



COVID-19 Literature Digest – 27/08/2021

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 The reports include both preprints, which should be treated with caution as they are NOT peer-reviewed and may be subject to change, and also research that has been subject to peer review and wider scrutiny.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Report for 27.08.2021 (please note that papers that have **NOT been peer-reviewed** are highlighted in red).

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Serology and immunology

Publication Date	Title/URL	Journal / Article type	Digest
14.08.2021	Favourable antibody responses to human coronaviruses in children and adolescents with autoimmune rheumatic diseases	Med (N Y) / Article	<ul style="list-style-type: none">• Study into the immune response of children and adolescents with juvenile idiopathic arthritis (JIA), juvenile dermatomyositis (JDM) and juvenile systemic lupus erythematosus (JSLE), against the seasonal human coronavirus (HCoV)-OC43 that frequently infects this age group• Sensitive flow cytometry-based assays were used to determine titres of antibodies that reacted with the spike and nucleoprotein of HCoV-OC43 and cross-reacted with SARS-CoV-2.• Autoimmune rheumatic diseases and their treatment were associated with a favourable ratio of spike to nucleoprotein antibodies. Despite immune dysfunction and immunosuppressive treatment, JIA, JDM and JSLE patients maintained comparable or stronger humoral responses than healthier peers, harbouring IgG antibodies that cross-reacted with SARS-CoV-2 spike.
25.08.2021	Sex Disparities and Neutralizing-Antibody Durability to SARS-CoV-2 Infection in Convalescent Individuals	mSphere / Article	<ul style="list-style-type: none">• Evaluation of serologic, demographic, and clinical correlates of functional antibody responses and durability to SARS-CoV-2, supporting growing evidence of sex discrepancies in COVID-19 disease morbidity and mortality, as well as functional neutralizing antibody responses to SARS-CoV-2.• In a cohort of 101 COVID-19 convalescent plasma (CP) donors, higher neutralizing antibody titers were found to be independently and significantly associated with male sex compared to female sex.• Higher convalescent antibody titers in male donors are associated with increased age and symptom grade.• Cardiometabolic comorbidities are associated with higher antibody titers independently of sex.

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Vaccines

Publication Date	Title/URL	Journal / Article type	Digest
24.08.2021	Antibody Response to a Fourth Dose of a SARS-CoV-2 Vaccine in Solid Organ Transplant Recipients: A Case Series	Transplantation / Research letter	<ul style="list-style-type: none"> • Study of the antibody responses to a 4th dose of SARS-CoV-2 vaccine in 18 solid organ transplant recipients (SOTRs) from 24.04.2021 – 16.06.2021 • After a fourth dose (post-D4), 5/8 (63%) participants with low-positive or negative titers showed boosting to high-positive titers. • Most participants with high-positive pre-D4 titers showed further boosting. • 7/11 (63%) SOTRs serially tested on similar assays, had increased titers post-D4. • Eleven of 16 participants (69%) receiving antiproliferative agents showed antibody boosting. • 3 participants with persistently negative post-D4 titers were kidney transplant recipients less than 5 years post-transplant taking tacrolimus and mycophenolate mofetil, and 2/3 were additionally taking corticosteroids.
24.08.2021	Weak antibody response to 3 doses of mRNA vaccine in kidney transplant recipients treated with belatacept	Am J Transplant / Article	<ul style="list-style-type: none"> • Only 4 of 62 belatacept-treated kidney transplant recipients (KTRs) developed anti-SARS-CoV-2 IgG with low antibody titers after 3 doses of BNT162b2 mRNA COVID-19 vaccine • In all 35 non-belatacept-treated KTRs seroprevalence was 37.1% after 3-vaccine doses. • In all 5 KTRs with prior COVID-19 history, mRNA vaccine induced strong antibody response with high antibody titers after 2 injections • 12 patients developed symptomatic COVID-19 following at least 1 vaccine injection. 75% were hospitalised and 50% died.
24.08.2021	Antibody response to the Janssen/Johnson & Johnson SARS-CoV-2 vaccine in patients with rheumatic and musculoskeletal diseases	Ann Rheum Dis / Letter	<ul style="list-style-type: none"> • Patients with rheumatic and musculoskeletal diseases (RMD) who received J&J vaccination had a lower rate of seroconversion compared with mRNA vaccines. • 29 days (28-32) after vaccination, anti-RBD antibody detectable in 36 of 45 receiving J&J versus 906 of 994 who completed mRNA vaccine series. • One in five participants who received J&J vaccination did not mount a detectable antibody response.
23.08.2021	Examining the Immunological Effects of COVID-19 Vaccination in Patients with Conditions	SSRN (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Study compares 600 participants with various immune-mediated inflammatory and chronic diseases recruited to the OCTAVE study and 231 healthy participants from the PITCH study.

