Public Health England

COVID-19 Literature Digest – 20/08/2021

Dear all,

Please find today's report below.

PHE's COVID-19 Literature Digest has been produced since February 2020. A selection of our previous Digests can be found here. This resource aims to highlight a small selection of recent COVID-19 papers that are relevant to UK settings, contain new data, insights or emerging trends. The Digest Team generate a report once per week (Fri). The reports include both preprints, which should be treated with caution as they are NOT peer-reviewed and may be subject to change, and also research that has been subject to peer review and wider scrutiny. The Digest is very rapidly produced and does not claim to be a perfect product; the inclusion or omission of a publication should not be viewed as an endorsement or rejection by PHE. We do not accept responsibility for the availability, reliability or content of the items included in this resource.

To join our email distribution list please send a request to COVID.LitDigest@phe.gov.uk. If you are interested in papers relating to behaviour and social science please contact COVID19.behaviouralscience@phe.gov.uk to sign up to receive the PHE Behavioural Sciences Weekly Report.

Best wishes,

Emma Farrow, James Robinson, Kester Savage
On behalf of the PHE COVID-19 Literature Digest Team

Report for 20.08.2021 (please note that papers that have **NOT been peer-reviewed** are highlighted in red).

Sections:

Transmission
Treatment
Modelling
Guidance and consensus statements (no digest)
Overviews, comments and editorials (no digest)

Serology and immunology

Publication Date	Title/URL	Journal / Article type	Digest
12.08.2021	Persistence of immunity to SARS-CoV-2 over time in the ski resort Ischgl	EBioMedicine / Research Paper	• New results from longitudinal community level study of Ischgl adult population. • Findings suggest seropositivity levels of around 40-45% can persist in a community for over 8 months, which may help reduce wild-type and B.1.1.7 [alpha] transmission at local level.
18.08.2021	Pan-Sarbecovirus Neutralizing Antibodies in BNT162b2-Immunized SARS-CoV-1 Survivors	N Engl J Med / Brief Report	• Authors assessed 8 survivors of SARS-CoV-1 infection in Singapore who subsequently received BNT162b2 [Pfizer] vaccine for neutralizing antibodies against both SARS-CoV-1 and SARS-CoV-2. • Show efficient induction of high-level and broad-spectrum pan-sarbecovirus neutralizing antibodies that can neutralize all variants of concern and five pre-emergent sarbecoviruses. • Related news item: https://www.nature.com/articles/d41586-021-02260-9
19.08.2021	Profile of humoral and cellular immune responses to single doses of BNT162b2 or ChAdOx1 nCoV-19 vaccines in residents and staff within residential care homes (VIVALDI): an observational study	Lancet Healthy Longev / Article	• 124 participants in 14 LTCFs, 89 staff / 35 residents (medium 87 years). • 18 staff / 12 (34%) residents had serological evidence of previous SARS-CoV-2 infection in blood samples median 40 days after vaccination. • All participants with previous infection had high antibody titres following vaccination independent of age. • In infection-naive participants, titres negatively correlated with age; significantly lower against spike protein from B.1.351[Beta] and P.1 [Gamma] variants. • Infection-naive residents have delayed antibody responses to first vaccine dose; consider for early second dose. • Associated comment: https://www.thelancet.com/journals/lanhl/article/PIIS2666-7568(21)00205-1/fulltext

Back to menu

Vaccines

Publication Date	Title/URL	Journal / Article type	Digest
18.08.2021	Impact of Delta on viral burden and vaccine effectiveness against new SARS-CoV-2 infections in the UK	Oxford University (non-peer reviewed) / Article	• A large community-based survey across the UK found that effectiveness of BNT162b2 (Pfizer) and ChAd0x1 (AstraZeneca) against any infections (new PCR positives) and infections with symptoms or high viral burden is reduced with the Delta variant. • Single dose of mRNA-1273 (Moderna) had similar or greater effectiveness compared to a single dose of BNT162b2 or ChAdOx1. Two doses remain at least as effective as protection afforded by prior natural infection. • Immunity following second doses differed significantly between BNT162b2 and ChAdOx1, with greater initial effectiveness against new PCR-positives but faster declines in protection against high viral burden and symptomatic infection with BNT162b2. • No evidence effectiveness varied by dosing interval, but protection higher among those vaccinated following a prior infection and younger adults. • With Delta, infections following two vaccinations had similar peak viral burden to those in unvaccinated individuals. • Associated news item: https://www.bmj.com/content/374/bmj.n2074.full
18.08.2021	New COVID-19 Cases and Hospitalizations Among Adults, by Vaccination Status — New York, May 3–July 25, 2021	MMWR Morb Mortal Wkly Rep / Early release	• In a real-world study in New York, USA (covering 3 May – 25 July 2021), overall age-adjusted COVID-19 vaccine effectiveness against hospitalisation was relatively stable (91.9%–95.3%). • However, effectiveness against infection for all adults declined from 91.7% to 79.8%. This coincided with a period of easing societal public health restrictions and increasing Delta variant circulation.
18.08.2021	Sustained Effectiveness of Pfizer-BioNTech and Moderna Vaccines Against COVID-19 Associated Hospitalizations Among Adults — United States, March–July 2021	MMWR Morb Mortal Wkly Rep / Early release	• Among 1,129 patients in 18 US States who received 2 doses of an mRNA vaccine (Pfizer-BioNTech or Moderna), vaccine effectiveness against COVID-19 hospitalisation was 86% at 2–12 weeks after vaccination and 84% at 13–24 weeks. Vaccine effectiveness was sustained among groups at risk for severe COVID-19.
17.08.2021	SARS-CoV-2 delta variant neutralisation after heterologous ChAdOx1-S/BNT162b2 vaccination	Lancet / Correspondence	• Study of plasma from ChAdOx1-S-primed vaccinees after homologous ChAdOx1-S [AstraZeneca, n=12) or heterologous BNT162b2 [Pfizer; n=11] boost to compare neutralising activity against variants of concern. • Robust inhibition of variants including Delta supports heterologous ChAdOx1-S / BNT162b2 vaccination.

