



UK Health
Security
Agency

COVID-19 Literature Digest – 26/11/2021

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 The reports include both preprints, which should be treated with caution as they are NOT peer-reviewed and may be subject to change, and also research that has been subject to peer review and wider scrutiny.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, or to be removed, 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Report for 26.11.2021 (please note that papers that have **NOT been peer-reviewed** are highlighted in red).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
22.11.2021	Serological responses to COVID-19 booster vaccine in England	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none">• Prospective, cohort study: antibody responses before/ after BNT162b2 booster in 750 adults aged ≥ 50 years• Primary immunisation two doses: (i) BNT162b2 given < 30 days apart; (ii) or ≥ 30 days apart; compared to (iii) AZD1222 given ≥ 30 days apart• 2-4 weeks after booster, antibody GMTs significantly higher in all three groups: (i) 18,104 (n=47; 76.3-fold), (ii) 13,980 (n=118; 15.9-fold), (iii) 10,799 (n=43; 57.2-fold)• Rapid serological responses to boosting observed, irrespective of vaccine type or schedule used for primary immunisation• Higher post-booster responses with longer interval between primary immunisation and boosting.
24.11.2021	mRNA COVID-19 vaccines induce enhanced antibody and cellular responses compared to ChAdOx1 or natural infection in children	Research Square (non-peer reviewed) / Article	<ul style="list-style-type: none">• Analyses antibody and cellular responses in children aged 12-16 years vaccinated with ChAdOx1 (Oxford-AstraZeneca, n=6) or mRNA COVID-19 vaccine (Moderna or Pfizer-BioNTech, n=9) using a 12-week extended-interval schedule• mRNA vaccination of seropositive children induces high antibody levels with one dose, but a second dose is required in infection-naïve children• Following second ChAdOx1 dose, antibody titres were higher than natural infection, but lower than mRNA vaccination• Vaccination induced live virus neutralising antibodies against Alpha, Beta and Delta variants, however, a second dose is required in infection-naïve children• CD4 T cell response was higher in 4 of 5 mRNA vaccinated children compared to ChAdOx1• Phenotyping showed predominantly early effector-memory CD4 T cell populations, with a type-1 cytotoxic cytokine signature, with IL-10.

17.11.2021	Pausing methotrexate improves immunogenicity of COVID-19 vaccination in patients with rheumatic diseases	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Neutralising SARS-CoV-2 antibodies were measured after second vaccination in 64 rheumatic patients on methotrexate therapy, 31 of whom temporarily paused medication without a fixed regimen • Young age (<60 years) and MTX-hold after vaccination were found to be the main factors influencing antibody response after vaccination, while BMI or MTX dose demonstrated no effect.
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Vaccines

Publication Date	Title/URL	Journal / Article type	Digest
18.11.2021	Duration of Effectiveness of Vaccines Against SARS-CoV-2 Infection and COVID-19 Disease: Results of a Systematic Review and Meta-Regression	SSRN (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Systematic review up to 27.10.2021 included 14 studies (3 RCTs, 6 test-negative case-control, 4 retrospective and 1 prospective cohort); vaccines evaluated were Pfizer-BioNTech (n=11), Moderna (n=8), Janssen (n=3), and Oxford-AstraZeneca (n=2) • On average, vaccine efficacy/effectiveness (VE) against infection decreased 1-6 months after full vaccination by 18.5 percentage points among all ages and 19.9 percentage points among older people; for symptomatic COVID-19 disease, VE decreased by 25.4 and 32.0 percentage points, respectively; and for severe COVID-19 disease, VE decreased by 8.0 and 9.7 percentage points, respectively • The majority of VE estimates against severe disease remained over 70% for all time points.
24.11.2021	Effectiveness of BNT162b2 and ChAdOx1 against SARS-CoV-2 household transmission - a prospective cohort study in England	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Authors estimated effectiveness of BNT162b2 and ChAdOx1 vaccines against acquisition and transmission of Alpha / Delta variants in this prospective household study • Between 02.02.2021 - 10.09.2021, 213 index cases and 312 contacts followed up • Delta lineages were 4.6 times more transmissible than Alpha; contacts >18 years old were 2.0 times more likely to acquire infection than children • Effectiveness of two vaccine doses against transmission of Delta: (i) 31% for BNT162b2; (ii) 42% for ChAdOx1, similar to effectiveness for Alpha • Protection against infection: (i) 71% for Alpha / 24% for Delta for BNT162b2; (ii) 26% vs 14% for ChAdOx1

