



UK Health
Security
Agency

COVID-19 Literature Digest – 22/10/2021

Dear all,

Please find [today's report](#) below.

UKHSA'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 The reports include both preprints, which should be treated with caution as they are NOT peer-reviewed and may be subject to change, and also research that has been subject to peer review and wider scrutiny.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 UKHSA. 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 Behavioural Sciences Weekly Report.

Best wishes,

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

Report for 22.10.2021 (please note that papers that have **NOT been peer-reviewed** are highlighted in red).

Sections:

[Serology and immunology](#)

[Vaccines](#)

[Diagnostics and genomics](#)

[Epidemiology and clinical - children and pregnancy](#)

[Epidemiology and clinical - long-term complications / sequelae](#)

[Epidemiology and clinical - risk factors](#)

[Epidemiology and clinical - other](#)

[Infection control / non-pharmaceutical interventions](#)

[Treatment](#)

[Modelling](#)

[Overviews, comments and editorials \(no digest\)](#)

Serology and immunology

Publication Date	Title/URL	Journal / Article type	Digest
15.10.2021	Immunogenicity of standard and extended dosing intervals of BNT162b2 mRNA vaccine	Cell / Article	<ul style="list-style-type: none">• UK study reviewing extended interval between BNT162b2 [Pfizer] jabs.• SARS-CoV-2 neutralizing antibody (NAb) levels were higher after extended dosing interval (6-14 weeks) compared to conventional 3-4 week regimen, accompanied by enrichment of CD4+ T cells expressing IL2.• A short dosing interval gives early protection, whereas an increased interval appears to improve peak neutralizing antibody levels.
20.10.2021	Immune Responses in Fully Vaccinated Individuals Following Breakthrough Infection with the SARS-CoV-2 Delta Variant in Provincetown, Massachusetts	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none">• Immune responses were assessed in 35 vaccinated individuals tested for SARS-CoV-2 in a cluster of Delta variant cases in Massachusetts, USA in July 2021• Vaccinated individuals who tested positive for SARS-CoV-2 demonstrated 28-fold higher binding antibody titers and 34-fold higher neutralising antibody titers against the delta variant than vaccinated individuals who tested negative.• Vaccinated individuals who tested positive also showed 4.4-fold higher Spike-specific CD8+ T cell responses against delta variant than vaccinated individuals who tested negative.
20.10.2021	Hybrid immunity improves B cells and antibodies against SARS-CoV-2 variants	Nature / Article	<ul style="list-style-type: none">• Analyses at single-cell level the memory B cells of five naive and five convalescent people vaccinated with the BNT162b2 mRNA (Pfizer-BioNTech)• Almost 6000 cells were sorted; over 3000 of them produced monoclonal antibodies against the spike protein and more than 400 neutralised the original Wuhan SARS-CoV-2 virus.• B.1.351 (Beta) and B.1.1.248 (Gamma) variants escaped almost seventy per cent of these antibodies while a much smaller portion was impacted by the B.1.1.7 (Alpha) and B.1.617.2 (Delta) variants.• Overall loss of neutralisation was always significantly higher in antibodies from naive people, in part due to the IGHV2-5;IGHJ4-1 germline, which was found only in convalescent people.

[Back to menu](#)

Vaccines

Publication Date	Title/URL	Journal / Article type	Digest
21.10.2021	Pfizer and BioNTech Announce Phase 3 Trial Data Showing High Efficacy of a Booster Dose of Their COVID-19 Vaccine	Pfizer (non-peer reviewed) / News	<ul style="list-style-type: none"> • A trial administered a booster of Pfizer-BioNTech COVID-19 vaccine to over 10,000 adult participants (aged ≥ 16 years) who had previously received the two-dose series • The booster restored vaccine protection against COVID-19 to the high levels achieved after the second dose; relative vaccine efficacy of 95.6% compared to those who did not receive a booster. Safety profile was favourable.
18.10.2021	Valneva Reports Positive Phase 3 Results for Inactivated, Adjuvanted COVID-19 Vaccine Candidate VLA2001	Valneva (non-peer reviewed) / Press release	<ul style="list-style-type: none"> • In a phase 3 trial (n=4,012 participants), COVID-19 vaccine candidate VLA2001 (Valneva) demonstrated superiority against ChAdOx1-S (AstraZeneca), in terms of geometric mean titer for neutralisation antibodies (GMT ratio=1.39; VLA2001 GMT 803.5; ChAdOx1-S, GMT 576.6), as well as non-inferiority in terms of seroconversion rates (SCR above 95% in both treatment groups) two weeks after the second vaccination in adults aged 30+ years. • VLA2001 induced broad T-cell responses with antigen-specific IFN-gamma-producing T-cells against the S- (74.3%), N- (45.9%) and M- (20.3%) proteins. • VLA2001 was well tolerated, demonstrating a statistically significant better tolerability profile compared to active comparator vaccine • Associated commentary: https://dx.doi.org/10.1136/bmj.n2551
13.10.2021	Safety and immunogenicity of CpG 1018 and aluminium hydroxide-adjuvanted SARS-CoV-2 S-2P protein vaccine MVC-COV1901: interim results of a large-scale, double-blind, randomised, placebo-controlled phase 2 trial in Taiwan	Lancet Respir Med / Article	<ul style="list-style-type: none"> • Phase 2 study: 3,854 participants (≥ 20 years) were randomly assigned to receive 2 doses [28 days apart] of either MVC-COV1901 (Medigen) COVID-19 vaccine (n=3304 participants) or placebo (n=549 participants) • For all participants in the vaccine group, at 28 days after the second dose against wild type SARS-CoV-2 virus, geometric mean titres (GMT) were 662.3 (408 IU/mL), the GMT ratio was 163.2, and the seroconversion rate was 99.8%; no vaccine-related Serious Adverse Events (SAEs) were recorded. • Preprint previously included.
20.10.2021	Effectiveness of BNT162b2 Vaccine against Delta Variant in Adolescents	N Eng J Med / Correspondence	<ul style="list-style-type: none"> • Study of 94,354 vaccinated adolescents matched with 94,354 unvaccinated controls • Estimated vaccine effectiveness against documented SARS-CoV-2 infection was 59% on days 14 through 20 after the first dose, 66% on days 21 to 27 after the first dose, and 90% on days 7 to 21 after the second dose.