17.08.2021	Immunogenicity and safety of inactivated whole virion Coronavirus vaccine with CpG (VLA2001) in healthy adults aged 18 to 55: a randomised phase 1 /2 clinical trial	medRxiv (non-peer reviewed) / Article	• Phase 1/2 trial of VLA2001 (Valneva) COVID-19 vaccine: between 16 December 2020 and 21 January 2021, 153 participants were randomised evenly between high and low dose groups. • In the high dose group, two weeks following the second dose, geometric mean titres were 530.4 for neutralizing antibodies and 2147.9 for S-binding antibodies. • There was a dose dependent response with 90.0% seroconversion (4-fold rise) at day 36 in the high dose group, which was significantly higher than rates in both the medium (73.5%) and low dose (51%) groups. • Antigen-specific interferon-γ T-cells reactive against the S, M and N proteins observed in 76%, 36% and 49% of high dose recipients, respectively. Vaccine was well-tolerated.
14.08.2021	Efficacy of inactivated SARS-CoV-2 vaccines against the Delta variant infection in Guangzhou: A test-negative case-control real-world study	Emerg Microbes Infect / Article	• Study of adults (18-59 years) during an outbreak of the Delta variant in May 2021 in Guangzhou city, China consisting of SARS-CoV-2 test-positive cases (n=74) and test-negative controls (n=292) • A single dose of either approved SARS-CoV-2 vaccine (China National Biotec Group or CoronaVac) yielded efficacy of 13.8% • Two-dose vaccination was 59.0% effective against COVID-19 overall, 70.2% against moderate COVID-19 and 100% against severe COVID-19 (might overestimate due to small sample size) • Effectiveness of two-dose vaccination against COVID-19 reached 72.5% among participants aged 40-59 years, and was higher in females than in males against COVID-19 and moderate diseases.
12.08.2021	Durability of mRNA-1273 vaccine-induced antibodies against SARS-CoV-2 variants	Science / Report	• Authors assess impact of variants B.1.1.7 (Alpha), B.1.351 (Beta), P.1 (Gamma), B.1.429 (Epsilon), B.1.526 (Iota), B.1.617.2 (Delta) on antibodies elicited by mRNA-1273 [Moderna] over seven months. • 8 volunteers in each of three age groups: 18-55, 55-70, 71+. • At peak response to 2nd vaccine dose, all individuals had responses to all variants. • Binding and functional antibodies against variants persisted in most subjects, albeit at low levels, for 6-months after primary series of vaccine. • Across all assays, B.1.351 had lowest antibody recognition.
09.08.2021	Comparison of two highly-effective mRNA vaccines for COVID-19 during periods of Alpha and Delta variant prevalence	medRxiv (non-peer reviewed) / Article	• Compares effectiveness of Moderna (mRNA-1273) and Pfizer-BioNTech (BNT162b2) vaccines in a US health system from January to July 2021. • Matched cohorts of vaccinated and unvaccinated individuals from Minnesota (n = 25,589 each) found both vaccines were highly effective against COVID-19 infection (Moderna: 86%; Pfizer: 76%) and hospitalisation (Moderna: 91.6%; Pfizer: 85%).

			• Delta variant increased from 0.7% in May to over 70% in July, at which point vaccine effectiveness against hospitalisation remained high (Moderna: 81%; Pfizer: 75%), but effectiveness against infection was lower for both vaccines (Moderna: 76%; Pfizer: 42%). • In fully vaccinated persons across sites in multiple states (Minnesota, Wisconsin, Arizona, Florida, and Iowa), Moderna conferred two-fold risk reduction against breakthrough infection compared to Pfizer (IRR = 0.50). • In Florida [currently experiencing COVID-19 surge], risk of infection in July after full vaccination with Moderna was about 60% lower than after full vaccination with Pfizer (IRR: 0.39).
19.08.2021	Reports of anaphylaxis after coronavirus disease 2019 vaccination, South Korea, 26 February to 30 April 2021	Eurosurveillance / Rapid communication	• During mass vaccination with 3.8 million doses of COVID-19 vaccinations (Oxford-AstraZeneca and Pfizer-BioNTech) in South Korea, 173 suspected cases of anaphylaxis were reported and 44 cases were confirmed using Brighton Collaboration case definitions. • The rates per million doses were 18.2 cases for Oxford-AstraZeneca and and 6.2 cases for Pfizer-BioNTech; median time of onset was 14 min after vaccination; most cases had recovered at the time of review.
10.08.2021	Acute tolerance of Moderna mRNA-1273 vaccine against COVID-19 in patients with cancer treated with radiotherapy	Lancet Oncol / Article	• 153 patients with cancer who had been treated with radiotherapy in the past 6 months were recruited to the experimental cohort between 28.03.2021 and 31.03.2021. There was a control group of 185. • Assessments were made as to the safety of the 2-dose Moderna mRNA-1273 vaccine. Early adverse events (local and systemic side-effects up to 7 days after each dose) and late adverse events (local and systemic side-effects up to 28 days after each dose) were reported. • Authors conclude that tolerance to the Moderna mRNA-1273 vaccine was not worse in patients who have undergone or are having radiotherapy. The safety profile of the Moderna mRNA-1273 vaccine does not raise any specific concerns in patients with cancer who received radiotherapy in the past 6 months.
18.08.2021	Effectiveness of COVID-19 Vaccines among Incarcerated People in California State Prisons: A Retrospective Cohort Study	medRxiv (non-peer reviewed) / Article	• Retrospective cohort study of 60,707 prisoners in California, USA: 49% received at least one BNT162b2 (Pfizer-BioNTech) or mRNA-1273 (Moderna) dose during the study period (22 Dec. 2020 to 1 Mar. 2021) • Estimated vaccine effectiveness from day 14 of first and second dose was 74% and 97%, respectively. • Effectiveness was similar among the subset of residents who were medically vulnerable (74% and 92% after first and second doses, respectively) and among the subset of residents who received the mRNA-1273 vaccine (71% and 96%). • Suggests mRNA vaccines are effective in preventing SARS-CoV-2 infections in a prison setting.