			<ul style="list-style-type: none"> • BNT162b2 and ChAdOx1 reduce transmission of Delta from breakthrough infections in household setting, though their protection against infection is low.
16.11.2021	HLA-A*03:01 is associated with increased risk of fever, chills, and more severe reaction to Pfizer-BioNTech COVID-19 vaccination	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • US survey of 17,440 participants in the Helix DNA Discovery Project about reaction to COVID-19 vaccination. • In BNT162b2 [Pfizer] recipients, HLA-A*03:01 was associated with a two-fold increase in risk of severe vaccine reactions. • Effect consistent across ages, sexes, and whether the person had previously had a COVID-19 infection.
23.11.2021	Reinfection with SARS-CoV-2: outcome, risk factors and vaccine efficacy in a Scottish cohort	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Scottish cohort study, investigating how protection against COVID-19 conferred by previous infection is modified by vaccination. • Rate of detected reinfection after two doses of vaccine was 1.35 times higher in those vaccinated before first infection than in those unvaccinated at first infection. • In unvaccinated individuals the protection against hospitalised COVID-19 conferred by previous infection is similar to that induced by vaccination. • In those with previous infection, vaccination reduces rates of reinfection and hospitalised COVID-19 by about 70%. • Combination of natural infection and vaccination provides maximal protection against new infection with SARS-CoV-2: prior vaccination does not impair this protection.
24.11.2021	Assessment of 4 Doses of SARS-CoV-2 Messenger RNA-Based Vaccine in Recipients of a Solid Organ Transplant	JAMA Netw Open / research letter	<ul style="list-style-type: none"> • Case series study [01.07.2021 to 05.08.2021]: a fourth dose (D4) of BNT162b2 (Pfizer-BioNTech) vaccine was given to 37 solid organ transplant recipients: 5 with weak response to 3 previous doses and 31 with no response to 3 previous doses. • Anti-SARS-CoV-2 antibodies were detected in 5/37 patients (13.5%) before dose 4 and in 18/37 patients (48.6%) 1 month later. • Four weeks after D4, a total of 32/37 patients (86.5%) had antibody concentrations less than 140 BAU/mL and all 37 patients (100%) had NAb titers less than 64 IU/mL. No breakthrough infection observed during follow-up.
23.11.2021	Assessment of Response to a Third Dose of the SARS-CoV-2 BNT162b2 mRNA Vaccine in Patients With Solid Tumors Undergoing Active Treatment	JAMA Oncol / Research Letter	<ul style="list-style-type: none"> • Single centre study between 15.08.2021 - 05.09.2021 with 37 patients with solid tumours who underwent serologic testing after receiving a third dose of the BNT162b2 mRNA vaccine • All but one patient had a positive serologic test result and, irrespective of the presence of chemotherapy in the treatment protocol, nearly all patients had excellent levels.