			<ul style="list-style-type: none"> • Estimated vaccine effectiveness against symptomatic Covid-19 was 57% on days 14 to 20 after the first dose, 82% on days 21 to 27 after the first dose, and 93% on days 7 to 21 after the second dose.
20.10.2021	BNT162b2 and ChAdOx1 nCoV-19 Vaccine Effectiveness against Death from the Delta Variant	N Engl J Med / Correspondence	<ul style="list-style-type: none"> • Cohort study using a national surveillance system in Scotland, UK identified 114,706 adults who tested positive for SARS-CoV-2 between 01.04.2021 and 16.08.2021. Sequencing data showed 99.5% of S-positive infections were caused by the delta variant. • Among those aged 40-59 years, vaccine effectiveness against death from Covid-19 was 88% for ChAdOx1 nCoV-19 (AstraZeneca) and 95% for BNT162b2 (Pfizer-BioNTech). Among those aged 60 years or older, vaccine effectiveness was 90% and 87%, respectively. • Overall, vaccine effectiveness against death from the delta variant 14 or more days after second vaccine dose was 91% for AstraZeneca and 90% for Pfizer-BioNTech.
19.10.2021	Neutralization of Mu and C.1.2 SARS-CoV-2 Variants by Vaccine-elicited Antibodies in Individuals With and Without Previous History of Infection	bioRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Authors measured the infectivity of viruses with Mu, C.1.2 and Delta+N501S spike proteins and determined their susceptibility to neutralization by convalescent and vaccine-elicited antibodies, both in unexperienced and experienced individuals. • Neutralising titers of sera from infection-experienced BNT162b2-vaccinated individuals up to 15-fold higher than vaccinated individuals without previous infection. • Individuals can raise a broadly neutralising humoral response by generating a polyclonal response to multiple spike protein epitopes that should protect against current and future variants.
20.10.2021	Long-term immunogenicity of BNT162b2 vaccination in older people and younger health-care workers	Lancet Respir Med / Correspondence	<ul style="list-style-type: none"> • Interim results of prospective cohort study comparing immune responses in a cohort of 82 fully vaccinated older people (median age 82.5) with those in 107 younger health-care workers (HCWs), measured 5 months after the completion of 2-doses of BNT162b2 [Pfizer] vaccine • All investigated markers of immunity were markedly reduced in older people at 6-month follow-up, suggesting that the 2-dose regimen elicits less durable immune responses than those in young adults. • Vaccine-specific memory B cells might be present despite reduced antibody concentrations but remain to be investigated in detail in older people
12.10.2021	Evaluation of COVID-19 vaccine breakthrough infections among immunocompromised patients fully vaccinated with BNT162b2	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • US / Pfizer study: Of 1,277,747 individuals ≥ 16 years, who received two BNT162b2 [Pfizer] doses, 225,796 (17.7%) identified as immunocompromised (IC). • Breakthrough infections 3 times higher in IC cohort (N=374 [0.18%] vs. N=604 in non-IC cohort [0.06%]).