Back to menu

Diagnostics and genomics

Publication Date	Title/URL	Journal / Article type	Digest
18.08.2021	A systematic review of the sensitivity and specificity of lateral flow devices in the detection of SARS-CoV-2	BMC Infect Dis / Research article	• Systematic Review of LFDs; 24 papers involving >26,000 tests from PubMed and Medxriv. • LFD performance is heterogeneous / dependent on manufacturer. • Great range of sensitivities (38.32–99.19%). Test performance doesn't appear dependent on operator.
12.08.2021	Accuracy of novel antigen rapid diagnostics for SARS-CoV-2: A living systematic review and meta-analysis	PLoS Med / Systematic review	• From a total of 14,254 articles, 133 analytical and clinical studies were included, resulting in 214 clinical accuracy datasets with 112,323 samples. • Across all meta-analysed samples, the pooled Ag-RDT sensitivity and specificity were 71.2% and 98.9% respectively. Sensitivity increased to 76.3% if analysis was restricted to studies that followed the Ag-RDT manufacturers' instructions. LumiraDx showed the highest sensitivity, with 88.2%. • Ag-RDTs detect the vast majority of SARS-CoV-2-infected persons within the first week of symptom onset and those with high viral load. They can have high utility for diagnostic purposes in the early phase of disease, making them a valuable tool to fight the spread of SARS-CoV-2.
31.08.2021	Ultrarapid detection of SARS-CoV-2 RNA using a reverse transcription-free exponential amplification reaction, RTF-EXPAR	Proc Natl Acad Sci U S A / Research Article	• In addition to a rapid sample-to-signal time of under 10 min, the "one-pot" format of the RTF-EXPAR assay, further increases the ease of use away from clinical testing laboratories, with significance for primary care and community settings, entertainment venues and border zones • As sensitive as PCR tests, the reported assay is faster because 1) it employs a method for generating DNA (the trigger strand) from RNA, bypassing the lengthy RT step, and 2) a quicker amplification process than PCR, called exponential amplification reaction (EXPAR), is used to amplify the trigger. • Additional comment https://www.birmingham.ac.uk/news/latest/2021/08/birmingham-researchers-confirm-speed-simplicity-and-sensitivity-for-new-covid-19-test.aspx
13.08.2021	Characterising the persistence of RT-PCR positivity and incidence in a community survey of SARS-CoV-2	medRxiv (non-peer reviewed) / Article	• Of 2,282 participants testing RT-PCR positive during round 8 of REACT-1 (during 6 to 22 January 2021), 896 (39%) provided up to two additional swabs for RT-PCR approximately 6 and 9 days after initial swab. • Estimated overall sensitivity of REACT-1 to detect virus on a single swab was 0.79; median duration of positivity following a positive test was 9.7 days.