	Potentially Leading to Diminished Immune Response Capacity – The OCTAVE Trial		<ul style="list-style-type: none"> • Overall 89% of patients within OCTAVE seroconverted 4 weeks after second vaccine dose of AstraZeneca or Pfizer vaccine, compared to 100% (n=93) of tested PITCH participants. • Failure to seroconvert was found at a higher proportion in some disease subgroups, particularly ANCA-Associated Vasculitis (AAV; 72.4%), haemodialysis with immunosuppression (16.7%) and hepatic disease (16.7%). All recruited AAV patients had received Rituximab. • Even in those who seroconverted, 40% of patients across disease cohorts generated lower levels of SARS-CoV-2 antibody reactivity compared to healthy subjects after two vaccines • Spike-specific T cell response across all patient sub-groups (including AAV) was similar to healthy individuals. • Linked BMJ News: https://dx.doi.org/10.1136/bmj.n2098
20.08.2021	To mix or not to mix? A rapid systematic review of heterologous prime-boost covid-19 vaccination	Expert Rev Vaccines / Systematic review	<ul style="list-style-type: none"> • Systematic review including 4 studies with 2,116 participants found heterologous administration of BNT162b2 (BNT) in ChAdOx1 (ChAd)-primed participants (ChAd/BNT) showed comparable immunogenicity to homologous BNT regimen • Compared with single-dose ChAdOX1 vaccination (ChAd) and homologous ChAdOX1 vaccination (ChAd/ChAd), heterologous ChAd/BNT was found to elicit higher immunogenicity and T cell responses. • Adverse events were more common with a heterologous regimen but these were tolerable and there were no serious adverse events.
27.08.2021	Risk of thrombocytopenia and thromboembolism after covid-19 vaccination and SARS-CoV-2 positive testing: self-controlled case series study	BMJ / Article	<ul style="list-style-type: none"> • Self-controlled case series study using UK national data on covid-19 vaccination and hospital admissions; comprised people vaccinated with first dose of either Oxford-AstraZeneca (ChAdOx1; n=19,608,008) or Pfizer-BioNTech (BNT162b2; n=9,513,625) and 1,758,095 people who had a positive SARS-CoV-2 test. • Found increased risk of thrombocytopenia after ChAdOx1 (incidence rate ratio 1.33 at 8-14 days) and after a positive SARS-CoV-2 test (5.27 at 8-14 days); increased risk of venous thromboembolism after ChAdOx1 (1.10 at 8-14 days) and after SARS-CoV-2 infection (13.86 at 8-14 days); and increased risk of arterial thromboembolism after BNT162b2 (1.06 at 15-21 days) and after SARS-CoV-2 infection (2.02 at 15-21 days). • Secondary analyses found increased risk of CVST after ChAdOx1 (4.01 at 8-14 days), after BNT162b2 (3.58 at 15-21 days), and after a positive SARS-CoV-2 test; increased risk of ischaemic stroke after BNT162b2 (1.12 at 15-21 days) and after a positive SARS-CoV-2 test; and increased risk of

			<p>other rare arterial thrombotic events after ChAdOx1 (1.21 at 8-14 days) and after a positive SARS-CoV-2 test.</p> <ul style="list-style-type: none"> • Suggests the risks of these haematological and vascular events were substantially higher and more prolonged after SARS-CoV-2 infection than after vaccination in the same population. • Associated editorial: https://www.bmj.com/content/374/bmj.n1994
25.08.2021	Safety of the BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Setting	N Engl J Med / Article	<ul style="list-style-type: none"> • Israeli study: data sets of 2.4 million BNT162b2 [Pfizer] vaccinated persons / 240,000 SARS-CoV-2 infected persons. • Vaccine: excess risk of myocarditis (2.7 events per 100,000 persons). Also lymphadenopathy, appendicitis and herpes zoster infection. • Infection: substantially increased risk of myocarditis (11.0 events per 100,000 persons). Additional serious adverse events, including pericarditis, arrhythmia, deep-vein thrombosis, pulmonary embolism, myocardial infarction, intracranial haemorrhage, and thrombocytopenia. • Vaccine appears protective against some adverse events such as anaemia and intracranial haemorrhage, likely because infection was prevented. • See linked editorial: https://www.nejm.org/doi/full/10.1056/NEJMe2112543
27.08.2021	Effectiveness of COVID-19 Vaccines in Preventing SARS-CoV-2 Infection Among Frontline Workers Before and During B.1.617.2 (Delta) Variant Predominance - Eight U.S. Locations, December 2020-August 2021	MMWR Morb Mortal Wkly Rep / Article	<ul style="list-style-type: none"> • In this frontline workers cohort, vaccine effectiveness (VE) point estimates declined from 91% predominance to 66% since Delta variant became predominant. • VE may also be declining as time since vaccination increases.
27.08.2021	Effectiveness of Pfizer-BioNTech and Moderna Vaccines in Preventing SARS-CoV-2 Infection Among Nursing Home Residents Before and During Widespread Circulation of the SARS-CoV-2 B.1.617.2 (Delta) Variant - National Healthcare Safety Network, March 1-August 1, 2021	MMWR Morb Mortal Wkly Rep / Article	<ul style="list-style-type: none"> • Two doses of mRNA vaccines 74.7% effective against infection among nursing home residents early in vaccination programme (March–May 2021). • When B.1.617.2 [Delta] variant circulation predominated, effectiveness declined to 53.1%. (based on 85,593 weekly reports to CDC from 14,917 facilities during June-July 2021). • Potential impact of waning immunity couldn't be determined
26.08.2021	Durability of antibody responses elicited by a single dose of Ad26.COV2.S and substantial increase following late boosting	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Study using sera from phase 1/2a and phase 2 clinical trials found a single dose of Ad26.COV2.S (Janssen) elicited durable neutralising and binding antibodies for at least 8 and 6 months, respectively, in adults (>18 years old) at levels similar to Day 29 responses.

