



UK Health
Security
Agency

COVID-19 Literature Digest – 08.10.2021

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 The reports include both preprints, which should be treated with caution as they are NOT peer-reviewed and may be subject to change, and also research that has been subject to peer review and wider scrutiny.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Report for 08.10.2021 (please note that papers that have **NOT been peer-reviewed** are highlighted in red).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
30.09.2021	A Systematic Review of the Protective Effect of Prior SARS-CoV-2 Infection on Repeat Infection	Eval Health Prof / Systematic Review	<ul style="list-style-type: none">• Systematic review including 10 studies, with a total population of 9,930,470 individuals and a median observation period ranging from 1 to 10.3 months. Eligible studies were retrieved on 18.08.2021• The weighted average risk reduction against reinfection was 90.4% and was observed up to 10 months. People with prior COVID-19 had a similar and durable level of protection when compared to those vaccinated against SARS-CoV-2.• Many papers included in this study followed patients infected with the wildtype strain of SARS-CoV-2 before the emergence and subsequent dominance of variant strains; the authors identified this as a limitation.
30.09.2021	Serological profile of first SARS-CoV-2 reinfection cases detected within the SIREN study	J Infect / Article	<ul style="list-style-type: none">• Report describes serological analysis of the first two reinfections as part of SARS-CoV-2 Immunity and Reinfection Evaluation (SIREN), a cohort study with over 44,000 healthcare workers• Both cases were mildly symptomatic and lacked live neutralising antibodies prior to reinfection• Evidence suggests that neutralising antibody titres are correlated with protection from reinfection
06.10.2021	Antibody persistence and neutralising activity in primary school students and staff: Prospective active surveillance, June to December 2020, England	EclinicalMedicine / Article	<ul style="list-style-type: none">• 1,344 staff and 835 students were tested in June 2020. Among the student cohort 11.5% and 11.3% had nucleoprotein and RBD antibodies, compared to 15.6% and 15.3% of staff. RBD antibodies correlated more strongly with neutralising antibodies than nucleocapsid antibodies.• Live virus neutralising activity was detected in 79.8% (n = 71/89) of nucleocapsid and 85.5% (71/83) of RBD antibody positive children.• Antibody results at baseline were significantly higher in students than staff but declined over time such that they were similar in the two groups after 24

			weeks. The immune response in children following SARS-CoV-2 infection was robust and sustained (>6 months)
05.07.2021	Characterization of humoral and SARS-CoV-2 specific T cell responses in people living with HIV	Nat Commun / Article	<ul style="list-style-type: none"> • Findings suggest majority of people living with HIV (PLWH) mount SARS-CoV-2 Spike- and Nucleoprotein-specific antibodies with neutralising activity and SARS-CoV-2-specific T cell responses at similar levels to HIV negative subjects. • Humoral and cellular responses to SARS-CoV-2 were detected 5-7 months post-infection. • Incomplete immune reconstitution on antiretroviral treatment (ART) and a low CD4:CD8 ratio may hamper development of immunity to SARS-CoV-2. • Preprint previously included.
29.09.2021	Decreasing humoral response among healthcare workers up to 4 months after two doses of BNT162b2 vaccine	J Infect / Correspondence	<ul style="list-style-type: none"> • Serological analysis of 138 samples from 17 [Pfizer-BioNTech] vaccinated healthcare workers: humoral response demonstrated median anti-S titer at 728 AU/mL one month after the first dose and an antibody peak one month after the second dose at 11720 AU/mL; this gradually decreased, reaching a plateau 4 months after second dose (3059 AU/mL). • Regarding variants of concern, 0/9, 5/9, 6/9 and 2/9 HCWs presented no or low neutralisation activities (i.e. with an effective dilution below 1:50) for the historical B, Alpha, Beta and Gamma strains, respectively.
30.09.2021	Estrogen Hormone Is an Essential Sex Factor Inhibiting Inflammation and Immune Response in COVID-19	Research Square (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Integrative network analysis indicates that estrogen hormones (e.g. estrone and estriol): 1) interact with ESR1/2 receptors, 2) can inhibit SARS-CoV-2 caused inflammation and immune response signalling in host cells; and 3) are associated with the distinct fatality rates between male and female COVID-19 patients. • A high level of estradiol protects young female COVID-19 patients; estrogen loss to an extremely low level in females after about 55 years of age increases fatality rate of women. • Medications which perturb the down-stream of ESR1/ESR2 may be effective or synergistic combined with other existing drugs for COVID-19 treatment.
28.09.2021	Neutralizing antibody responses following natural SARS-CoV-2 infection: Dynamics and correlation with commercial serologic tests	J Clin Virol / Article	<ul style="list-style-type: none"> • Results support the use of VIDAS SARS-CoV-2 IgG, Euroimmun Anti-SARS-CoV-2 ELISA IgG, Euroimmun Anti-SARS-CoV-2 QuantiVac ELISA IgG and Microblot-Array COVID-19 IgG assays to monitor neutralizing antibody response following natural SARS-CoV-2 infection. • Only a minority (16.9%) of the participants in this study lost Nabs within in at least 6 months. • Depending on the immunoassay, 21% to 33% of the participants became seronegative, and 16.9% had a loss of neutralizing antibodies.