			• Greater median duration of positivity found where there was low N-gene Ct value, symptomatic persons, or for infection with Alpha variant. • Estimated proportion of positive individuals detected on first swab was higher for those with an initially low N-gene Ct value and those who were pre-symptomatic. • Compared to swab-positivity, estimates of infection incidence during REACT-1 included sharper features with evident transient increases around the time of key changes in social distancing measures.
13.08.2021	Diagnostic accuracy of rapid point-of-care tests for diagnosis of current SARS-CoV-2 infections in children: A systematic review and meta-analysis	medRxiv (non-peer reviewed) / Article	• Systematic review: 17 studies (6355 paediatric study participants) all compared antigen tests against RT-PCR. One study was at low risk of bias. • Pooled overall diagnostic sensitivity and specificity of rapid point-of-care tests in paediatric populations was 64.2% and 99.1%, respectively; in symptomatic children it was 71.8% and 98.7%; and in asymptomatic children it was 56.2% and 98.6%.
13.08.2021	Rapid genome sequencing in hospitals to identify potential vaccine-escape SARS-CoV-2 variants	Lancet Infect Dis / Correspondence	• Case study: rapid sequencing by London front-line hospital laboratories • All positive patient nose and throat swabs, 07.07.2021 onward / PCR-based genotyping of all new cases in 3 hospitals • Two cases of potential vaccine-escape variant from B.1.621 lineage, both unvaccinated, living 5 miles apart, with no known epidemiological contact or recent travel. Finding indicates ongoing community transmission.
13.08.2021	Combined epidemiological and genomic analysis of nosocomial SARS-CoV-2 infection early in the pandemic and the role of unidentified cases in transmission	Clin Microbiol Infect	• 44 putative transmission clusters were found through epidemiological analysis, which included 234 cases and all 86 nosocomial cases. SARS-CoV-2 genome sequence was obtained from 168/234 (72%) of these cases in epidemiological clusters, including 77/86 (90%) nosocomial cases. • 75/168 (45%) linked, sequenced cases were not refuted by applying genomic data, creating 14 final clusters accounting for 59/77 (77%) sequenced nosocomial cases. • Nosocomial cases decreased to 0-2/day despite continuing daily admissions of around 40-50 cases community-onset SARS-CoV-2 and before the impact of introducing universal face-masks or banning hospital visitors. • Genomics was necessary to accurately resolve transmission clusters Our data supports unidentified cases, such as healthcare workers or asymptomatic patients, as important vectors of transmission.
11.08.2021	Evolutionary analysis of the Delta and Delta Plus variants of the SARS-CoV-2 viruses	J Autoimmun / Article	• Structural analysis examined distinctions between Delta and Delta Plus variants. • Delta Plus had a significant number of high-prevalence mutations (≥20 %) compared to Delta.

			• Delta Plus has new mutations in ORF1a (A1146T, P1604L, A3209V, V3718S, and T3750I); these mutations alter the local structure to evade antibody binding.

Back to menu

Epidemiology and clinical - children and pregnancy

Publication Date	Title/URL	Journal / Article type	Digest
17.07.2021	Risk of infection and transmission of SARS-CoV-2 among children and adolescents in households, communities and educational settings: A systematic review and meta-analysis	J Glob Health / Article	• Systematic review (90 studies). Compared to adults, children (<10 years) showed comparable national (risk ratio (RR) = 0.87) and subnational (RR = 0.81) prevalence in population-screening studies, and lower odds of infection in community/household contact-tracing studies (odds ratio (OR) = 0.62). Adolescents observed comparable risk (OR = 1.22) with adults. • In educational-settings, children attending daycare/preschools (OR = 0.53) were at lower-risk when compared to adults. Odds of infection among primary (OR = 0.85) and high-schoolers (OR = 1.30) was comparable to adults. • Overall, children and adolescents had lower odds of infection in educational-settings compared to community and household clusters.
18.08.2021	Pre-activated antiviral innate immunity in the upper airways controls early SARS-CoV-2 infection in children	Nat Biotechnol / Article	• Study provides evidence via single cell RNA sequencing that children's airway immune cells are primed for virus sensing, resulting in a stronger early innate antiviral response to SARS-CoV-2 infection than in adults.
10.08.2021	Clinical outcomes and antibody response in COVID-19-positive paediatric solid organ transplant recipients	Pediatr Infect Dis J / Brief report	• Report on the clinical and laboratory manifestations and outcomes of 25 paediatric solid organ transplant (SOT) recipients who tested positive for SARS-CoV-2. • Twenty-one (84%) developed a mild disease; 22 of 23 (96%) had a positive serologic response. Two patients (8%), both kidney transplant recipients with additional comorbidities, developed a severe disease, emphasizing the need for close monitoring in this population • During the acute phase of infection, 23 (92%) of patients were symptomatic, a high percentage, particularly in the paediatric population. All the patients fully recovered clinically from the COVID-19 disease
12.08.2021	Deaths in Children and Adolescents Associated With COVID-19 and MIS-C in the United States	Pediatrics / Article	• Analysis of 112 SARS-CoV-2 associated deaths from 25 participating jurisdictions. • Deaths associated with SARS-CoV-2 among individuals <21 years of age during February–July 2020 occurred predominantly among older adolescents, males, Black (non-Hispanic) and Hispanic persons, and persons with underlying medical conditions.

			• Ninety-six decedents (86%) had at least one underlying condition, the most common being obesity, asthma, and developmental disorders. Decedents with COVID-19 disease were more likely than those with MIS-C to have underlying medical conditions.
10.08.2021	COVID-19 Vaccination During Pregnancy: Coverage and Safety	Am J Obstet Gynecol / Original research	• London NHS Foundation Trust cohort study: 1328 pregnant women who gave birth 01.03.21 - 04.07.21. • Under one third accepted COVID-19 vaccination during pregnancy; they experienced similar pregnancy outcomes. • Lower uptake among younger women, non-white ethnicity, and lower socioeconomic background.
13.08.2021	Immediate Pre-Partum SARS-CoV-2 Status and Immune Profiling of Breastmilk: A Case-Control Study	Front Immunol / Article	• 21 women from a study group of 37 (56.8%) developed symptomatic COVID-19. Study confirms no viral RNA and a distinct immunological profile in breastmilk according to mother's SARS-CoV-2 status. Severity of disease (symptomatic or asymptomatic infection) did not affect the immunological profile in breast milk. • Concentrations of cytokines, chemokines and growth factors were higher in breastmilk of the study group compared with the control group at 1st week postpartum. Immune compounds concentrations decreased on time, particularly in the control group milk samples. • Lack of viral RNA in breastmilk supports its safety, and concurs with recent epidemiological data, as several small observational studies reported on the absence of infection in infants fed by breastmilk of SARS-CoV-2 positive woman or inadvertently fed with SARS-CoV-2 RNA-positive milk

