or confirmed COVID-19 identified from Electronic Patient Records (EPR) (at King's College Hospital, London). • There were 1477 patients admitted with COVID-19 and 214 CTPA scans performed, of which n = 180 (84%) were requested outside of critical care. The diagnostic yield for PE was 37%. The overall proportion of PE in patients with COVID-19 was 5.4%. • Even outside of the critical care environment, PE in hospitalised patients with COVID-19 is common. Of note, approaching half of PE events were diagnosed on hospital admission. More data are needed to identify an optimal diagnostic pathway in patients with COVID-19.
15.07.2020	Outcome of hospitalisation for COVID-19 in patients with Interstitial Lung Disease: An international multicentre study	medRxiv (non-peer reviewed) / Article	• An international multicentre audit assessed outcomes following COVID-19 in European patients (n=349) with Interstitial Lung Disease (ILD) versus those without in a contemporaneous age, sex and comorbidity matched population. • Patients with ILD are at increased risk of death from COVID-19 (HR 1.60, Confidence Intervals 1.17-2.18 p=0.003), particularly those with poor lung function (HR 1.72, 1.05-2.83) and obesity (HR 1.98, 1.13−3.46).
15.07.2020	Early triage of critically ill COVID-19 patients using deep learning	Nat Commun / Article	• Show that a deep learning-based survival model can predict the risk of COVID-19 patients developing critical illness based on clinical characteristics at admission. • This model was developed using a cohort of 1590 patients from 575 medical centres, with internal validation performance of concordance index 0.894. • Further validated the model on three separate cohorts from Wuhan, Hubei and Guangdong provinces consisting of 1393 patients with concordance indexes of 0.890, 0.852 and 0.967 respectively. • This model was used to create an online calculation tool designed for patient triage at admission to identify patients at risk of severe illness, ensuring that patients at greatest risk of severe illness receive

			appropriate care as early as possible and allow for effective allocation of health resources.
12.06.2020	Symptom clusters in Covid19: A potential clinical prediction tool from the COVID Symptom study app	medRxiv (non-peer reviewed) / Article	• Unsupervised time series clustering over symptom presentation was performed on data collected from a training dataset of completed cases enlisted early from the COVID Symptom Study Smartphone application, yielding six distinct symptom presentations. *This study is over a month old and was included as it receiving a lot of media attention.*

Treatment

Publication Date	Title/URL	Journal/ Article type	Digest
17.07.2020	Dexamethasone in Hospitalized Patients with Covid-19 — Preliminary Report	NEJM / Original article	• In this controlled, open-label trial (RECOVERY) comparing a range of possible treatments in patients who were hospitalized with Covid-19, the authors randomly assigned patients to receive oral or intravenous dexamethasone for up to 10 days or to receive usual care alone. The primary outcome was 28-day mortality. Here, they report the preliminary results of this comparison. • A total of 2104 patients were assigned to receive dexamethasone and 4321 to receive usual care. Overall, 482 patients (22.9%) in the dexamethasone group and 1110 patients (25.7%) in the usual care group died within 28 days after randomization. • In patients hospitalized with Covid-19, the use of dexamethasone resulted in lower 28-day mortality among those who were receiving either invasive mechanical ventilation or oxygen alone at randomization but not among those receiving no respiratory support.
17.07.2020	Hydroxychloroquine in Nonhospitalized Adults With Early COVID-19: A Randomized Trial	Ann Intern Med / Original research	• Oral hydroxychloroquine did not substantially reduce symptom severity in adult outpatients with early, mild COVID-19 (n=341) in a randomized, double-blind, placebo-controlled trial conducted from 22 Mar through 20 May 2020.
17.07.2020	High versus standard doses of corticosteroids in COVID-19 patients with an acute respiratory distress syndrome: a controlled observational comparative study	medRxiv (non-peer reviewed) / Article	• A study of 573 COVID-19 patients allocated to either high doses (HD) or standard doses (SD) of corticosteroids examined mortality, risk of need for mechanical ventilation (MV) or death, and risk of developing a severe case of ARDS. • After adjusting by baseline characteristics, HD were associated with a higher mortality than SD (adjusted-OR 2.46, 95% CI 1.58-3.83, p<0.001)

			and with an increased risk of needing MV or death (adjusted-OR 2.50, p=0.001). Interaction analysis showed that HD increased mortality exclusively in elderly patients. • Risk of developing a severe ARDS was similar between groups.
17.07.2020	Effect of corticosteroid treatment on 1376 hospitalized COVID-19 patients. A cohort study	medRxiv (non-peer reviewed) / Article	• 1444 patients were admitted to their hospital with a positive RT-PCR test for SARS-CoV-2, 559 patients (39%) were exposed to corticosteroids during hospital stay, 844 (61%) were not exposed to corticosteroids. • Found treatment with corticosteroids did not affect hospital mortality in patients with COVID-19 after balancing for confounding variables (adjusted p = 0.25). • Patients in the corticosteroids cohort had reduced risk of ICU admission (adjusted p <0.001).

Overviews, comments and editorials

Publication Date	Title/URL	Journal/ Article type
20.07.2020	Encouraging results from phase 1/2 COVID-19 vaccine trials	The Lancet / Comment
15.07.2020	Survivorship after COVID-19 ICU stay	Nat Rev Dis Primers / Comment
17.07.2020	COVID-19 in people with diabetes: understanding the reasons for worse outcomes	The Lancet Diabetes & Endocrinology / Review
17.07.2020	Potential factors linked to high COVID-19 death rates in British minority ethnic groups	The Lancet Infectious Diseases / Correspondence
18.07.2020	Obesity and covid-19: the unseen risks	Bmj / Letter
17.07.2020	Serology testing in the COVID-19 pandemic response	The Lancet Infectious Diseases / Personal view
17.07.2020	Sewage monitoring is the UK's next defence against covid-19	Bmj / Feature
19.07.2020	Covid-19: Is the UK government marginalising scientists?	Bmj / News
17.06.2020	The Lancet–Chatham House Commission on improving population health post COVID-19	The Lancet / Correspondence

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