			<ul style="list-style-type: none"> • Seroreversion observed by some commercial tests did not always correlate with the absence of antibody neutralizing capacity.
05.10.2021	One-year sustained cellular and humoral immunities of COVID-19 convalescents	Clin Infect Dis	<ul style="list-style-type: none"> • Cohort study of 101 COVID-19 convalescents found that SARS-CoV-2-specific IgG antibodies and also NAb can persist among over 95% COVID-19 convalescents from 6 months to 12 months after disease onset. • At least 19/71 (26%) of COVID-19 convalescents (double positive in ELISA and MCLIA) had detectable circulating IgM antibody against SARS-CoV-2 at 12m post-disease onset. • Positive SARS-CoV-2-specific T-cell responses (at least one of the SARS-CoV-2 antigen S1, S2, M and N protein) observed in 71/76 (93%) and 67/73 (92%) of convalescents at 6m and 12m, respectively. • Both antibody and T-cell memory levels were positively associated with disease severity in this cohort.

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Vaccines

Publication Date	Title/URL	Journal / Article type	Digest
01.10.2021	Efficacy of COVID-19 vaccines in immunocompromised patients: A systematic review and meta-analysis	medRxiv (non-peer reviewed) / Systematic Review	<ul style="list-style-type: none"> • Systematic review between 1.12.2020 and 3.09.2021 included 42 observational studies. • Among immunocompromised groups, transplant recipients had the lowest pooled risk ratio of 0.06 followed by haematological cancer patients at (0.36), solid cancer patients (0.40) and immune-mediated inflammatory diseases (IMID) patients (0.66) [all GRADE=Moderate]. • Following second dose, the lowest pooled risk ratio was again seen in transplant recipients at (0.29 (GRADE=Moderate), haematological cancer patients at 0.68 (GRADE=Low), IMID patients at 0.79 (GRADE=Low) and solid cancer at 0.92 (GRADE=Low). • Limitations include: observational studies; not controlled for co-morbidities or age; heterogeneity in definition of immunocompromised state; different vaccine types.
29.09.2021	Serologic response to coronavirus disease 2019 (COVID-19) vaccination in patients with immune-mediated inflammatory diseases: a systematic review and meta-analysis	Gastroenterology / Systematic review	<ul style="list-style-type: none"> • Search on 01.08.2021 for observational studies found 25 studies for inclusion (n=5360). Most participants received mRNA vaccines. • Meta-analysis demonstrated that 82.3% of patients with immune-mediated inflammatory diseases (IMIDs) achieved a serologic response to a 2-dose

			<p>regimen of COVID-19 mRNA vaccines, which was statistically lower than the control cohort.</p> <ul style="list-style-type: none"> • On meta-regression, anti-CD20 therapy was associated with lower response rates. Anti-TNF therapy also showed a trend toward lower response rates • A third vaccine dose should be considered for patients with IMiDs.
01.09.2021	Humoral and cellular immune responses upon SARS-CoV-2 vaccines in patients with anti-CD20 therapies: A systematic review and meta-analysis of 1342 patients	medRxiv (non-peer reviewed) / Systematic Review	<ul style="list-style-type: none"> • Systematic review up to 21.08.2021 included 23 studies (1342 patients). • Overall rate of humoral response was 41% and overall rate of cell-mediated immune responses was 71% • Longer time interval since last anti-CD20 therapy was associated with higher humoral response rates (>6 months 63% vs <6 months 20%). • Anti-CD20 treated kidney transplant recipients showed the lowest vaccination response rates compared to patients with haematological malignancies or autoimmune diseases. • Heterogeneous rates of humoral and cellular immunogenicity suggests patients with history of anti-CD20 therapies should be individually assessed.
05.10.2021	Evaluation of Immune Response and Disease Flares in Metabolic-Associated Fatty Liver Disease (MAFLD) Patients Following SARS-CoV-2 Vaccination: A Prospective Study	SSRN (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Prospective observational study included 50 patients with metabolic associated fatty liver disease (MAFLD) and 50 healthy controls, all receiving two doses of CoronaVac COVID-19 vaccine. • Findings: vaccination in MAFLD patients was safe and well tolerated; MAFLD patients showed robust immune response after vaccination (82% by day 57) although neutralising antibody titer in both groups fell below seropositivity cut-off value on day 180 (MAFLD group 0.928 / non-MAFLD group 0.907); vaccination did not affect MAFLD disease status.
07.10.2021	Protection Across Age Groups of BNT162b2 Vaccine Booster against Covid-19	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • The effect of booster vaccinations in Israel was examined using Ministry of Health data from 30.07.2021 to 05.10.2021 (n=4,616,994 persons). • Confirmed infection rates were ~10-fold lower in the booster versus non-booster group (ranging 8.8-17.8 across five age groups) and 4.7-11.4 fold lower in the secondary analysis. • Severe illness rates in the primary and secondary analysis were 19.1-fold and 6.5-fold lower for ages 60+, and 20.7-fold and 2.9-fold lower for ages 40-60. • For ages 60+, COVID-19 associated death rates were 13.9-fold lower in the primary analysis and 4.6-fold lower in the secondary analysis.
01.10.2021	Immune Memory Response After a Booster Injection of mRNA-1273 for Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2)	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Participants immunised 6-8 months earlier with a primary series of two doses of 50 µg (n=173) or 100 µg (n=171) of Moderna vaccine were administered a booster injection of 50 µg.