Back to menu

Epidemiology and clinical - long-term complications / sequelae

Publication Date	Title/URL	Journal / Article type	Digest
20.08.2021	Spectrum, risk factors and outcomes of neurological and psychiatric complications of COVID-19: a UK-wide cross-sectional surveillance study	Brain Commun / Article	• Of 267 cases 95 (36%) were female, and 44 (18%) were from BAME groups. 113 (42%) <60 years. COVID-19 was confirmed or probable in 239 (90%) patients, and possible in 10% of cases. Comorbidities were common, with 196 (81%) cases having at least one • Cerebrovascular events were reported in 131 cases (49%), followed by other central disorders (95, 36%) including delirium (28, 11%), central inflammatory (25, 9%), psychiatric (25, 9%), and other encephalopathies (17, 7%), including a

			severe encephalopathy (n = 13) not meeting delirium criteria; and peripheral nerve disorders (41, 15%). • Presentations spanned pre-symptomatic, early and later phases of COVID-19, implying different pathophysiological processes may occur, and these may act synergistically in driving neurological complications. • Study has identified older age and a higher pre-COVID-19 frailty score to be associated with poor outcome, and the effect of these factors overshadowed the effects of specific neurological diagnoses.
06.08.2021	Long Covid in adults discharged from UK hospitals after Covid-19: A prospective, multicentre cohort study using the ISARIC WHO Clinical Characterisation Protocol	Lancet Reg Health Eur	• At least 90 days after initial onset 55% of the 327 participants reported not feeling fully recovered. Persistent symptoms were reported by 93% with fatigue the most common (83%) Breathlessness was reported by 54% and 47% reported an increase in MRC dyspnoea scale. New or worse disability was reported by 24% of participants. • Survivors of Covid-19 experienced long-term symptoms, new disability, increased breathlessness, and reduced quality of life. These findings were present in young, previously healthy working age adults, and were most common in younger females.
20.08.2021	Risk Predictors and Symptom Features of Long COVID Within a Broad Primary Care Patient Population Including Both Tested and Untested Patients	Pragmat Obs Res / Article	• Observational UK study using data from Platform C19, a research database linking primary care electronic health record data (EHR) with patient-reported questionnaire information from patients aged 18–85 between 07.08.2020 and 22.01.2021 • Risk predictors of long COVID were age ≥40 years, female sex, frailty, visit to A&E, and hospital admission for COVID-19 symptoms. Aches and pain, appetite loss, confusion and disorientation, diarrhoea, and persistent dry cough were symptom features statistically more common in long COVID. • Of 3151 patients with self-diagnosed, clinician-diagnosed, or test-confirmed COVID-19, 310 (9.8%) had long COVID, defined here as reporting symptoms ≥ 4 weeks. Only 34.2% long COVID patients had test-confirmed COVID-19.
10.08.2021	Persistent Endotheliopathy in the Pathogenesis of Long COVID Syndrome	J Thromb Haemost / Brief report	• Among 50 patients reviewed at median 68 days following SARS-CoV-2 infection thrombin generation assays revealed significantly shorter lag times, increased endogenous thrombin potential (ETP) and peak thrombin in convalescent COVID-19 patients; these changes were independent of ongoing acute phase response or active NETosis. • EC biomarkers including VWF:Ag, VWFpp and FVIII:C were significantly elevated in convalescent COVID-19 compared to controls, as were plasma soluble thrombomodulin (sTM) levels. • Sustained endotheliopathy was more frequent in older, comorbid patients and those requiring hospitalisation.

			• Plasma VWF:Ag and VWFpp levels correlated inversely with 6-minute walk tests. • Associated commentary: https://www.rcsi.com/dublin/news-and-events/news/news-article/2021/08/blood-clotting-may-be-the-root-cause-of-long-covid-syndrome

Back to menu

Epidemiology and clinical – risk factors

Publication Date	Title/URL	Journal / Article type	Digest
18.08.2021	COVID-19 infection, hospitalisation and death Amongst People with Rare Autoimmune Rheumatic Disease in England. Results from the RECORDER Project	medRxiv (non-peer reviewed) / Article	• Analysis of health records identified a cohort of 168,680 people with rare autoimmune rheumatic diseases (RAIRD) in England, of whom 1874 (1.11%) tested COVID-19 positive. Mortalities with COVID-19 listed on the death certificate occurred in 713 (0.42%) people with RAIRD. • Compared to the general population, the age standardised infection rate was 1.54 times higher and the age/sex standardised mortality rate for COVID-19 related death was 2.41 times higher in people with RAIRD. These increases were seen despite shielding policies. • No evidence of an increase in deaths from other causes in the RAIRD population.
16.08.2021	Risk of COVID-19 death in cancer patients: an analysis from Guy's Cancer Centre and King's College Hospital in London	Br J Cancer / Article	• Observational cohort study with 306 SARS-CoV-2-positive cancer patients. 71% had mild/moderate and 29% had severe COVID-19. Seventy-two patients died of COVID-19 (24%), of whom 35 died <7 days. • An increased risk of COVID-19 severity and death (including within 7 days) was observed for haematological patients compared to those with solid malignancies. This is likely explained by the intense immunosuppressive treatment received by these patients. • Findings provide further evidence of the increased risk of COVID-19 mortality for male and Asian cancer patients, and those with haematological malignancies or a cancer diagnosis >2 years.
16.08.2021	Multiple sclerosis is not associated with an increased risk for severe COVID-19: a nationwide retrospective cross-sectional study from Germany	Neurol Res Pract / Article	• Among 157,524 patients hospitalised with COVID-19 in Germany, 551 had a concurrent MS diagnosis (0.3%). • Univariate analysis found lower rates of ICU admission (17.1% versus 22.7%), lower use of ventilation (9.8% versus 14.5%) and lower in-hospital mortality (11.1% versus 19.3%) among COVID-19 patients with comorbid MS.