			<ul style="list-style-type: none"> • Highest incidence rates in IC cohort: organ transplant recipients; those with >1 IC condition, antimetabolite usage, primary immunodeficiencies, and hematologic malignancies.
15.10.2021	Efficacy and safety of a third SARS-CoV-2 vaccination in multiple sclerosis vaccine non-responders	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Norwegian study: 130 anti-CD20- or fingolimod-treated patients with multiple sclerosis (pwMS) with low or absent humoral immunity despite full vaccination. • Third dose of BNT162b2 [Pfizer] / mRNA-1273 [Moderna] associated with significantly increased levels of anti-SARS-CoV-2 SPIKE RBD IgG. • Assumed protective humoral immunity: 25% among patients using anti-CD20 therapy; 7% among those treated with fingolimod.
22.10.2021	Effectiveness of Pfizer-BioNTech mRNA Vaccination Against COVID-19 Hospitalization Among Persons Aged 12–18 Years — United States, June–September 2021	MMWR Morb Mortal Wkly Rep / Article	<ul style="list-style-type: none"> • Among hospitalised U.S. patients aged 12–18 years (n=179 case-patients, n=285 controls), vaccine effectiveness of 2 doses of Pfizer-BioNTech vaccine against COVID-19 hospitalisation during June–September 2021 was 93%.
15.10.2021	Rapid Review Update 1: What is the ongoing effectiveness, immunogenicity, and safety of COVID-19 vaccines in persons who have had a prior, confirmed COVID-19 infection?	National Collaborating Centre for Methods and Tools / Rapid review	<ul style="list-style-type: none"> • Rapid review includes evidence available up to 06.11.2021 • Vaccination in individuals with previous COVID-19 infection (“previously-infected”) may be slightly more effective compared to those without previous infection, although breakthrough infection numbers were low in both groups (low certainty). • Only two studies compared rates of infection in previously-infected people who were vaccinated compared to those who were not vaccinated, therefore vaccination effectiveness could not be determined (very low certainty). • Across the 13 studies reporting on the humoral immune response to vaccination, previously-infected people were likely have a stronger response than those without prior infection after two doses, with magnitude of difference decreasing over time (moderate certainty).
13.10.2021	Breakthrough SARS-CoV-2 infections in 620,000 U.S. Veterans, February 1, 2021 to August 13, 2021	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Authors compare SARS CoV-2 infection by vaccination status in 620,000 Veterans (2.7% of US population). • Vaccine protection declined: 91.9% March to 53.9% mid-August. • Declines greatest for Janssen vaccine (declined to 3%), followed by Pfizer (50%) and Moderna (64%). • Patterns of breakthrough infection over time were consistent by age, despite rolling vaccine eligibility, implicating Delta as primary determinant of infection.
21.10.2021	A UK Survey Examining the Experience of Adults With Mastocytosis Receiving COVID-19 Vaccination	Hemasphere / Research Letter	<ul style="list-style-type: none"> • Anonymous patient survey (n=227) regarding reactions after the 1 dose of the COVID-19 vaccine in adults. Data collected between 26.01.2021, and 21.05.2021.

			<ul style="list-style-type: none"> • Results provide support for the safety of COVID-19 vaccination in patients with mastocytosis. A low rate of anaphylaxis (1.5% of patients) was observed, which must be balanced against the risk of infection and complications of COVID-19 itself.
20.10.2021	Safety and tolerability of mRNA COVID-19 vaccines in people with antiphospholipid antibodies	Lancet Rheumatol / Correspondence	<ul style="list-style-type: none"> • Italian study, assessing safety and tolerability of COVID-19 vaccines in people with antiphospholipid antibodies. • 102 vaccinated patients surveyed; 52 with antiphospholipid syndrome / 50 with antiphospholipid antibodies without clinical features of the syndrome. • mRNA COVID-19 vaccines have an acceptable safety and tolerability profile. No major adverse effects nor thrombotic events were reported. Side-effects seem frequent, but mild and transient in nature.

[Back to menu](#)

Diagnosics and genomics

Publication Date	Title/URL	Journal / Article type	Digest
15.10.2021	SARS-CoV-2 variants of concern and variants under investigation in England: technical briefing 25	Gov.uk / Technical briefing	<ul style="list-style-type: none"> • Includes detailed variant surveillance analyses which contribute to risk assessments and designation of new VOCs and VUIs. • New sub-lineage of Delta designated as AY.4.2, with spike mutations A222V and Y145H is currently increasing in frequency, accounting for around 6% of sequences generated in the week commencing 27.09.2021 • Delta with E484Q, which may be antigenically significant, was first identified on 03.08.2021. Includes graphic of phylogenetic tree of UK Delta with E484Q, E484K • 43 of 56 Delta with E484K sequences detected in England have been linked to epidemiological data, detected across 9 English regions, with the majority in the North West.
14.10.2021	Variation at Spike position 142 in SARS-CoV-2 Delta genomes is a technical artifact caused by dropout of a sequencing amplicon	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Authors investigate effect of a deletion found in the genome of all Delta lineage SARS-CoV-2. • Spike G142D should be considered a lineage-defining mutation of Delta.
18.10.2021	Bees can be trained to identify SARS-CoV-2 infected samples	bioRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Dutch study: honeybees trained via Pavlovian conditioning to identify SARS-CoV-2 infected minks (Neovison vison). • Honeybee-based diagnostics may offer a reliable and rapid test; a low-input addition to the currently available testing methods, particularly for remote and developing communities.