			<ul style="list-style-type: none"> • A 5x10¹⁰ vp booster dose at 6 months elicited a steep and robust 9-fold increase in 18–55-year-old adults at Day 7 post boost compared to Day 29 levels following the initial immunisation. • A lower booster dose of 1.25x10¹⁰ vp at 6 months in adults 18–55 and ≥65 years of age also elicited a 6–7.7 fold increase at Day 28 post boost compared to Day 29 levels following the initial immunisation, with similar magnitude of post-boost responses in both age groups.
21.08.2021	Poliovirus Vaccination Induces a Humoral Immune Response That Cross Reacts With SARS-CoV-2	Front Med (Lausanne) / Article	<ul style="list-style-type: none"> • Analysis of Sera from 204 adults and children, who were immunized with the poliovirus vaccine, and evaluation of the effects of polio-immune serum on SARS-CoV-2-induced cytopathology in cell culture • Poliovirus vaccination induces an adaptive humoral immune response; the antibodies created bind the RNA-dependent RNA polymerase (RdRp) protein of both poliovirus and SARS-CoV-2, thereby preventing SARS-CoV-2 infection

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Diagnostics and genomics

Publication Date	Title/URL	Journal / Article type	Digest
19.08.2021	ONS: Impact of Delta and calendar time on symptoms reported by individuals testing swab positive – preliminary analysis of data (to 12 July 2021), 22 July 2021	Gov.uk (non-peer reviewed) / Research and analysis	<ul style="list-style-type: none"> • Authors model percentage of individuals newly testing positive or negative over time who reported any symptoms and, of those reporting any symptoms, the percentage reporting each specific symptom (up to 12 July 2021) • Findings do not suggest any major shift away from the importance of the classic four symptoms in positive cases with the emergence of the Delta variant in the UK • Recent reports of associations with sore throat may reflect background increases in other respiratory infections/hay fever, potentially with SARS-CoV-2 isolated incidentally.
23.08.2021	Correlation of SARS-CoV-2 Subgenomic RNA with Antigen Detection in Nasal Midturbinate Swab Specimens	Emerg Infect Dis / Article	<ul style="list-style-type: none"> • SARS-CoV-2 sgRNA detected in all samples from antigen-positive participants (28/28), consistent with identification of active viral replication and potential shedding. • Among antigen-negative participants, sgRNA detection varied between SARS-CoV-2 RNA-positive midturbinate (0/4) and nasopharyngeal (13/16) swab specimens.

			<ul style="list-style-type: none"> Nasopharyngeal swab specimens are expected to have higher viral loads but this isn't the sole explanation.
24.08.2021	Symptoms and SARS-CoV-2 positivity in the general population in the UK	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> Analyses data from the COVID-19 Infection Survey from 26 April 2020 to 7 August 2021: included 27,692 participants testing SARS-CoV-2 positive (of whom 48% self-reported symptoms) and a comparator group of 3,806,692 test-negative visits (457,215 participants) There was a small increase in sore throat reporting in symptomatic positive episodes and negative visits from April-2021. After May-2021 when Delta emerged there were substantial increases in headache and fever in positives, but not in negatives. Although specific symptom reporting in symptomatic positive episodes vs. negative visits varied by age, sex, and ethnicity, only small improvements in symptom-based infection detection were obtained; e.g. adding fatigue/weakness or all eight symptoms to the classic four symptoms (cough, fever, loss of taste/smell) increased sensitivity from 74% to 81% to 90% but tests per positive from 4.6 to 5.3 to 8.7.
26.08.2021	Sensitivity and specificity of the antigen-based anterior nasal self-testing programme for detecting SARS-CoV-2 infection in schools, Austria, March 2021	Eurosurveillance / Rapid communication	<ul style="list-style-type: none"> Authors evaluate performance of the antigen-based anterior nasal screening programme implemented in all Austrian schools, combining nationwide antigen-based screening data obtained in March 2021 from 5,370 schools (Grade 1–8) with an RT-qPCR-based prospective cohort study comprising a representative sample of 244 schools. Considering a range of assumptions, only a subset of infected individuals are detected with the programme (low to moderate sensitivity) and non-infected individuals mainly tested negative (very high specificity).
24.08.2021	SARS-CoV-2 Wastewater Surveillance for Public Health Action	Emerg Infect Dis / Article	<ul style="list-style-type: none"> Paper describe the key uses, barriers, and applicability of SARS-CoV-2 wastewater surveillance for supporting public health decisions and actions.
22.08.2021	Delta variant and mRNA Covid-19 vaccines effectiveness: higher odds of vaccine infection breakthroughs	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> Observational case-case study covering a period of VOC replacement in Portugal from Alpha to Delta dominance (17 May and 4 July 2021): 2,097 positive cases analysed. Individuals infected with Delta were more frequently vaccinated (n=162; 12%) than individuals infected with Alpha (n=38; 5%). Significantly higher odds of mRNA vaccine infection breakthrough found for partial (OR=1.70) and complete vaccination (OR=1.96) in Delta cases compared to Alpha cases, suggesting lower mRNA vaccine effectiveness against Delta cases.