			• This finding was stable across sex and MS subtype but was attenuated by age-stratification, confirming equal odds of in-hospital mortality between COVID-19 patients with and without MS (log OR: 0.09).
18.08.2021	Peripheral Artery Disease and COVID-19 Outcomes: Insights from the Yale DOM-CovX Registry	medRxiv (non-peer reviewed) / Article	• Study of 3,830 patients consecutively admitted with SARS-CoV-2 between 1 March and 10 November 2020 (50.5% female, mean age 63.1), of whom 18.3% (n = 693) had peripheral arterial disease (PAD). • PAD was independently associated with increased mortality (OR=1.45) and major adverse cardiovascular events (OR=1.48). PAD was not independently associated with stroke and myocardial infarction.

Back to menu

Epidemiology and clinical – other

Publication Date	Title/URL	Journal / Article type	Digest
16.08.2021	Association of Age and Pediatric Household Transmission of SARS-CoV-2 Infection	JAMA Pediatr / Original investigation	• Cohort study of 6280 households with paediatric index cases, the adjusted odds of household transmission by children aged 0 to 3 years was 1.43 compared with children aged 14 to 17 years.
02.08.2021	Age-Associated Neurological Complications of COVID-19: A Systematic Review and Meta-Analysis	Front Aging Neurosci / Systematic Review	• Systematic review of case reports and series (239 papers): neurological injury associated with COVID-19 infection was observed across the lifespan, with and without comorbidities and with all disease severities. • Older individuals are more susceptible to developing life-threatening COVID-19 and cerebrovascular disease (e.g. stroke). • Mild but inverse correlation with age observed with CNS inflammatory diseases, such as encephalitis, as well as taste and/or smell disorders. • Increased age also associated with comorbid cardiovascular risk factors, including hypertension, diabetes mellitus, and lipid disorders, but not with obesity. • Potential pathophysiological mechanisms of neurological symptoms and long-term consequences of infection are discussed.
17.08.2021	The Immunopathogenesis of Neuroinvasive Lesions of SARS-CoV-2 Infection in COVID-19 Patients	Front Neurol / Review	• In this review recent findings on the mechanisms by which SARS-CoV-2 accesses the central nervous system (CNS) and induces neurological dysregulation are summarized. • A wide range of neurological symptoms have been associated with COVID-19; alongside a neurotropic behaviour and neuroinvasive properties, the virus may trigger neurological defects by triggering a cytokine storm.

			• Current evidence strongly suggests that patients surviving COVID-19 are at high risk of developing neurological disease. There are concerns that even when the pandemic is over, SARS-CoV-2 might persist within the CNS and cause chronic and latent infection in a large proportion of the population including those who suffered only mild respiratory symptoms.
11.08.2021	Shedding of Infectious SARS-CoV-2 Despite Vaccination when the Delta Variant is Prevalent - Wisconsin, July 2021	medRxiv (non-peer reviewed) / Article	• Authors analyse viral load data from a laboratory in Wisconsin, USA at a time of increasing prevelance of the Delta variant • No difference observed in viral loads when comparing unvaccinated individuals to those with vaccine "breakthrough" infections; individuals with breakthrough infections frequently test positive with viral loads consistent with the ability to shed infectious viruses. • Notably, 68% of individuals infected despite vaccination tested positive with Ct <25, including at least 8 asymptomatic. • Results suggest vaccinated individuals who become infected with Delta may be sources of SARS-CoV-2 transmission to others.
13.08.2021	Evolutionary trajectory of SARS-CoV-2 and emerging variants	Virol J / Review	• Review highlighting the origins of all known human coronaviruses (HCoVs) and mapping positively selected-for mutations within their proteins in order to discuss the evolutionary trajectory of SARS-CoV-2. • The impact of mutations on virus transmission, pathogenicity, and neutralization by natural or vaccine-mediated immunity are discussed • The authors suggest that SARS-CoV-2 is evolving to become less pathogenic in humans and the pandemic is driven by asymptomatic, pre-symptomatic, or otherwise unrecognized cases. • Reduced pathogenicity combined with mounting population-level immunity will likely cause a reduction of severe cases of COVID-19, leading to an apparent abatement of the pandemic, followed by endemic circulation of low pathogenic variants.
18.08.2021	Ethnic variation in outcome of people hospitalised during the first COVID-19 epidemic wave in Wales (UK): an analysis of national surveillance data using Onomap, a name-based ethnicity classification tool	BMJ Open / Original research	• Surveillance data from 77,555 PCR tests by Public Health Wales was used in addition to data from the records of 4046 hospitalised patients. Data included admission to intensive care units (ICU) and linked to records of 1309 COVID-19 in-hospital deaths • Ethnicity categorised using name-based ethnicity classifier, Onomap, a validated tool developed by UCL that has been found effective in 30 other published studies in healthcare, epidemiology and public health. • While white groups were more likely to be tested for SARS-CoV-2, BAME groups were more likely to test positive. Likelihood of dying was significantly higher for hospitalised males even after adjusting for age and ethnicity