			<ul style="list-style-type: none"> • Neutralising antibody levels one month after booster dose were 1.7-fold higher than those one-month post primary series second injection meeting the prespecified criteria for non-inferiority. • Reactogenicity after booster dose similar to that after the second dose in the primary series of two doses of mRNA-1273 (50 or 100 µg) with no serious adverse events reported at one-month follow-up.
01.10.2021	Effectiveness of mRNA-1273 against Delta, Mu, and other emerging variants	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Test-negative case-control study included 8,153 COVID-19 cases and their matched (1:5) controls. • Two-doses of mRNA-1273 (Moderna) vaccine displayed vaccine effectiveness (VE) of 86.7% against Delta infection, 98.4% against Alpha, 90.4% against Mu, 96-98% against other identified variants, and 79.9% against unidentified variants. • VE against Delta moderately declined with increasing time since vaccination (94.1% at 14-60 days to 80.0% at 151-180 days). Waning was less pronounced for non-Delta variants. • VE against Delta lower among individuals aged ≥65 years (75.2% than those aged 18-64 years (87.9%). VE against Delta hospitalisation was 97.6%. One-dose VE was 77.0% against Delta infection.
06.10.2021	Waning of BNT162b2 Vaccine Protection against SARS-CoV-2 Infection in Qatar	N Engl J Med / Article	<ul style="list-style-type: none"> • National study: as of 07.09.2021, estimated 90% population ≥ 12 years of age received at least one vaccine dose / 80% both. • BNT162b2 (Pfizer) protection appeared to wane rapidly following its peak; decline accelerating after 4th month to reach approx. 20% in months 5 through 7 after 2nd dose; variant-specific effectiveness waned in same pattern. • Protection against hospitalisation and death persisted at a robust level for 6 months after 2nd dose. • Context 9% of population ≥ 50 years old.
04.10.2021	Effectiveness of mRNA BNT162b2 COVID-19 vaccine up to 6 months in a large integrated health system in the USA: a retrospective cohort study	Lancet / Article	<ul style="list-style-type: none"> • Vaccine effectiveness (VE) of BNT162b2 [Pfizer] against Delta was 75% (and against delta-related hospital admissions 93%) over study period (14.12.2020 - 08.08.2021). • 1 month after fully vaccinated: VE 93% against Delta; fell to 53% (39–65) up to 5 months later. Against other variants: VE 97% waned to 67% at 4–5 months. • Reduction in VE against SARS-CoV-2 infections over time probably primarily due to waning immunity with time, not delta escaping vaccine protection.
02.10.2021	Different dose regimens of a SARS-CoV-2 recombinant spike protein vaccine (NVX-CoV2373) in younger	PLoS Med / Article	<ul style="list-style-type: none"> • Phase 2 study (n = 1,288) found that a two-dose regimen of 5 µg NVX CoV2373 (Novavax) COVID-19 vaccine is highly immunogenic and well tolerated in both younger (18-59 years) adults.

	and older adults: A phase 2 randomized placebo-controlled trial		<ul style="list-style-type: none"> • In older adults (60-84 years), the 2-dose regimen of 5 µg was also well tolerated and showed sufficient immunogenicity to support its use in late-phase efficacy studies. • Preprint previously included
03.10.2021	Recombinant adjuvanted zoster vaccine and reduced risk of COVID-19 diagnosis and hospitalization in older adults	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Cohort study of 149,244 recipients of recombinant adjuvanted zoster vaccine (RZV) matched to 298,488 unvaccinated individuals. • RZV vaccination was associated with a 16% lower risk of COVID-19 diagnosis and 32% lower risk of hospitalisation (adjusted hazard ratios 0.84 and 0.68, respectively). • In the test-negative design, 8.4% of 75,726 test-positive cases and 13.1% of 340,898 test-negative controls had received ≥1 RZV dose. The adjusted odds ratio was 0.84. • Results suggest RZV elicits heterologous protection, possibly through trained immunity.

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Diagnostics and genomics

Publication Date	Title/URL	Journal / Article type	Digest
01.10.2021	A Rapid Antibody Screening Haemagglutination Test for Predicting Immunity to Sars CoV-2 Variants of Concern	Research Square (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Authors developed a hemagglutination test (HAT) which correlated with neutralising antibodies in two independent cohorts from 798 convalescents. • Home-dwelling older individuals (80-99 years, n=89) had significantly lower antibodies after one dose of Pfizer-BioNTech vaccine than younger adult vaccinees (n=310) and naturally infected individuals (n=307). • Second vaccine dose boosted and broadened antibody repertoire to variants of concern (VOC) in naïve but not previously infected, older and younger adults. • Over 75% of older adults responded after two vaccinations to alpha and delta, but only 59-62% to beta and gamma, compared to 96-97% of younger vaccinees and 68-76% of infected individuals. • Overall, the HAT provides a surrogate marker for neutralising antibodies and could be used as an inexpensive rapid test.
01.10.2021	Viral detection and identification in 20 min by rapid single-particle fluorescence in-situ hybridization of viral RNA	Sci Rep / Article	<ul style="list-style-type: none"> • A rapid fluorescence in situ hybridization (FISH) protocol capable of detecting influenza virus, avian infectious bronchitis virus and SARS-CoV-2 specifically and quantitatively in approximately 20 min.