			<ul style="list-style-type: none"> • Lower mean Ct values observed for the Delta cases versus Alpha, regardless of vaccination status. Delta variant cases revealed a Ct-value mean increase of 2.24 between unvaccinated and fully vaccinated breakthrough cases, compared with 4.49 in Alpha cases, suggesting lower impact of vaccine on viral load.
24.08.2021	The continuous evolution of SARS-CoV-2 in South Africa: a new lineage with rapid accumulation of mutations of concern and global detection	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Authors report identification of a potential variant of interest assigned to lineage C.1.2, first identified in May 2021 and evolved from C.1 • Emergence of C.1.2 was associated with increased substitution rate, as previously observed with the emergence of the Alpha, Beta and Gamma VOCs • C.1.2 contains multiple substitutions (R190S, D215G, N484K, N501Y, H655Y and T859N) and deletions (Y144del, L242-A243del) within the spike protein, which have been observed in other VOCs and are associated with increased transmissibility and reduced neutralisation sensitivity • Accumulation of additional mutations (C136F, Y449H and N679K) may also impact neutralisation sensitivity or furin cleavage.
24.08.2021	Mutation Y453F in the spike protein of SARS-CoV-2 enhances interaction with the mink ACE2 receptor for host adaption	bioRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Authors investigate functional properties of "Cluster 5" mutations previously identified in mink-associated virus (miSARS-CoV-2) spilled back over into humans. • Y453F mutation located in the RBD domain of miSARS-CoV-2 enhances binding to mink ACE2 and other orthologs of Mustela species without compromising, and even enhancing, its ability to utilise human ACE2 for entry. Additionally, Y453F spike exhibited resistance to convalescent serum. • Structural analysis suggests Y34 of mink ACE2 was better suited to interact with Phe rather than Tyr at position 453 of the viral RBD.
20.08.2021	Mutations that adapt SARS-CoV-2 to mustelid hosts do not increase fitness in the human airway	bioRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Authors investigate the molecular basis of mink and ferret adaptation and demonstrate the spike mutations Y453F, F486L, and N501T all specifically adapt SARS-CoV-2 to use mustelid ACE2. • Risk assessment of these mutations suggests mink-adapted viruses are unlikely to pose an increased threat to humans, as Y453F attenuates the virus replication in human cells and all 3 mink-adaptations have minimal antigenic impact. • Certain SARS-CoV-2 variants emerging from circulation in humans may naturally have a greater propensity to infect mustelid hosts and therefore these species should continue to be surveyed for reverse zoonotic infections.

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Epidemiology and clinical - children and pregnancy

Publication Date	Title/URL	Journal / Article type	Digest
26.08.2021	Global characteristics and outcomes of SARS-CoV-2 infection in children and adolescents with cancer (GRCCC): a cohort study	Lancet Oncol / Article	<ul style="list-style-type: none">• Global cohort of 1500 children and adolescents with cancer and COVID-19• Severe disease can occur, particularly in patients receiving intensive chemotherapy, or with lymphopenia and neutropenia• Mortality lower than reported for adults with cancer and SARS-CoV-2; more than four times that reported in general paediatric population.
21.08.2021	Prevalence of Smell or Taste Dysfunction Among Children With COVID-19 Infection: A Systematic Review and Meta-Analysis	Front Pediatr / Systematic review	<ul style="list-style-type: none">• Systematic review including 18 studies found the following results in children with COVID-19, for the pooled prevalence of 1) smell dysfunction - 15.97% 2) taste dysfunction - 9.20% 3) smell or taste dysfunction - 15.50% 4) smell and taste dysfunction - 20.21%• Higher smell or taste dysfunction rates were associated with being female, younger age, smaller sample size, patients in Asia, and with comorbidities.• Limitations of the study were discussed in terms of the heterogeneity of assessment methods and the low or moderate quality of the included studies
21.08.2021	SARS-CoV-2 in diabetic pregnancies: a systematic scoping review	BMC Pregnancy Childbirth / Systematic review	<ul style="list-style-type: none">• Review of 49 eligible papers found pregnant women with diabetes mellitus are more likely to get infected and are at an increased risk of a severe course of COVID-19.• The prognosis of pregnant women with diabetes mellitus and COVID-19 may be associated with simplified viral uptake by ACE2, a higher basal value of pro-inflammatory cytokines, being hypoxemic as well as platelet activation, embolism, and preeclampsia.• COVID-19 may cause new onset diabetes mellitus, and that vertical transmission from mother to baby might be possible.