			• No evidence from this study that BAME groups were more likely to die from COVID-19 than white British or Irish groups, even after adjusting for gender, age and social deprivation

Back to menu

Infection control / non-pharmaceutical interventions

Publication Date	Title/URL	Journal / Article type	Digest
17.08.2021	Measuring the scientific effectiveness of contact tracing: Evidence from a natural experiment	Proc Natl Acad Sci U S A / Article	• Exploiting the events surrounding a data error, this experiment provides evidence that cases subject to proper contact tracing were associated with a reduction in subsequent new infections of 63% and a reduction in subsequent COVID-19–related deaths of 66% across a 6-week period. • These findings suggest that tracing may be even more effective than indicated by previous correlational research.
17.08.2021	Do school closures and school reopenings affect community transmission of COVID-19? A systematic review of observational studies	BMJ Open / Original research	• Systematic review: 40 studies included, with data from 150 countries; 32 studies assessed school closures and 11 examined re-openings. • Substantial heterogeneity between school closure studies, with half of the studies at lower risk of bias reporting reduced community transmission by up to 60%, and half reporting null findings. • Three of the four school reopening studies at lower risk of bias reported no associated increases in transmission. • Suggests school re-openings, in areas of low transmission and with appropriate mitigation measures, were generally not accompanied by increasing community transmission.

Back to menu

Transmission

Publication Date	Title/URL	Journal / Article type	Digest
19.07.2021	Estimating SARS-CoV-2 Circulation in the School Setting: A Systematic Review and Meta-Analysis	SSRN (non-peer reviewed) / Article	• Systematic review included: 21 screening studies reporting infections, (n>120,000;, 15 studies on contact tracing (n=112,622); and 9 studies on seroprevalence (n=17,879). • Screening studies estimated 0·31% point prevalence in schools. In contact tracing studies, onward viral transmission was limited (SAR = 2·54%).

			• Young index cases were 74% significantly less likely than adults to favour viral spread (OR = 0·26) and data from seroprevalence studies shows that children are 43% less likely than adults to test positive for antibodies (OR = 0·57). Overall, data suggests that schools did not develop into hotspots for SARS-CoV-2 transmission.
17.08.2021	Aerosols from speaking can linger in the air for up to nine hours	Build Environ / Article	• To understand the role of speech aerosols in the spread of COVID-19 globally, the lifetime and size distribution of the aerosols are studied through a combination of light scattering observation and aerosol sampling. • Speech aerosols in the size range of about 0.3–2 μm (after dehydration) had the longest lifetime compared to larger aerosols (2–10 μm). • Findings suggest that speech aerosols have the potential to transmit respiratory viruses across long duration (hours), and long-distance (over social distance) through the airborne route.
13.08.2021	Transmission dynamics and epidemiological characteristics of Delta variant infections in China	medRxiv (non-peer reviewed) / Article	• Among 167 patients infected with the Delta variant in an outbreak in Guangdong, China the mean estimates of latent and incubation periods were 4.0 days and 5.8 days, respectively. Relatively higher viral load observed in Delta cases vs wild-type infections. • Secondary attack rate among close contacts of Delta cases was 1.4%, and 73.9% of the transmissions occurred before onset. • Index cases without vaccination (OR: 2.84) or with one dose of vaccination (OR: 6.02) were more likely to transmit infection to their contacts than those who had received 2 doses of vaccination.
02.08.2021	Aerosol transmission of SARS-CoV-2 due to the chimney effect in two high-rise housing drainage stacks	J Hazard Mater / Article	• Authors investigated two stack aerosol-related outbreaks of COVID-19 in high rise buildings in Hong Kong • Tracer gas was injected into drainage stacks via the water closet of the index case and concentrations were monitored in the bathrooms and along the facades of infected and non-infected flats and in roof vents. • Measured tracer gas distribution agreed with the observed distribution of infected cases. • Phylogenetic analysis demonstrated clonal spread from a point source in cases along the same vertical column. • Results suggests stack aerosols may spread indoors via pipe leaks, facilitating long-range aerosol transmission of SARS-CoV-2 through drainage pipes via the "chimney effect".