			<ul style="list-style-type: none"> • The limit of detection (LOD) of the assay was comparable to the most sensitive lateral flow assays (LOD ~ 102 PFU/ mL for SARS-CoV-2). • Adaptable both as a lab technique and a future diagnostic tool in enveloped viruses with an accessible genome, this workflow can be used in virus cultures, combined nasal and throat swabs with added virus and likely patient samples without previous purification.
28.09.2021	B.1.617.2 enters and fuses lung cells with increased efficiency and evades antibodies induced by infection and vaccination	Cell Rep / Report	<ul style="list-style-type: none"> • Results demonstrate immune evasion, enhanced colon- and lung cell entry, and augmented syncytium formation by B.1.617.2. • Evasion of antibody-mediated neutralization by B.1.617.2 is more prominent than observed for B.1.1.7, but less prominent when compared to B.1.351 • Treatment of infection with bamlanivimab alone will be ineffective, but data indicates that casirivimab, imdevimab, and etesevimab will remain effective treatment options for B.1.617.2-infected patients, especially when administered early after infection. • The B.1.617.2 S protein is able to cause more cell-to-cell fusion than the wild type S protein, which may suggest that B.1.617.2 could cause more tissue damage, and thus be more pathogenic, than previous variants. Viral spread via syncytium formation could contribute to efficient inter- and intra-host spread of this variant.
03.10.2021	Appearance of IgG to SARS-CoV-2 in saliva effectively indicates seroconversion in mRNA vaccinated immunocompromised individuals	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Immunocompromised individuals (n=404) and healthy controls (n=82) participated in a prospective clinical trial encompassing two doses of Pfizer-BioNTech vaccine • IgG responses to the SARS-CoV-2 spike full-length trimeric glycoprotein (Spike-f) and S1 subunit in saliva in the HIV and hematopoietic stem cell transplantation (HSCT)/chimeric antigen receptor T cell therapy (CAR-T) groups were comparable to healthy controls • In contrast, primary immunodeficiencies (PID), solid organ transplantation (SOT), and chronic lymphocytic leukaemia (CLL) patients all displayed weaker responses • Salivary IgG levels strongly correlated with serum IgG titers on days 21 and 35 ($\rho=0.8079$ and 0.7768); suggests saliva sampling is highly suitable for screening low responding/vulnerable groups for revaccination.

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Epidemiology and clinical - children and pregnancy

Publication Date	Title/URL	Journal / Article type	Digest
07.10.2021	Illness characteristics of COVID-19 in children infected with the SARS-CoV-2 Delta variant	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> Analyses data for 109,626 UK school-aged children from the COVID Symptom Study (reported 28.12.2021 to 08.07.2021) to examine characteristics of Delta variant infection In total, 694 (276 younger [5-11 years], 418 older [12-17 years]) symptomatic children tested positive for Alpha infection and 706 (227 younger and 479 older) with Delta infection Median illness duration was short with either variant (overall cohort: 5 days with Alpha, 5 days with Delta) The seven most prevalent symptoms were common to both variants; symptom burden over the first 28 days was slightly greater with Delta compared with Alpha infection (in younger children, 3 with Alpha, 4 with Delta; in older children 5 with Alpha and 6 with Delta); odds of several symptoms were higher with Delta than Alpha infection, including headache and fever.
29.09.2021	Methods for Estimation of SARS-CoV-2 Seroprevalence and Reported COVID-19 Cases in U.S. Children, August 2020 - May 2021	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> Analysis of 67,321 serum specimens among children and adolescents in 14 U.S. states from August 2020 through May 2021; the majority of children did not have detectable SARS-CoV-2 nucleocapsid antibodies. Case-based surveillance underestimated the number of children infected with SARS-CoV-2; estimated ratios of infections to reported confirmed/probable COVID-19 cases varied by state and type of immunoassay, ranging from 0.8-13.3 in May 2021.

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Epidemiology and clinical - long-term complications / sequelae

Publication Date	Title/URL	Journal / Article type	Digest
07.10.2021	Physical, cognitive, and mental health impacts of COVID-19 after hospitalisation (PHOSP-COVID): a UK multicentre, prospective cohort study	Lancet Respir Med / Article	<ul style="list-style-type: none"> UK multicentre, long-term follow-up study of 1077 discharged COVID-19 adults (aged ≥18 years). At follow-up (medium 5.9 months): 239/830 participants (29%) felt fully recovered; 158/806 (20%) had a new disability; 124/641 (19%) experienced a health-related change in occupation.