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Epidemiology and clinical - long-term complications / sequelae

Publication Date	Title/URL	Journal / Article type	Digest
29.07.2021	Cardiopulmonary Exercise Testing in Patients with Post-COVID-19 Syndrome	Med Clin (Barc) / Article	<ul style="list-style-type: none"> • Cross-sectional study of 200 adults with history of SARS-CoV-2 infection and a cardiopulmonary exercise testing (CPET) performed between 45 and 120 days after the viral episode. • Compared to asymptomatic subjects, patients with post-COVID-19 syndrome showed significantly lower main peak VO₂ (25.8±8.1mL/min/kg vs. 28.8±9.6mL/min/kg), developed symptoms more frequently during CPET (52.7% vs. 13.7%) and were less likely to reach the anaerobic threshold (50.9% vs. 72.7%); these findings were not modified when adjusting for confounders.
23.08.2021	Chemosensory dysfunctions induced by COVID-19 can persist up to 7 months: A study of over 700 healthcare workers	Chem Senses / Article	<ul style="list-style-type: none"> • Study of 704 healthcare workers using self-assessment to report olfactory, gustatory and trigeminal sensitivity found evidence chemosensory dysfunction 3 to 7 months following SARS-CoV-2 infection. • 20% of infected participants reported scores in a formal test that are indicative of hyposmia/anosmia. Approximately 10% of the patients exhibit parosmia and/or phantosmia. Women are more heavily affected than men. • Persistent chemosensory dysfunctions may be a sign of chronic central nervous system alterations and there is evidence that SARS-CoV-2 can infect olfactory sensory neurons in humans
23.08.2021	What can the neurological manifestations of COVID-19 tell us: a meta-analysis	J Transl Med / Meta-analysis	<ul style="list-style-type: none"> • Findings from 168 articles (n = 292,693) suggest that nervous system expression in COVID-19 is diverse and pervasive but easily underestimated • Meta-analysis showed that the most common neurological manifestations of COVID-19 were myalgia (33%), smell impairment (33%), taste dysfunction (33%), altered mental status (32%), headache (29%), encephalopathy (26%), alteration of consciousness (13), stroke (12%), dizziness (10%), vision impairment (6%), intracerebral haemorrhage (5%), seizure (4%), encephalitis (2%), Guillan-Barré Syndrome (GBS) (1%) • Research has so far failed to provide an answer to the question of which neurological manifestations are the most insidious and which are the most difficult to recover from.

25.08.2021	Fibromyalgia: a new facet of the post-COVID-19 syndrome spectrum? Results from a web-based survey	RMD Open / Article	<ul style="list-style-type: none"> • Analysis of the responses from 616 individuals (77.4% women) to a set of 28 questions gathering demographic information, features and duration of acute COVID-19, comorbid diseases, and other individual's attributes such as height and weight, 6±3 months after the COVID-19 diagnosis. • Findings suggest that clinical features of fibromyalgia (FM) are common in patients who recovered from COVID-19, with an estimated prevalence of ~31%. Obesity and male gender affect the risk of developing post-COVID-19 FM or FibroCOVID.
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Epidemiology and clinical – risk factors

Publication Date	Title/URL	Journal / Article type	Digest
20.08.2021	Follow-up of renal transplant recipients after acute COVID-19-A prospective cohort single-center study	Immun Inflamm Dis / Article	<ul style="list-style-type: none"> • Study with 104 adult kidney-transplant patients found that post-COVID-19 syndrome, the presence of symptoms and laboratory abnormalities persisting >8 weeks beyond onset of acute COVID-19, is frequent in the renal transplant population, and in some of is associated with significant morbidity. • Only 11.53% of renal transplant recipients who survived acute COVID-19 were free of symptom and new-onset laboratory abnormalities during the median follow-up of 64. Three patients died from sepsis after discharge. 47 patients (45.2%) experienced clinical complications, while 74 patients (71.2%) had one or more laboratory abnormalities. • The most common clinical complications included shortness of breath (19.2%), tiredness (11.5%), peripheral neuropathy (7.7%), self-reported cognitive impairments (5.7%), and dry cough (7.7%).
24.08.2021	SARS-CoV-2 infection and venous thromboembolism after surgery: an international prospective cohort study	Anaesthesia / Article	<ul style="list-style-type: none"> • 128,013 elective and emergency patients undergoing surgery during Oct 2020, from 115 countries: substudy of 4418 (3.5%) with SARS-CoV-2 diagnosis. • Recent and peri-operative SARS-CoV-2 infection independently associated with increased incidence of postoperative VTE. • In patients with pre-operative SARS-CoV-2, ongoing symptoms were associated with an increased rate of postoperative VTE, irrespective of how long before surgery the diagnosis was made.

23.08.2021	From swab testing to health outcomes within the T2DM population: impact of diabetes background on covid19 progression	Diabetes Res Clin Pract / Article	<ul style="list-style-type: none"> • Data from 125,021 T2DM patients, of whom 1,882 tested positive for SARS-CoV-2. 49.4% were hospitalized within 30 days, 11.8% were admitted to an ICU, and 27.1% died. • Likelihood of death increased with age, male sex, liver and renal impairment, Hba1c above 8%, and former smoking. Hospitalization and ICU admission were mainly affected by age, male sex, hypertension, and metabolic control. ICU admissions were lower in very elderly people
09.08.2021	The Association Between Anti-diabetic Agents and Clinical Outcomes of COVID-19 in Patients with Diabetes: A Systematic Review and Meta-Analysis	Arch Med Res / Systematic review	<ul style="list-style-type: none"> • 31 studies with 66,914 patients included in qualitative and quantitative synthesis. • Metformin might be beneficial in decreasing mortality and poor composite outcomes, including intubation ventilation, ARDS, ICU admission, disease progression in diabetic patients infected with SARS-CoV-2. Its long-term home use is strongly supported because of its anti-inflammatory and antiviral effects. • DPP-4 inhibitors, sulfonylurea/glinides, SGLT-2 inhibitors, and GLP-1RA were found to not increase risk of death or poor composite outcomes of COVID-19 in patients with diabetes. Current evidence is insufficient to draw a solid conclusion regarding the effects of α-glycosidase inhibitors or TZD on clinical outcomes of COVID-19 in diabetic patients.