			<ul style="list-style-type: none"> • A statistically significant increase in antibody levels was noted, including in patients who had shown a moderate or minimal response following the second dose.
23.11.2021	Anti-SARS-CoV-2 immunogenicity decay and incident cases six months after Sinovac-CoronaVac inactivated vaccine in autoimmune rheumatic diseases patients: phase 4 prospective trial	Research Square (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Phase 4 prospective trial including 828 autoimmune rheumatic diseases (ARD) patients and a matched control group of 223 people, all vaccinated with CoronaVac (Sinovac). • From day 69 to day 210, anti-S1/S2IgG positivity and GMT reduced 23.8% and 38% in ARD group and 20% and 51% in control group. • In the same period, NAb positivity and activity declined 41% and 54% in ARD and 39.7% and 47% in control group. • Analysis found that male (OR=0.56), prednisone (OR=0.56), anti-TNF (OR=0.66), abatacept (OR=0.29) and rituximab (OR=0.32) use were associated with a substantial reduction on IgG response at day 210 in ARD patients.

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Diagnosics and genomics

Publication Date	Title/URL	Journal / Article type	Digest
22.11.2021	Saliva is superior over nasopharyngeal swab for detecting SARS-CoV2 in COVID-19 patients	Sci Rep / Article	<ul style="list-style-type: none"> • From 152 patients, 80 (52.63%) tested positive and 72 (47.37%) were negative for SARS-CoV-2 in nasopharyngeal swabs (NPS) sample. In saliva, 129 (92.14%) were tested positive and 11 (7.86%) were negative on the day of admission to hospital. • These findings suggest that saliva has better diagnostic yield than NPS for diagnosis of SARS-CoV2 infection. COVID-19 patients also show a higher viral load and prolonged period of SARS-CoV-2 RNA shedding in saliva. • Study limitations include lack of samples on the early onset of the disease and from asymptomatic individuals.
24.11.2021	Detection of cross-reactive immunoglobulin A against the severe acute respiratory syndrome-coronavirus-2 spike 1 subunit in saliva	PLoS One / Research article	<ul style="list-style-type: none"> • Study (n=137) to establish whether secretory immunoglobulin A (SIgA) in saliva cross-reacts with SARS-CoV-2 spike 1 subunit in individuals who have not been infected with this virus. • 46.7% of saliva samples contained Cross-reactive SIgA (CRSA) against SARS-CoV-2 spike 1. Levels of CRSA decreased with age • Study limited by small number of participants.

			<ul style="list-style-type: none"> • Although vaccines stimulate the production of cross-reactive antibodies, no significant association was found between vaccines and cross-reactive antibodies.
23.11.2021	Impaired Dendritic Cell Homing in COVID-19	Front Med (Lausanne) / Brief research report	<ul style="list-style-type: none"> • An investigation into the impact of SARS-CoV-2 on antigen-presenting cells using multiplexed immunofluorescence found SARS-CoV-2 appears to be impairing the maturation of dendritic cells (DCs) • The lungs of COVID-19 autopsy cases (n=19) in different stages of diffuse alveolar damage (DAD) were used and the cell population of professional antigen-presenting cells (APC) were compared • An increased count of myeloid dendritic cells (mDCs) found in later stages of DAD was attributed to a combination of an impaired upregulation of maturation markers and a subsequent failure of homing to lymph nodes. An effective T cell response is prevented.

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Epidemiology and clinical - children and pregnancy

Publication Date	Title/URL	Journal / Article type	Digest
17.11.2021	Durability of anti-Spike antibodies in the infant after maternal COVID-19 vaccination	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Authors quantified anti-S IgG in (i) 92 2-month and 6-month-old infants with mothers vaccinated in pregnancy, (ii) 12 6-month-old infants after maternal infection. • Detectable anti-S IgG in (i) vaccinated group: 94% of infants (58/62) at 2 months; 60% (18/30) at 6 months. (ii) Natural infection group: 8% (1/12) of infants at 6-month timepoint. • Vaccination resulted in significantly higher maternal and cord titers at delivery; significantly greater antibody persistence in infants at 6 months, compared to natural infection.
25.11.2021	COVID-19 vaccine surveillance report: Week 47	UKHSA / Report	<ul style="list-style-type: none"> • Preliminary data looking at women who gave birth in England during January-August 2021 (n=355,299) suggests women receiving COVID-19 vaccination prior to delivery (n=24,759) had good birth outcomes. • The stillbirth rate for vaccinated women was 3.35 per 1,000, a similar rate for unvaccinated women (3.60 per 1,000). • The proportion of vaccinated women giving birth to babies with low birthweight (5.28%) was similar to the proportion for unvaccinated women (5.36%)