			<ul style="list-style-type: none"> • Four clusters with different severities of mental and physical health impairment (n=767): very severe (131 patients, 17%), severe (159, 21%), moderate along with cognitive impairment (127, 17%), mild (350, 46%). • Predictors of not recovering included female sex, comorbidities, middle age, and requiring invasive mechanical ventilation during admission. • Persistently elevated serum C-reactive protein was positively associated with cluster severity. • Linked comment: https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00447-1/fulltext
06.10.2021	MRI and CT coronary angiography in survivors of COVID-19	Heart / Article	<ul style="list-style-type: none"> • UK prospective multimodality two-centre observational study: 52 patients recovering from severe COVID-19 do not have evidence of left ventricular dysfunction or a major excess in persistent myocardial injury compared with 10 comorbidity-matched volunteers. • Patients demonstrate right but not left ventricular dysfunction. Previous reports of left ventricular myocardial abnormalities following COVID-19 may reflect pre-existing comorbidities.
05.10.2021	Long COVID following mild SARS-CoV-2 infection: characteristic T cell alterations and response to antihistamines	J Investig Med / Original research	<ul style="list-style-type: none"> • Prospective observational study with 49 patients, recruited between November 2020 and April 2021, in long COVID group (symptoms >84 days after acute infection) and 16 controls who were asymptomatic after acute infection. • T cell changes specific to long COVID include reduced CD4+ EM cells, and increased PD-1 on both CD4+ and CD8+ CM cells. PD-1 is a coinhibitor, contributing to T cell memory, and is associated with T cell exhaustion in chronic viral infection. Detection of T cell perturbations so late after infection suggests that SARS-CoV-2 could persist for longer than originally assumed. • Increased CD28, a costimulator essential for signal transduction and T cell triggering, was limited to those who had made an uneventful recovery from COVID-19 and may represent a 'healthy' immune response to SARS-CoV-2.

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Epidemiology and clinical – risk factors

Publication Date	Title/URL	Journal / Article type	Digest
04.10.2021	The epidemiology, pathophysiological mechanisms, and management toward COVID-19 patients with Type 2 diabetes: A systematic review	Prim Care Diabetes / Systematic Review	<ul style="list-style-type: none"> • Systematic review of 82 papers, retrieved on 31.08.2021, including only retrospective studies and prospective cohort studies, fundamental research, and guidelines. • A high proportion of patients with COVID-19 have comorbid diabetes, which could result in a higher risk of poor prognosis. • In patients with diabetes, the binding of the SARS-CoV-2 to the ACE2 receptor, resulting in acute inflammation and release of cytokines, further exacerbates an already impaired immune function and increases the risk of inflammatory cytokine storm.
03.10.2021	COVID-19 risk factors amongst 14,786 care home residents: An observational longitudinal analysis including daily community positive test rates of COVID-19, hospital stays, and vaccination status in Wales (UK) between 1st September 2020 and 1st May 2021	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Analysis of 14,786 older care home residents in Wales, UK (01.09.2020 to 01.05.2021) found increased odds of a positive test associated with age (OR 1.01 per year of age), community positive test rate (OR 1.13 per percent increase in positive test rate), hospital inpatients (OR 7.40), and residents in care homes with non-specialist dementia care (OR 1.42). • Decreased odds of a positive test associated with having a positive test prior to the observation period (OR 0.58) and either one or two doses of a vaccine (0.21 and 0.05 respectively).
07.10.2021	Occupational risk of COVID-19 in the first versus second epidemic wave in Norway, 2020	Euro Surveill / Rapid Communication	<ul style="list-style-type: none"> • Study compared residents of Norway aged 20–70 years (3,559,694 on 1 January 2020) in occupations that typically entail close contact with others and age-matched individuals in other professions • Nurses, physicians, dentists and physiotherapists had 2–3.5 times the odds of COVID-19 infection during the first pandemic wave. • In the second wave, bartenders, waiters, food counter attendants, transport conductors, travel stewards, childcare workers, pre-school and primary school teachers had approximately 1.25–2 times the odds of infection. • Bus, tram and taxi drivers had an increased odds of infection in both waves (odds ratio: 1.2–2.1). • Occupation was of limited relevance for the odds of severe infection [hospitalisation].
28.09.2021	Determinants of SARS-CoV-2 entry and replication in airway mucosal tissue and susceptibility in smokers	Cell Rep Med / Article	<ul style="list-style-type: none"> • Authors find SARS-CoV-2 infection present in all examined head & neck tissues (collected post-mortem at autopsy from 27 COVID-19 patients), with a notable tropism for the nasal cavity and tracheal mucosa. • SARS-CoV-2 RNA levels were significantly higher amongst smokers (both current and former) compared to non-smokers.