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Epidemiology and clinical – other

Publication Date	Title/URL	Journal / Article type	Digest
19.08.2021	The Delta SARS-CoV-2 variant has a higher viral load than the Beta and the historical variants in nasopharyngeal samples from newly diagnosed COVID-19	J Infect / Research letter	<ul style="list-style-type: none"> • Analysis of results from 738 COVID-19 patients, of whom 332 were infected with historical SARS-CoV-2, 249 with Alpha, 98 with Beta and 59 with Delta variants. Relative viral load (VL) was assessed from CT values (for ORF1ab and N target genes) • Concerning the ORF1ab target gene, the Delta variant presented a VL ten times higher than the historical variants (median 7.83 log₁₀ copies/ml). A two-fold difference was also observed between the Delta variant and the Alpha and Beta variants. • For the N gene, the Delta variant presented a 5-fold higher VL than the historical variants. A 2.5-fold higher difference was observed in VL levels between the Delta variant and the Beta variant. The Alpha and Delta variants had similar VL.

24.08.2021	The SARS-CoV-2 Alpha variant is associated with increased clinical severity of disease	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • In a prospective clinical cohort study B.1.1.7 (Alpha) lineage was responsible for a third wave of SARS-CoV-2 infection in Scotland, UK and associated with 5-fold higher transmission rate than second wave B.1.177 lineage • Of 1475 patients, 364 were infected with B.1.1.7, 1030 with B.1.177 and 81 with other lineages between 1 November 2020 and 30 January 2021 • Positive association was found between increased clinical severity and lineage (B.1.1.7 versus non-B.1.1.7; cumulative odds ratio: 1.40) • Viral load was higher in B.1.1.7 samples than in non-B.1.1.7 samples, as measured by cycle threshold (Ct) value (mean Ct change: -2.46).
22.08.2021	SARS-CoV-2 escape from a highly neutralizing COVID-19 convalescent plasma	Proc Natl Acad Sci U S A / Article	<ul style="list-style-type: none"> • Plasma samples, collected between March and May 2020 from 20 convalescent COVID-19 patients, with were tested by enzyme-linked immunosorbent assay. • Over a period of 80 days and under constant pressure SARS-CoV-2 can use mutations in both the N-terminal domain and the receptor-binding domain to generate a variant completely resistant to plasma neutralization.
20.08.2021	The association between immunosuppressants use and COVID-19 adverse outcome: National COVID-19 cohort in South Korea	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Population-based retrospective cohort study using a nationwide healthcare claims database in South Korea (up to 15 May 2020) analysed 4,349 hospitalised patients aged 40+ years, of whom 1,356 were immunosuppressants users and 2,903 were non-users. • Patients using immunosuppressants were at increased odds of the primary outcome of all-cause death, ICU admission and mechanical ventilation use (IPTW OR 1.32), and patients who used corticosteroids were at increased odds of the primary outcome (IPTW OR 1.33).
26.08.2021	SARS-CoV-2 infection and transmission in school settings during the second COVID-19 wave: a cross-sectional study, Berlin, Germany, November 2020	Eurosurveillance / Rapid communication	<ul style="list-style-type: none"> • Study of oro-nasopharyngeal swabs and blood samples from 24 randomly selected schools and connected households in Germany (n=1,119 participants). • SARS-CoV-2 infection occurred in eight classes, each affecting 1–2 individuals. Six of nine infected students were asymptomatic at testing. • Infection prevalence was 2.7% for students, 1.4% for staff and 2.3% household members. IgG antibodies detected in 2.0%, 1.4% and 1.4% respectively. • Prevalence increased with inconsistent facemask-use in school, walking to school, and case-contacts outside school. • After 1 week, no school-related secondary infections appeared in affected classes; the attack rate in connected households was 1.1%.