[Back to menu](#)

Epidemiology and clinical - children and pregnancy

Publication Date	Title/URL	Journal / Article type	Digest
14.10.2021	Virologic features of SARS-CoV-2 infection in children	J Infect Dis / Article	<ul style="list-style-type: none">• 110 children with a median age of 10 years. Age did not impact SARS-CoV-2 viral load. Children were most infectious within the first five days of illness, and severe disease did not correlate with increased viral loads.• Symptomatic and asymptomatic children can carry high quantities of live, replicating SARS-CoV-2, creating a potential reservoir for transmission and evolution of genetic variants.• Paediatric SARS-CoV-2 sequences were representative of those in the community and novel variants were identified. Editorial: https://doi.org/10.1093/infdis/jiab511
15.10.2021	Clinical characteristics and pregnancy outcomes of women diagnosed with SARS-CoV-2 in London's most ethnically diverse borough: A cross-sectional study	Obstet Med / Article	<ul style="list-style-type: none">• Cross-sectional study of 32 women with SARS-CoV-2 compared to background departmental figures from the three months prior to the outbreak.• Pregnant women from Black and Asian backgrounds are more at risk of admission with coronavirus disease, even within an area of high ethnic diversity; however, they are not more severely affected than women nationally.• Babies born to women with SARS-CoV-2 infection are more likely to be born premature, or by caesarean delivery. There was no difference in birthweight centile for gestational age.

[Back to menu](#)

Epidemiology and clinical - long-term complications / sequelae

Publication Date	Title/URL	Journal / Article type	Digest
20.10.2021	Symptom Persistence Despite Improvement in Cardiopulmonary Health – Insights from longitudinal CMR, CPET and lung function testing post-COVID-19	EClinicalMedicine / Research Paper	<ul style="list-style-type: none">• 58 patients recruited between 14.03.2020 – 25.05.2020 in UK study of longitudinal trajectories of cardiopulmonary abnormalities and symptoms following hospitalisation with COVID-19, via symptom-questionnaires, cardiac and lung magnetic resonance imaging (CMR), cardiopulmonary exercise test (CPET), and spirometry.

		<ul style="list-style-type: none"> • At 6 months: (i) cardiac abnormalities on CMR improved in majority, similar to controls; (ii) parenchymal abnormalities, lung function impairment and CPET improved but still abnormal relative to controls; (iii) nearly half the patients continue to experience symptoms. • Dissociation between persistent cardiopulmonary symptoms and CMR/CPET parameters underscore need to examine alternative mechanisms for symptom persistence in patients. • Preprint included previously
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[Back to menu](#)

Epidemiology and clinical – risk factors

Publication Date	Title/URL	Journal / Article type	Digest
20.10.2021	SARS-CoV-2 infection in heart transplant recipients: a systematic literature review of clinical outcomes and immunosuppression strategies	Heart Fail Rev / Systematic review	<ul style="list-style-type: none"> • Systematic review of relevant case reports and case review articles from 01.01.2020 – 27.08.2021 identified total of 33 eligible studies • SARS-CoV-2 infection in heart transplant and heart-kidney transplant recipients in our cohort had a worse mortality (20.2%) than SARS-CoV-2 infection in the general US population but new left ventricular dysfunction was rare
18.10.2021	Proton-pump inhibitor use is not associated with severe COVID-19-related outcomes: a propensity score-weighted analysis of a national veteran cohort	Gut / Letter	<ul style="list-style-type: none"> • Study of 97,674 US veterans: 14,958 (15.3%) tested COVID-19 positive, of whom 6262 (41.9%) were current proton pump inhibitor [PPI] users, and 8696 (58.1%) were non-users. • After weighting, PPI use versus non-use was not associated with the composite primary outcome (oxygen therapy, ICU admission, mechanical ventilation or death; 8.2% vs 8.0%; OR 1.03) or secondary outcome (ICU admission, mechanical ventilation or death; 23.4% vs 22.9%; OR 1.03). • There were no significant interactions between age and PPI use on composite or individual outcomes.
14.10.2021	COVID-19 infection in adult patients with hematological malignancies: a European Hematology Association Survey (EPICOVIDEHA)	J Hematol Oncol / Article	<ul style="list-style-type: none"> • Study included 3801 patients with hematological malignancies (HM) with confirmed COVID-19; severe/critical COVID-19 observed in 63.8% of patients (n = 2425); 2778 patients (73.1%) were hospitalised, of whom 689 (18.1%) were admitted to intensive care units (ICUs); and 1185 patients (31.2%) died. • Primary cause of death was COVID-19 in 688 patients (58.1%), HM in 173 patients (14.6%), and a combination of both COVID-19 and progressing HM in 155 patients (13.1%).