			<ul style="list-style-type: none"> • An association between smoking and higher SARS-CoV-2 viral infection in the human proximal airway may explain increased susceptibility of smokers to developing severe COVID-19.
16.09.2021	Hyperglycemia in acute COVID-19 is characterized by insulin resistance and adipose tissue infectivity by SARS-CoV-2	Cell Metab / Article	<ul style="list-style-type: none"> • US study, 3,854 COVID-19 inpatients (01.03.2020 - 15.05.2020); clear association between hyperglycemia (glucose > 170 mg/dL) and adverse outcomes. • Hyperglycaemia associated with 15-fold increased risk for intubation / 3.6-fold for death. • Authors' data suggest that SARS-CoV-2 may trigger adipose tissue dysfunction to drive insulin resistance and adverse outcomes in acute COVID-19.
04.10.2021	Understanding inequalities in COVID-19 outcomes following hospital admission for people with intellectual disability compared to the general population: a matched cohort study in the UK	BMJ Open / Article	<ul style="list-style-type: none"> • 506 patients with intellectual disability (ID) were matched with a control group using a 1:3 ratio to compare outcomes from the International Severe Acute Respiratory and emerging Infections Consortium WHO Clinical Characterisation Protocol UK. • After 5 days in hospital, 16.6% of ID patients had died compared with only 6.5% of controls. This trend continued so that at 20 days 39.3% of ID patients had died compared with 32.7% of controls • Significant disparities in healthcare were observed between people with ID and the general population during the COVID-19 pandemic, which may have contributed to excess mortality in this group.
03.10.2021	Association of Health Status and Nicotine Consumption with SARS-CoV-2 positivity rates	BMC Public Health / Article	<ul style="list-style-type: none"> • First population-based study (n = 8214) to assess behavioural risk factors for SARS-CoV2 infection. • Inverse epidemiological association between smoking and infection found, contrary to findings from predominantly severely ill COVID-19 patients.
07.10.2021	COVID-19 in lung transplant recipients-Risk prediction and outcomes	PLoS One / Article	<ul style="list-style-type: none"> • Retrospective analysis in a high-volume lung transplant centre between 19.03.2020 and 18.05.2021. Impact of COVID-19 on physical and psychological health, clinical outcomes, and mortality were analyzed including follow-up visits up to 12 weeks after infection in survivors. • Out of 1,046 patients in follow-up, 31 acquired COVID-19 during the pandemic. 12/31 (39%) died and 26 (84%) were hospitalized. • Mortality and morbidity of COVID-19 in lung transplant recipients is high, especially in case of a pre-existing chronic lung allograft dysfunction (CLAD) and significant co-morbidities.
05.10.2021	Associations of Disease-Modifying Therapies With COVID-19 Severity in Multiple Sclerosis	Neurology / Research Article	<ul style="list-style-type: none"> • An international cohort study of people with multiple sclerosis who contracted COVID-19 (657 suspected, 1,683 confirmed). • Rituximab was associated with increased risk of hospitalisation, ICU admission, and need for artificial ventilation.

- Ocrelizumab was associated with hospitalisation and ICU admission.
- Preprint previously included

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Epidemiology and clinical – other

Publication Date	Title/URL	Journal / Article type	Digest
06.10.2021	Coronavirus (COVID-19) Infection Survey, characteristics of people testing positive for COVID-19, UK: 6 October 2021	Office for National Statistics / COVID-19 Infection Survey	<ul style="list-style-type: none"> • Analysis of UK national statistics suggests that between July 2020 and September 2021, the risk of reinfection was higher in the period after 17 May 2021, when the Delta variant was the dominant strain, compared with the period before. • Estimated number of reinfections in the UK is low overall (11.8 per 100,000 participant days at risk); reinfections more likely to cause serious illness are even lower (5.5 per 100,000 participant days at risk). • Participants with lower viral load in their initial infection were at a higher risk of reinfection.
02.10.2021	Spatial Risk Factors for Pillar 1 COVID-19 Excess Cases and Mortality in Rural Eastern England, UK	Risk Anal / Article	<ul style="list-style-type: none"> • Secondary analysis of patient records in a confined area of eastern England, covering persons who tested positive for SARS-CoV-2 through end May 2020 • Residence area data on air quality, deprivation levels, care home bed capacity, age distribution, rurality, access to employment centres, and population density was obtained and considered as risk factors for excess cases and excess deaths in the 28 days after confirmation of positive Covid status. • The number of cases in lower super output areas (LSOAs) were clearly dependent on the age demographic of the populations and their lack of ruralness. Older profile and less rural areas had more cases and more deaths. • The results indicate that deprivation was an important predictor of poor outcomes subsequent to infection during the early part of the Covid epidemic in rural England.
06.10.2021	Thromboembolic Risk in Hospitalized and Nonhospitalized COVID-19 Patients: A Self-Controlled Case Series Analysis of a Nationwide Cohort	Mayo Clin Proc / Article	<ul style="list-style-type: none"> • Scottish study using individual-level record linkage of five health databases covering the whole population of 5.5 million between March 2018 and October 2020 • The risk of thromboembolism was significantly elevated especially in the 7 days following a positive test. Risk of myocardial infarction, stroke,