Infection control / non-pharmaceutical interventions

Publication Date	Title/URL	Journal / Article type	Digest
21.07.2021	Experimental investigation of indoor aerosol dispersion and accumulation in the context of COVID-19: Effects of masks and ventilation	Physics of Fluids / Article	<ul style="list-style-type: none"> • Experimental study of exhaled aerosol using a seated manikin in a relatively large indoor environment. • All tested face masks provided protection in immediate vicinity of the host; however, leakages reduced mask efficiency relative to the ideal filtration efficiency of the mask material. • At 2 m distance from host there was significant aerosol build-up in the indoor space over a long duration (10 h). • The apparent exhalation filtration efficiency is significantly lower than the ideal filtration efficiency of the mask material; nonetheless, high-efficiency masks offered substantially higher apparent filtration efficiencies (60% and 46% for R95 and KN95 masks, respectively) than the more commonly used cloth (10%) and surgical masks (12%). • Analysis of ventilation suggests relatively low air-change rates (2 h⁻¹) can lead to lower aerosol build-up compared to the best performing mask in an unventilated space. • Press release: https://uwaterloo.ca/news/media/study-supports-widespread-use-better-masks-curb-covid-19
20.08.2021	SARS-CoV-2 aerosol transmission in schools: the effectiveness of different interventions	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Modelling study: the most effective single intervention to reduce virus particle concentration in a classroom containing one infectious individual was natural ventilation by fully opening six windows all day during winter (14-fold decrease in cumulative dose), followed by universal use of surgical face masks (8-fold decrease). • In spring/summer, natural ventilation was only effective (≥ 2-fold decrease) when windows were fully open all day. In winter, partly opening two windows all day or fully opening six windows at the end of each class was also effective (≥ 2-fold decrease). Opening windows during yard and lunch breaks only had minimal effect (≤ 1.2-fold decrease). • One HEPA filter was as effective as two windows partly open all day during the winter (2.5-fold decrease) while two filters were more effective (4-fold decrease).

- Combined interventions were the most effective (≥ 30 -fold decrease).

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Transmission

Publication Date	Title/URL	Journal / Article type	Digest
20.08.2021	Public health impact of mass sporting and cultural events in a rising COVID-19 prevalence in England	K Hub (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Data from the EURO 2020 soccer matches hosted at Wembley stadium, London identified very high numbers of individuals who tested positive for COVID-19 and were traced, including those who were potentially infectious (3,071) and those who acquired their infection during the tournament period (6,784). • Other events with similar numbers of spectators found lower case numbers e.g. the All England Lawn Tennis Championships at Wimbledon, London had 299 potentially infectious and 582 potentially acquired cases. • Infections associated with EURO 2020 may be attributed to circumstances (e.g. once in a generation experience) unlikely to be replicated for the forthcoming sporting season • Authors highlight mitigations such as wearing face coverings on transport to/from events, and improving indoor spectator gathering places (e.g. pubs) by minimising crowding and improving ventilation. • Associated press release: https://www.gov.uk/government/news/government-data-shows-mass-events-can-take-place-safely-but-fans-urged-to-remain-cautious-in-crowds-and-get-vaccinated
24.08.2021	Superspreaders drive the largest outbreaks of hospital onset COVID-19 infections	Elife / Article	<ul style="list-style-type: none"> • Authors applied a combined statistical approach to infer and examine SARS-CoV-2 transmission networks within a UK hospital environment during the first wave. • Uneven pattern of transmission; patients much more likely to be infected by other patients than by HCWs. • Data consistent with a pattern of superspreading, whereby 21% of individuals caused 80% of transmission events.

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Treatment

Publication Date	Title/URL	Journal / Article type	Digest
19.08.2021	Remdesivir and Mortality in Patients with COVID-19	Clin Infect Dis / Article	<ul style="list-style-type: none"> • Retrospective cohort study with 1,138 patients hospitalized between 28.02.2020 – 28.05.2020, comparing those receiving remdesivir (RDV) (n=286) to those receiving best supportive care (BSC) (n=852). • 400 receiving BSC received hydroxychloroquine. Corticosteroids were used in 12.6% of RDV group and 23% of BSC group. • Treatment with RDV was associated with lower mortality compared to BSC. These findings remain the same in the subgroup with baseline use of low-flow oxygen.
20.08.2021	Deconstructing the Treatment Effect of Remdesivir in the Adaptive COVID-19 Treatment Trial-1: Implications for Critical Care Resource Utilization	Clin Infect Dis / Article	<ul style="list-style-type: none"> • Analysis of data from 1051 patients enrolled on the Adaptive COVID-19 Treatment Trial-1 (ACTT-1) using different modelling approaches to characterize the effect of remdesivir on progression of recovery, improvement in respiratory therapy requirement, deterioration in respiratory therapy requirement, and death. • Remdesivir was found to speed time to recovery and reduce the overall demand for hospital care
22.08.2021	Optimal timing of remdesivir initiation in hospitalized COVID-19 patients administered with dexamethasone	Clin Infect Dis / Article	<ul style="list-style-type: none"> • In a cohort of 10,445 COVID-19 patients, hospitalized between 21.01.2020 and 31.01.2021, 1544 patients received dexamethasone during hospitalization. • Exposure group consisted of 93 patients who had initiated remdesivir prior to dexamethasone and 373 who co-initiated the two treatments together; Non-exposure group (1,068) were given remdesivir after dexamethasone or had no remdesivir use. • Initiation of remdesivir prior to or simultaneously with dexamethasone was associated with significantly shorter time to clinical improvement and positive IgG antibody, lower risk of in-hospital death, in addition to shorter length of hospital stay in patients with moderate COVID-19.
23.08.2021	Intranasal Corticosteroids are Associated with Better Outcomes in Coronavirus Disease 2019 (COVID-19)	J Allergy Clin Immunol Pract / Article	<ul style="list-style-type: none"> • Data of 72,147 patients from the Cleveland Clinic COVID-19 Research Registry (CCRR) was used to perform a propensity score matching for treatment with intranasal corticosteroids (INCS) prior to SARS-CoV-2 infection (01.04.2020 – 31.03.2021) • 10,187 (14.1%) were utilizing INCS prior to SARS-CoV-2 infection. Compared to non-users, INCS users demonstrated lower risk for hospitalization, ICU admission, and in-hospital mortality.