			<ul style="list-style-type: none"> • Highest mortality was observed in acute myeloid leukemia (199/497, 40%) and myelodysplastic syndromes (118/279, 42.3%). • Mortality rate significantly decreased between the first and second waves (581/1427, 40.7% vs. 439/1773, 24.8%). • In multivariable analysis, age, active malignancy, chronic cardiac disease, liver disease, renal impairment, smoking history, and ICU stay correlated with mortality; acute myeloid leukaemia was a higher mortality risk than lymphoproliferative diseases.
19.10.2021	Association between warfarin and COVID-19-related outcomes compared with direct oral anticoagulants: population-based cohort study	J Hematol Oncol / Article	<ul style="list-style-type: none"> • Population-based UK cohort study: 92,339 warfarin users and 280,407 direct oral anticoagulants (DOACs) users were included. • Lower risk of all outcomes was associated with warfarin versus DOACs [testing positive for SARS-CoV-2, HR 0.73; COVID-19-related hospital admission, HR 0.75; COVID-19-related deaths, HR 0.74]. • A lower risk of negative control outcomes associated with warfarin versus DOACs was also observed [being tested for SARS-CoV-2, HR 0.80; non-COVID-19 deaths, HR 0.79]. • Overall, this study shows no evidence of harmful effects of warfarin on severe COVID-19 disease.
13.10.2021	Associations between HIV infection and clinical spectrum of COVID-19: a population level analysis based on US National COVID Cohort Collaborative (N3C) data	Lancet HIV / Article	<ul style="list-style-type: none"> • A US data set from 01.01.2020 to 08.05.2021 included 1,436,622 adult COVID-19 cases in the USA of whom 13,170 had HIV infection. • People with HIV had higher odds of COVID-19 death (adjusted odds ratio 1.29) and hospitalisation (1.20), but lower odds of mild or moderate COVID-19 (0.61) than people without HIV. • Elevated odds were higher among older age groups, male, Black, African American, Hispanic, or Latino adults. • A lower CD4 cell count (<200 cells per µL) was associated with all the adverse COVID-19 outcomes, while viral suppression was only associated with reduced hospitalisation. • Associated commentary: https://dx.doi.org/10.1016/s2352-3018(21)00272-1
15.10.2021	Factors associated with severity of COVID-19 disease in a multicenter cohort of people with HIV in the United States, March-December 2020	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • US study of COVID-19 in people with HIV (PWH); identifying predictors of disease severity. • Of 16,056 PWH in care, 649 diagnosed with COVID-19 between March-December 2020. • HIV viral load suppression and antiretroviral therapy (ART) status were not associated with hospitalization, although the majority of PWH were suppressed (86%).

			<ul style="list-style-type: none"> • Chronic kidney disease (CKD), chronic obstructive pulmonary disease, diabetes, hypertension, obesity, and increased cardiovascular and hepatic fibrosis risk scores were associated with higher risk of hospitalization. • PWH who were older, not on ART, with current CD4 <350, diabetes, and CKD were overrepresented amongst PWH who required intubation or died.
13.10.2021	Combination therapy of infliximab and thiopurines, but not monotherapy with infliximab or vedolizumab, is associated with attenuated IgA and neutralisation responses to SARS-CoV-2 in inflammatory bowel disease	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Study risk of severe COVID-19 for patients with inflammatory bowel disease (IBD) on immunomodulator and biologic therapy. • Infliximab/thiopurine combination therapy: significantly lower IgA, a range of lower IgG responses and impaired neutralising antibody responses. • Infliximab or vedolizumab monotherapy: significantly reduced IgG responses - but no significant reduction in IgA and neutralising antibody responses. • May explain why individuals on infliximab/thiopurine combination therapy are at greater risk of severe COVID-19 than patients on monotherapy.
08.10.2021	COVID-19 in Multiple Sclerosis: Clinically reported outcomes from the UK Multiple Sclerosis Register	Mult Scler Relat Disord / Article	<ul style="list-style-type: none"> • Clinical data collection identified 196 UK Multiple Sclerosis (MS) patients with confirmed COVID-19 infection during the first two waves of the pandemic. • Of 85 patients hospitalised, 63.5% were due to COVID-19; median stay in hospital was 9 days regardless of survival. • Patients with MS were less likely to be admitted to hospital in second wave, and their likelihood of death also reduced. • Hospitalised patients in the second wave more likely to be younger, less disabled, and not to have progressive MS. • Older, male patients with comorbidity, increased disability and progressive MS were associated with increased rates of hospitalization; being on a disease modifying treatments was associated with lower likelihood of being admitted.
20.10.2021	Asthma Phenotypes and COVID-19 Risk: A Population-based Observational Study	Am J Respir Crit Care Med / Article	<ul style="list-style-type: none"> • 434,348 asthma and 748,327 matched patients were included, using electronic medical records to identify patients and matched controls. Asthma was phenotyped by medication, exacerbation history, and type-2 inflammation • More severe asthma was associated with more severe COVID-19 outcomes, but type-2 inflammation was not. The risk of COVID-19 hospitalisation appeared to be similar to the risk with influenza or pneumonia. • Limitations: data from wave 1, prior to the availability of COVID-19 vaccination and before the routine use of corticosteroids and other treatments in hospitalised patients; associations with outcomes may have changed subsequently.