Back to menu

Treatment

Publication Date	Title/URL	Journal / Article type	Digest
18.08.2021	Inhaled High Dose Nitric Oxide is a Safe and Effective Respiratory Treatment in Spontaneous Breathing Hospitalized Patients with COVID-19 pneumonia	Nitric Oxide / Article	• Multicentre study to evaluate the feasibility and effects of high-dose inhaled nitric oxide (NO) in non-intubated spontaneously breathing patients with COVID-19 • Twenty-nine COVID-19 patients received a total of 217 intermittent inhaled NO treatments for 30 min at 160 ppm between March and June 2020 • In this cohort, inhaled NO at 160 ppm for 30 min twice daily promptly improved the respiratory rate of tachypneic patients and systemic oxygenation of hypoxemic patients. No adverse events were observed and none of the participants were readmitted or had long-term COVID-19 sequelae.
09.08.2021	Effect of anakinra on mortality in patients with COVID-19: a systematic review and patient-level meta-analysis	Lancet Rheumatol / Systematic review	• Systematic review with data on 1185 patients from nine studies suggests that Anakinra could be an effective and safe immunomodulatory treatment to prevent unfavourable outcomes in moderate-to-severe cases of pneumonia due to COVID-19. • Anakinra showed a significant survival benefit when given without dexamethasone, but not with dexamethasone co-administration. Anakinra was not associated with a significantly increased risk of secondary infections when compared with standard of care • Additional comment: https://dx.doi.org/10.1016/s2665-9913(21)00249-6
16.08.2021	Systemic corticosteroids for the treatment of COVID-19	Cochrane Database Syst Rev / Review	• 11 RCTs in 8075 participants: 3072 participants randomised to corticosteroid, majority received dexamethasone (n = 2322). • Moderate-certainty evidence: slightly reduce all-cause mortality in people hospitalised with COVID-19. • Low-certainty evidence: reduction in ventilator-free days (limitations noted). • No evidence for asymptomatic or mild disease (non-hospitalised participants).

Back to menu

Modelling

Publication Date	Title/URL	Journal / Article type	Digest
14.08.2021	SARS-CoV-2 infection in UK university students: lessons from September-December 2020 and modelling insights for future student return	R Soc Open Sci / Article	• Overall distribution of university outbreaks in late 2020 were consistent with expected importation of infection from arriving students. • In term time, larger halls of residence posed higher risks for larger attack rates. This was not mitigated by segmentation into smaller households.

			• Although community spillover can occur, occasionally even large outbreaks do not give any detectable signal of spillover to the local population. • Staggering return of students to university residence is of limited value in reducing transmission in term time; student adherence to testing and self-isolation are likely to be more important. • Very frequent asymptomatic testing (all students every 3 days) would be necessary to prevent a major outbreak in the context of a more transmissible variant (as currently dominant in the UK). • Preprint previously included
13.08.2021	Impact of university re-opening on total community COVID-19 burden	PLoS One / Article	• Dynamic transmission model of COVID-19 in a mid-sized city currently experiencing a low infection rate. Consideration is given to screening interventions as a mitigation strategy • Evaluation, in terms of cumulative COVID-19 infections, time to peak infections, and the timing and peak level of critical care occupancy, of the impact of 20,000 university students arriving on 1 September • Modelling indicates that if arriving students reduce their contacts by 40% compared to pre-COVID levels, the total number of infections in the community increases by 115% (from 3,515 to 7,551), with 70% of the incremental infections occurring in the general population, and an incremental 19 associated deaths.
18.08.2021	Non-pharmaceutical interventions, vaccination and the Delta variant: epidemiological insights from modelling England's COVID-19 roadmap out of lockdown	medRxiv (non-peer reviewed) / Article	• Modelling suggests the roadmap out of lockdown in England was successful in offsetting increased transmission resulting from lifting non-pharmaceutical interventions (NPIs) with increasing population immunity through vaccination. • With the emergence of Delta [estimated transmission advantage of 73% over Alpha], fully lifting NPIs on 21 June 2021 as originally planned may have led to 3,400 peak daily hospital admissions: delaying until 19 July reduced peak hospitalisations by three-fold to 1,400 per day. • There was substantial uncertainty in epidemic trajectory, with particular sensitivity to estimates of vaccine effectiveness and the intrinsic transmissibility of Delta.
13.08.2021	SARS-CoV-2 variants: levels of neutralisation required for protective immunity	medRxiv (non-peer reviewed) / Article	• Modelling study integrates published data on in vitro neutralisation and clinical protection to examine vaccine efficacy against existing SARS-CoV-2 variants of concern (VOC). • Findings suggest neutralising activity against ancestral SARS-CoV-2 is highly predictive of neutralisation of VOC. All vaccines show similar drop in neutralisation to the variants. • Neutralisation levels remain strongly correlated with protection from infection with SARS-CoV-2 VOC (r=0.81).

			• Protection against symptomatic infection may drop below 50% within the first year after vaccination for some current vaccines. • Booster vaccination should enable high levels of immunity that prevent severe infection outcomes with current SARS-CoV-2 VOC, at least in the medium term. • Associated news item: https://www.nature.com/articles/d41586-021-02237-8

Back to menu

Guidance and consensus statements

Publication Date	Title/URL	Journal / Article type
17.08.2021	The long-term sequelae of COVID-19: an international consensus on research priorities for patients with pre-existing and new-onset airways disease	Lancet Respir Med / Position Paper

Back to menu

Overviews, comments and editorials

Publication Date	Title/URL	Journal / Article type
17.08.2021	The animal origin of SARS-CoV-2	Science / Perspective
09.08.2021	Predicted COVID-19 positive cases, hospitalisations, and deaths associated with the Delta variant of concern, June-July, 2021	Lancet Digit Health / Comment
15.08.2021	Time for action: towards an intersectional gender approach to COVID-19 vaccine development and deployment that leaves no one behind	BMJ Glob Health / Commentary
16.08.2021	Persistent SARS-CoV-2 infection: the urgent need for access to treatment and trials	Lancet Infect Dis / Comment
19.08.2021	How universities can make reopening safer this autumn	BMJ / Opinion

Back to menu

Produced by the PHE COVID-19 Literature Digest Team

To sign-up, email COVID.LitDigest@phe.gov.uk
A selection of previous digests can be found here