			<p>pulmonary embolism (PE), and deep vein thrombosis (DVT) were all significantly higher in the week following a positive test.</p> <ul style="list-style-type: none"> • The risk of PE and DVT was particularly high and remained significantly elevated 8 weeks following a positive test
05.10.2021	Duration of Viral Nucleic Acid Shedding and Early Reinfection with the Severe Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in Health Care Workers and First Responders	J Infect Dis / Article	<ul style="list-style-type: none"> • A mean duration of nucleic acid shedding of 30.1 days was estimated by analysing gaps of varying lengths between subsequent positive and negative nucleic acid amplification test (NAAT) results of 137 persons March to September 2020. The mean time to reinfection was 89.1 days. • These findings were used to conclude that a 90-day period between positive NAAT results can reliably define reinfection in immunocompetent persons although reinfection can occur at shorter intervals.
04.10.2021	Spatiotemporal analysis of the first wave of COVID-19 hospitalisations in Birmingham, UK	BMJ Open / Article	<ul style="list-style-type: none"> • Analysis included all hospitalisations (n=4040) for COVID-19 to University Hospitals Birmingham NHS Foundation Trust between 01.02.2020 and 30.09.2020. • Age, ethnic minority status and a general measure of socioeconomic deprivation could reasonably predict the small areas of Birmingham with a relatively high incidence of COVID-19 hospitalisations. • Analysis demonstrates that geospatial statistical methods can provide daily predictions of disease epidemiology at small spatial scales and could be used to target intervention programmes and prioritise the rollout of vaccination
06.10.2021	An observational study of breakthrough SARS-CoV-2 Delta variant infections among vaccinated healthcare workers in Vietnam	EclinicalMedicine / Article	<ul style="list-style-type: none"> • 62 fully vaccinated healthcare workers took part in this study. All tested positive for SARS-CoV-2 between 11.06.2021 – 25.06.2021, 7-8 weeks after a second dose of the Oxford-AstraZeneca vaccine. • 22 whole genome sequences of SARS-CoV-2 were obtained from 22 fully vaccinated staff members and all were assigned to the SARS-CoV-2 Delta variant. • Whilst most were asymptomatic or mildly symptomatic, viral loads inferred from Ct values were 251 times higher than in cases infected with the original strain in the first wave.
02.10.2021	Nosocomial outbreak caused by the SARS-CoV-2 Delta variant in a highly vaccinated population, Israel, July 2021	Euro Surveill / Rapid Communication	<ul style="list-style-type: none"> • The index case, in an outbreak of 42 diagnosed cases, was a fully vaccinated haemodialysis patient in their 70s. They was not tested for SARS-CoV-2 on admission, because their symptoms were mistaken for possible bloodstream infection exacerbating congestive heart failure. • Of the 42 cases diagnosed in this outbreak, 38 were fully vaccinated with two doses of the Pfizer vaccine, one was recovered with one vaccination and three were unvaccinated.

		<ul style="list-style-type: none"> • Several transmissions probably occurred between two individuals both wearing surgical masks, and in one instance using full PPE, including N-95 mask, face shield, gown and gloves. • The shortest interval between vaccination and infection was 142 days (5 months), and many of our case patients advanced to severe disease.
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Infection control / non-pharmaceutical interventions

Publication Date	Title/URL	Journal / Article type	Digest
05.10.2021	Rapid inactivation of SARS-CoV-2 by titanium dioxide surface coating	Wellcome Open Res / Research article	<ul style="list-style-type: none"> • Testing of Titanium dioxide (TiO₂) coating of surfaces as an infection control measure. • Tiles coated with TiO₂ 120 days previously were able to inactivate SARS-CoV-2 under ambient indoor lighting with 87% reduction in titres at 1h / complete loss by 5h exposure. • SARS-CoV-2 on untreated surface was still fully infectious at 5 h post-addition of virus.
05.10.2021	Understanding the effectiveness of government interventions against the resurgence of COVID-19 in Europe	Nat Commun / Article	<ul style="list-style-type: none"> • Modelling study linking case and death data was used to estimate effectiveness of 17 non pharmaceutical interventions (NPIs) in Europe's second wave. • Business and educational institution closures, gathering bans reduced transmission, but by less than in first wave. • Results suggest stringent safety measures made schools safer compared to first wave.
01.10.2021	Multicomponent Strategies to Prevent SARS-CoV-2 Transmission — Nine Overnight Youth Summer Camps, United States, June–August 2021	MMWR Morb Mortal Wkly Rep	<ul style="list-style-type: none"> • During June–August 2021, a total of 7,173 campers and staff members attended nine U.S. overnight camps that implemented multiple prevention strategies including high vaccination coverage (>93% among eligible persons aged ≥12 years); prearrival and frequent screening testing (38,059 tests); and additional concomitant prevention measures. • Nine laboratory-confirmed COVID-19 cases and no secondary infections were detected. • Suggests high vaccination coverage coupled with multiple prevention strategies is crucial for averting COVID-19 outbreaks in congregate settings.

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Transmission

Publication Date	Title/URL	Journal / Article type	Digest
02.10.2021	The Alpha variant was not associated with excess nosocomial SARS-CoV-2 infection in a multi-centre UK hospital study	J Infect / Article	<ul style="list-style-type: none"> • Analysis of 4184 sequences, sampled from patients with COVID-19 from nine UK hospitals between 16.11.2020 to 10.01.21 to determine impact of variants on nosocomial transmission • Healthcare-acquired infections were no more likely to be identified as the Alpha variant than community acquired infections. • There was no significant difference in the number of patients involved in nosocomial outbreaks caused by the Alpha variant compared to outbreaks caused by other lineages. • Suggests currently implemented infection control measures may be as effective against more transmissible variants.

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Treatment

Publication Date	Title/URL	Journal / Article type	Digest
03.10.2021	Tocilizumab administration for the treatment of hospitalized patients with COVID-19: A systematic review and meta-analysis	Respirology / Systematic review	<ul style="list-style-type: none"> • 52 papers up to 31.03.2021 (9 RCTs, 43 observational studies) were included in both qualitative and quantitative analyses. The total population of participants was 27,004, of whom 8048 (29.8%) received tocilizumab (TCZ) • Study provides evidence for the role of TCZ in the management of COVID-19, demonstrating that its use is associated with lower mortality and risk of intubation or need for mechanical ventilation in hospitalized COVID-19 patients. The benefit of TCZ is greater when administered concomitantly with systemic corticosteroids.
01.10.2021	Merck and Ridgeback's Investigational Oral Antiviral Molnupiravir Reduced the Risk of Hospitalization or Death by Approximately 50 Percent Compared to Placebo for Patients with Mild or Moderate COVID-19 in Positive Interim Analysis of Phase 3 Study	Merck (non-peer reviewed) / News	<ul style="list-style-type: none"> • Interim analysis of 775 patients with mild-to-moderate COVID-19 who initially enrolled in the Phase 3 MOVE-OUT trial (up to 05.08.2021); 7.3% of patients who received the oral antiviral Molnupiravir were hospitalised through day 29, compared with 14.1% of placebo group who were hospitalised or died • Merck will seek emergency use authorisation in the U.S. and submit applications to regulatory agencies worldwide. • Associated commentary: https://www.bmj.com/content/375/bmj.n2422