01.10.2021	Association Between Tumor Necrosis Factor Inhibitors and the Risk of Hospitalization or Death Among Patients With Immune-Mediated Inflammatory Disease and COVID-19	JAMA Netw Open / Original investigation	<ul style="list-style-type: none"> • Cohort study of adult patients (n=6077) with immune-mediated inflammatory diseases (IMIDs) and COVID-19, from 12.03.2020 – 01.02.2021 • Tumour necrosis factor (TNF) inhibitors in combination with azathioprine/6-mercaptopurine therapy, methotrexate monotherapy, azathioprine/6-mercaptopurine monotherapy, or Janus kinase inhibitor monotherapy were each associated with significantly higher odds of hospitalization or death compared with TNF inhibitor monotherapy. • Added commentary: https://dx.doi.org/10.1001/jamanetworkopen.2021.29707
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[Back to menu](#)

Epidemiology and clinical – other

Publication Date	Title/URL	Journal / Article type	Digest
15.10.2021	Ischemic stroke associated with COVID-19: a systematic review and meta-analysis	J Neurol / Systematic review	<ul style="list-style-type: none"> • Systematic review (up to 24.03.2021) included 10 studies, comprising 26,691 participants and 280 patients with ischemic stroke and COVID-19. • Pooled prevalence of ischemic stroke in COVID-19 was 2%. • Pooled proportions of hypertension, hyperlipidemia and diabetes in COVID-19-related ischemic stroke was 66%, 48% and 40%, respectively. • Pooled proportion of females was 36%. • Cryptogenic stroke subtype was associated with a high trend (pooled proportion 35%).
18.10.2021	Acute kidney injury in patients hospitalised with COVID-19 from the ISARIC WHO CCP-UK Study: a prospective, multicentre cohort study	Nephrol Dial Transplant / Article	<ul style="list-style-type: none"> • UK study with 85,687 patients from 254 hospitals between 17.01.2020 – 05.12.2020 found acute kidney injury (AKI), which is associated with an increased risk of mortality, common in adults hospitalised with COVID-19. • Of 85,687 patients, 2,198 (2.6%) received acute kidney replacement therapy (KRT). Of 41,294 patients with biochemistry data, 13,000 (31.5%) had biochemical AKI: 8,562 stage 1 (65.9%), 2,609 stage 2 (20.1%) and 1,829 stage 3 (14.1%) • Risk factors for kidney replacement therapy (KRT) were chronic kidney disease (CKD, male sex and black race. The main risk factors for biochemical AKI were admission respiratory rate >30 breaths per minute, CKD and black race • Reduced rates of AKI later in the pandemic could not be explained by the use of dexamethasone or remdesivir

14.10.2021	Cardiac SARS-CoV-2 infection is associated with pro-inflammatory transcriptomic alterations within the heart	Cardiovasc Res / Article	<ul style="list-style-type: none"> • 95 consecutive autopsy used cases to quantify virus load and characterize cardiac involvement in COVID-19 through in-situ hybridization, immunohistochemistry and RNA-sequencing • SARS-CoV-2 virus load was detected in the cardiac tissue of 41/95 deceased (43%). • Cardiac infection induced transcriptomic alterations mainly linked to immune response and destruction of cardiomyocytes. Increased pro-inflammatory gene expression was detected in SARS-CoV-2-infected cardiac tissue but no increased SARS-CoV-2 associated immune cell infiltration was observed.
20.10.2021	Cardiac iron overload promotes cardiac injury in patients with severe COVID-19	Infection / Correspondence	<ul style="list-style-type: none"> • Investigation into iron metabolism in left ventricular myocardium of 7 patients who had died due to severe COVID-19 and assessment of cardiac iron content as well as ferroptosis pathways in these patients. • Iron concentration in left ventricular myocardium of patients who had died due to COVID-19 was significantly elevated • Results show a direct association between intracellular iron accumulation, ferroptosis and SARS-CoV-2 infection in the heart during lethal severe disease courses of COVID-19
14.10.2021	REACT-1 study of coronavirus transmission: September 2021 final results	Gov.uk (non-peer reviewed) / Independent report	<ul style="list-style-type: none"> • Round 14 of REACT-1 showed limited evidence of exponential growth (R 1.03). • The epidemic was growing in those aged 17 years and below (R 1.18, with 0.99 probability that R>1) however, for those aged 18-54, the epidemic was decreasing (R 0.81). • Highest weighted prevalence in round 14 was found in children aged 5-12 years (2.32%) and 13-17 years (2.55%). • Higher prevalence also observed in: i) people of Black ethnicity (1.41%) compared with white ethnicity (0.78%); and ii) those in households of 6 or more people (1.75%) compared to 0.33% for single person households • Weighted prevalence lower in vaccinated vs unvaccinated persons (0.56% and 1.73%, respectively). • All positive samples from this round that could be sequenced were found to be Delta variant.