19.08.2021	Intravenous bamlanivimab use associates with reduced hospitalization in high-risk patients with mild to moderate COVID-19	J Clin Invest / Article	<ul style="list-style-type: none"> • 2,335 patients received single-dose bamlanivimab infusion between 12.11.2020 and 17.02.2021 and compared with a propensity-matched control of 2,335 untreated patients with mild to moderate COVID-19 • Bamlanivimab monotherapy was associated with a statistically significant lower rate of all-cause hospitalization at 28 days after infusion, with greater effects demonstrated at 14 and 21 days. Reductions were also observed in the rates of ICU admissions and mortality.
26.08.2021	Janus kinase inhibitors and major COVID-19 outcomes: time to forget the two faces of Janus! A meta-analysis of randomized controlled trials	Clin Rheumatol / Meta-analysis	<ul style="list-style-type: none"> • Data from 4 randomised controlled trials (1338 subjects) with documented COVID-19 infection, using the following Janus kinase inhibitors: baricitinib, ruxolitinib, tofacitinib, and nezulcitinib. • Treatment with JAK inhibitor reduced the risk for COVID-19 death by 43%, compared to control, and led to a significant decrease in the risk for mechanical ventilation or extracorporeal membrane oxygenation (ECMO) initiation by 36%. • Limitations identified include the number of studies and the emergence of variants concern.
20.08.2021	Efficacy of Thymosin Alpha 1 in the Treatment of COVID-19: A Multicenter Cohort Study	Front Immunol / Article	<ul style="list-style-type: none"> • In a cohort of 2,282 patients, 306 received Thymosin Alpha 1 (Tα1) therapy. • Use of Tα1 was associated with poor clinical outcomes and a higher non-recovery rate, especially when applied late or in severe cases • Patients receiving Tα1 therapy had comparable disease severity, although the patients in the Tα1 group included a slightly larger proportion of critically ill patients (59/306 vs. 240/1,976).
24.08.2021	Effect of Anticoagulant Administration on the Mortality of Hospitalized Patients With COVID-19: An Updated Systematic Review and Meta-Analysis	Front Med (Lausanne) / Systematic review	<ul style="list-style-type: none"> • Review of 11 observational studies enrolling 20,748 hospitalized COVID-19 patients • Pooled meta-analysis showed anticoagulation therapy, compared with non-anticoagulation therapy, was associated with a 30% lower relative risk of mortality. The evidence of benefit was stronger among critically ill COVID-19 patients in ICU • Severe bleeding events were not associated with the administration of anticoagulants

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Modelling

Publication Date	Title/URL	Journal / Article type	Digest
25.08.2021	The impact of long-term non-pharmaceutical interventions on COVID-19 epidemic dynamics and control: the value and limitations of early models	Proc Biol Sci / Research article	<ul style="list-style-type: none">• This paper evaluates the accuracy of an early epidemiological compartment model over time to understand the value and limitations of models during unfolding epidemics.
26.08.2021	Comparing antiviral strategies against COVID-19 via multiscale within-host modelling	R Soc Open Sci / Article	<ul style="list-style-type: none">• Introducing a stochastic agent-based model of COVID-19 intracellular dynamics, incorporating essential steps of the viral life cycle targeted by treatment options.• Modelling reveals that using both antiviral and convalescent plasma therapies in combination can be very effective in reducing the length of infection, but that a delay in the commencement of treatment reduces these synergistic effects.• Early treatment with either therapy alone can increase the duration of infection, with infectious virions still present after the decline of other markers of infection.

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Guidance and consensus statements

Publication Date	Title/URL	Journal / Article type
23.08.2021	Information for healthcare professionals on myocarditis and pericarditis following COVID-19 vaccination	Public Health England / Guidance

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Overviews, comments and editorials

Publication Date	Title/URL	Journal / Article type
20.08.2021	Covid-19 booster vaccines: What we know and who's doing what	BMJ / News
23.08.2021	Covid-19 vaccines: GPs boost uptake by calling patients and teaming up with community groups	BMJ / News
20.08.2021	Chronic SARS-CoV-2, a Cause of Post-acute COVID-19 Sequelae (Long-COVID)?	Front Microbiol / Article

27.08.2021	Understanding long COVID: a modern medical challenge	Lancet / Editorial
24.08.2021	Monitoring non-pharmaceutical public health interventions during the COVID-19 pandemic	Sci Data / Comment
24.08.2021	Covid-19: Which countries are doing well on test and trace-and how can we tell?	BMJ / Feature
27.08.2021	Airborne transmission of respiratory viruses	Science / Review
20.08.2021	Covid-19: UK approves first monoclonal antibody treatment	BMJ / News
20.08.2021	Evidence on the efficacy of ivermectin for COVID-19: another story of apples and oranges	BMJ Evid Based Med / Letter

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