01.10.2021	Remdesivir treatment in hospitalized patients with COVID-19: a comparative analysis of in-hospital all-cause mortality in a large multi-center observational cohort	Clin Infect Dis / Accepted manuscript	<ul style="list-style-type: none"> • US study: 28,855 hospitalised COVID-19 patients treated with Remdesivir (RDV) matched to 16,687 non-RDV patients. Baseline oxygenation levels also matched. • RDV associated with reduction in mortality at 14-days and 28-days. • Benefit also seen for patients on low-flow oxygen, high-flow oxygen/non-invasive ventilation and invasive mechanical ventilation/ECMO • RDV initiated upon hospital admission was associated with improved survival among COVID-19 patients.
28.09.2021	Real World Long-term Assessment of The Efficacy of Tocilizumab in Patients with COVID19: Results From A Large De-identified Multicenter Electronic Health Record Dataset in the United States	Int J Infect Dis / Article	<ul style="list-style-type: none"> • Analysis of data, updated September 2020, from 87 hospitals with longitudinal data, including demographics, diagnostic (ICD10) codes, vital signs, medications, and laboratory data. • In a cohort of 20,409 patients included for analysis, 1,510 patients received tocilizumab (TCZ) • TCZ use was not associated with improved mortality in patients hospitalized with COVID-19. Whilst survival curves showed a short-term trend towards better outcomes in the TCZ group, this was likely driven by the subgroup of patients who required a moderate amount of supplemental oxygen. The positive effects subsided in the long-term observation.
05.10.2021	Tocilizumab and remdesivir in hospitalized patients with severe COVID-19 pneumonia: a randomized clinical trial	Intensive Care Med / Article	<ul style="list-style-type: none"> • 434 of 649 participants with severe COVID-19 were randomly assigned to tocilizumab plus remdesivir and 215 to placebo plus remdesivir. 566 patients (88.2%) received corticosteroids during the trial to day 28. Patients were followed for 60 days. • Serious adverse events (SAEs) occurred in 128 (29.8%) of the tocilizumab plus remdesivir cohort and 72 (33.8%) placebo plus remdesivir patients; 78 (18.2%) and 42 (19.7%) patients, respectively, died by day 28. • Tocilizumab plus remdesivir did not shorten the median time to hospital discharge to day 28 compared with placebo plus remdesivir, which was 14 days for both cohorts
30.09.2021	COVIDrugNet: a network-based web tool to investigate the drugs currently in clinical trial to contrast COVID-19	Sci Rep / Article	<ul style="list-style-type: none"> • An easy-to-use freely accessible web app depicting the continuous evolving scenario of the ongoing drug clinical trials.
07.10.2021	Efficacy and Safety of Therapeutic-Dose Heparin vs Standard Prophylactic or Intermediate-Dose Heparins for Thromboprophylaxis in High-risk Hospitalized Patients With	JAMA Intern Med / Original investigation	<ul style="list-style-type: none"> • US randomised clinical trial of 253 hospitalised adult COVID-19 patients with very elevated D-dimer levels: (i) standard prophylactic or intermediate-dose low-molecular-weight heparin (LMWH) or unfractionated heparin (UFH) or (ii) therapeutic-dose LMWH. • Therapeutic-dose LMWH reduced major thromboembolism and death. Treatment effect not seen in ICU patients.

[COVID-19: The HEP-COVID
Randomized Clinical Trial](#)

• Invited commentary:
<https://dx.doi.org/10.1001/jamainternmed.2021.6212>

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Guidance and consensus statements

Publication Date	Title/URL	Journal / Article type
06.10.2021	COVID-19 vaccination in patients with heart failure: a position paper of the Heart Failure Association of the European Society of Cardiology	Eur J Heart Fail / Position Paper

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Overviews, comments and editorials

Publication Date	Title/URL	Journal / Article type
06.10.2021	The role of viral genomics in understanding COVID-19 outbreaks in long-term care facilities	Lancet Microbe / Article
05.10.2021	Mechanisms of SARS-CoV-2 entry into cells	Nat Rev Mol Cell Biol / Review Article
04.10.2021	COVID-19 and metabolic disease: mechanisms and clinical management	Lancet Diabetes Endocrinol / Review
21.09.2021	Echoes Through Time: The Historical Origins of the Droplet Dogma and its Role in the Misidentification of Airborne Respiratory Infection Transmission	SSRN (non-peer reviewed) / Article
05.10.2021	Masks and Respirators for the 21st Century: Policy Changes Needed to Save Lives and Prevent Societal Disruption	Johns Hopkins Center for Health Security / Report

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