[Back to menu](#)

Infection control / non-pharmaceutical interventions

Publication Date	Title/URL	Journal / Article type	Digest
14.10.2021	Rapid inactivation of SARS-CoV-2 after exposure to Vapour Hydrogen Peroxide	J Hosp Infect / Letter to the editor	<ul style="list-style-type: none"> • Study investigating inactivation of SARS-CoV-2 (dried from multiple media) using a commercial vaporised hydrogen peroxide (VHP) generator. • Inactivation of SARS-CoV-2 to below detection limit within five minutes of injection of VHP to enclosure.
21.10.2021	Rapid, dose-dependent and efficient inactivation of surface dried SARS-CoV-2 by 254 nm UV-C irradiation	Euro Surveill / Research	<ul style="list-style-type: none"> • An experimental study evaluated the efficacy of 254 nm ultraviolet (UV)-C irradiation treatment to inactivate surface dried high-titre SARS-CoV-2. • Drying for 2 hours did not have a major impact on infectivity, indicating that exhaled virus in droplets or aerosols stays infectious on surfaces for some time. • Short exposure of high titre surface dried virus ($3-5 \times 10^6$ IU/ml) with UV-C light (16 mJ/cm²) resulted in total inactivation of SARS-CoV-2. • Dose-dependency experiments revealed that 3.5 mJ/cm² were still effective to achieve a > 6-log reduction in viral titres, whereas 1.75 mJ/cm² lowered infectivity only by one order of magnitude.

[Back to menu](#)

Treatment

Publication Date	Title/URL	Journal / Article type	Digest
18.10.2021	Colchicine for the treatment of COVID-19	Cochrane Database Syst Rev / Systematic review	<ul style="list-style-type: none"> • Living systematic review of 3 randomised controlled trials (n=4488) up to 21.05.2021 found colchicine probably had little or no benefit in people hospitalised with moderate or severe COVID-19 • Colchicine probably results in a slight reduction of the risk of admission to hospital or death within 28 days among patients with mild or asymptomatic infection. • Limitations and gaps in the existing available evidence are identified in detail
14.10.2021	Association between glucocorticoids treatment and viral clearance delay in patients with COVID-19: a systematic review and meta-analysis	BMC Infect Dis / Systematic review	<ul style="list-style-type: none"> • Systematic review (up to 20.04.2021) included 38 studies, comprising 9572 COVID-19 patients. • Glucocorticoid treatment was associated with delayed viral clearance in COVID-19 patients (adjusted RR 1.52), based on moderate-quality evidence. • In subgroup analyses, risk of viral clearance delay was significant both for patients who are mild or moderately ill (adjusted RR 1.86), and severely or critical ill (adjusted RR 1.59); however, this risk significantly increased for

			patients taking high doses (unadjusted RR 1.85) or medium doses (adjusted RR 1.86), rather those taking low doses (adjusted RR 1.38).
18.10.2021	Corticosteroid use in ARDS and its Application to Evolving Therapeutics for Coronavirus Disease 2019 (COVID-19): A Systematic Review	Pharmacotherapy / Systematic review	<ul style="list-style-type: none"> • Systematic review evaluated corticosteroid use in patients with acute respiratory distress syndrome (ARDS; both non-COVID-19 and COVID-19); included 15 studies, comprising 8877 patients. • Findings suggest corticosteroids are associated with improvements in mortality and ventilator-free days in critically ill patients with both COVID-19 and non-COVID-19 ARDS, and evidence suggests their use should be encouraged in these settings. • Substantial differences in the corticosteroid regimens utilised in these trials mean questions remain regarding the optimal corticosteroid agent, dose, and duration in patients with ARDS.
15.10.2021	The Effectiveness of Convalescent Plasma for the Treatment of Novel Corona Virus Disease 2019: A Systematic Review and Meta-Analysis	Front Med (Lausanne) / Systematic review	<ul style="list-style-type: none"> • Sixteen randomized controlled trials (RCTs) were included (n=16,296) up to 19.07.2021 • Meta-analysis demonstrates that convalescent plasma (CCP) can significantly reduce 28-day mortality of severe or critical COVID-19 patients and the duration of mechanical ventilation (MV). No significant difference was observed in the length of hospital stay, the duration of ICU, the rate of ICU, and MV. • Limitations included quality of some of the evidence and that the results of three large sample studies will obscure the results of other studies, especially the study of RECOVERY • Further evidence is needed to prove the safety of CCP treatment
18.10.2021	Open Science Discovery of Oral Non-Covalent SARS-CoV-2 Main Protease Inhibitor Therapeutics	bioRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Results of COVID Moonshot: an open-science structure-enabled drug discovery campaign targeting SARS-CoV-2 main protease. • All compound designs, crystallographic data, assay data and synthesized molecules were shared rapidly and openly.
14.10.2021	Effectiveness of therapeutic heparin versus prophylactic heparin on death, mechanical ventilation, or intensive care unit admission in moderately ill patients with covid-19 admitted to hospital: RAPID randomised clinical trial	BMJ / Research article	<ul style="list-style-type: none"> • Of 465 SARS-CoV-2 positive participants recruited between 29.05.2020 and 12.04.2021 with elevated D-dimer levels, 228 and 237 were randomised to therapeutic and prophylactic dose heparin respectively • Findings did not reveal a significant reduction in the primary composite outcome of death, mechanical ventilation, or ICU admission with therapeutic heparin. However, therapeutic heparin was associated with a substantially decreased odds of all cause death and low risk of major bleeding.
18.10.2021	Colchicine in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial	Lancet Respir Med / Article	<ul style="list-style-type: none"> • UK randomised controlled trial: hospitalised COVID-19 patients were randomly allocated to receive colchicine plus usual care (n=5610) or usual care alone (n=5730).

			<ul style="list-style-type: none"> • Results suggest colchicine was not associated with reductions in 28-day mortality, duration of hospital stay, or risk of progressing to invasive mechanical ventilation or death. • Preprint previously included
19.10.2021	Monoclonal Antibody Treatment of Breakthrough COVID-19 in Fully Vaccinated Individuals with High-Risk Comorbidities	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • US cohort of 1395 persons who developed breakthrough infections, mostly during Delta surge: 527 (37.8%) had anti-spike monoclonal antibody treatment / 868 (62.2%) did not. • Treatment associated with significantly lower rates of hospitalization and oxygen supplementation • Number needed to treat to prevent one hospitalization: 225 among lowest-risk patient group; 4 among groups with highest numbers of medical comorbidity.
18.10.2021	Efficacy of interferon beta-1a plus remdesivir compared with remdesivir alone in hospitalised adults with COVID-19: a double-blind, randomised, placebo-controlled, phase 3 trial	The Lancet Respiratory Medicine / Article	<ul style="list-style-type: none"> • Phase 3 trial across five countries (Japan, Mexico, Singapore, South Korea, USA): 969 hospitalised COVID-19 patients were assigned to interferon beta-1a plus remdesivir group ('Interferon group', n=487) or placebo plus remdesivir group ('Placebo group', n=482) between 05.08.2020 and 11.11.2020. • Estimated mortality at 28 days was 5% in the interferon group and 3% in the placebo group (hazard ratio 1.33). • Patients not requiring high-flow oxygen were more likely to have at least one related adverse event in the interferon group (33 [7%] of 442 patients) than in the placebo group (15 [3%] of 435). • In patients requiring high-flow oxygen, 24/35 (69%) had an adverse event and 21 (60%) had a serious adverse event in the interferon group compared with 13/33 (39%) who had an adverse event and eight (24%) who had a serious adverse event in the placebo group.

[Back to menu](#)

Modelling

Publication Date	Title/URL	Journal / Article type	Digest
14.10.2021	Modelling airborne transmission of SARS-CoV-2 using CARA: Risk assessment for enclosed spaces	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • COVID Airborne Risk Assessment (CARA) methodology enables risk assessments against airborne transmission of SARS-CoV-2 viruses. • Approach links physical, mechanical, biological domains, benchmarked with clinical and experimental data.

		<ul style="list-style-type: none"> • Findings include: (i) 20% of infected hosts emit approx. 2 orders of magnitude more viral-containing particles; (ii) surgical-type masks led to 5-fold reduction in emissions; (iii) slightly open window in winter equivalent to full window opening in summer. • A critical threshold value approach is proposed, to define an acceptable risk level in a given indoor setting.
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[Back to menu](#)

Overviews, comments and editorials

Publication Date	Title/URL	Journal / Article type
19.10.2021	The immunology of asymptomatic SARS-CoV-2 infection: what are the key questions?	Nat Rev Immunol / Comment
15.10.2021	Differential Kinetics of Immune Responses Elicited by Covid-19 Vaccines	N Engl J Med / Correspondence
14.10.2021	Trying to Block SARS-CoV-2 Transmission With Intranasal Vaccines	JAMA / News
19.10.2021	COVID-19 vaccination in patients with immunity-mediated kidney disease	Nat Rev Nephrol / Comment
08.10.2021	Understanding and managing uncertainty and variability for wastewater monitoring beyond the pandemic: Lessons learned from the United Kingdom national COVID-19 surveillance programmes	J Hazard Mater / Article
18.10.2021	COVID-19 and liver injury: role of inflammatory endotheliopathy, platelet dysfunction and thrombosis	Hepatol Commun / Review
20.10.2021	Children primed and ready for SARS-CoV-2	Nat Microbiol / News and Views

[Back to menu](#)



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