			<ul style="list-style-type: none"> • The proportion of premature births was 6.51% for vaccinated and 5.99% for unvaccinated women. • Press release: https://www.gov.uk/government/news/new-ukhsa-study-provides-more-safety-data-on-covid-19-vaccines-in-pregnancy
26.11.2021	Risk for Stillbirth Among Women With and Without COVID-19 at Delivery Hospitalization - United States, March 2020-September 2021	MMWR Morb Mortal Wkly Rep / Article	<ul style="list-style-type: none"> • Among 1,249,634 delivery hospitalisations during March 2020–September 2021, U.S. women with COVID-19 (21,653 deliveries) were at increased risk for stillbirth compared with women without COVID-19 (adjusted relative risk [aRR] = 1.90). • This association was higher during the period of Delta variant predominance (aRR = 4.04) than during the pre-Delta period (aRR = 1.47).
20.11.2021	Decidual immune response following COVID-19 during pregnancy varies by timing of maternal SARS-CoV-2 infection	bioRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Authors collected decidua basalis tissues at delivery from women with symptomatic COVID-19 during second (2nd Tri COVID, n=8) or third trimester (3rd Tri COVID, n=8) and SARS-CoV-2-negative controls (Control, n=8). • 2nd Tri COVID: significantly increased T cells; 3rd Tri COVID: significantly increased macrophages, NK cells and T cells. • Suggests innate and adaptive immune responses at maternal-fetal interface in maternal SARS-CoV-2 infections late in pregnancy; infections earlier in pregnancy show evidence of a resolving immune response.

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Epidemiology and clinical - long-term complications / sequelae

Publication Date	Title/URL	Journal / Article type	Digest
20.11.2021	Persistent symptoms following SARS-CoV-2 infection among children and young people: a meta-analysis of controlled and uncontrolled studies	J Infect / Systematic review	<ul style="list-style-type: none"> • Systematic review of 22 published and unpublished studies (n=23,141) between 01.12.2019 – 31.07.2021 reporting children and young people (CYP) aged ≤19 years with confirmed or probable SARS-CoV-2 with symptoms persisting beyond acute illness. • Pooled prevalence of symptoms across all studies was high; however when meta-analysis was restricted to studies with a SARS-CoV-2 negative control group, most reported persistent symptoms were equally common in SARS-CoV-2 positive cases and SARS-CoV-2 negative controls. • Higher study quality was associated with lower prevalence of all symptoms, except loss of smell and cognitive symptoms.
17.11.2021	Care Models for Long COVID: A Rapid Systematic Review	medRxiv (non-peer reviewed) / Systematic Review	<ul style="list-style-type: none"> • Systematic review; best-available evidence about care models for persons living with Long COVID.

			<ul style="list-style-type: none"> • Search on 27.05.2021: 12 eligible international care model papers; 7/12 were conceptual models without a description of implementation. • 22 care model principles; top five were multidisciplinary teams (92%), integrated care (67%), self-management (58%), coordination of care (58%), evidence-based care (58%). • 10 distinct care model components; top five: standardized symptom assessment (92%), referral system (83%), follow-up system (83%), virtual care (83%), and home-base care (58%). • Overall, evidence remains scarce. No risk of bias assessment as most were conceptual papers
22.11.2021	Association of COVID-19 with arterial and venous vascular diseases: a population-wide cohort study of 48 million adults in England and Wales	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • UK cohort study quantifying association between time since COVID-19 diagnosis and vascular disease, overall and by age, sex, ethnicity, and pre-existing disease. • Across whole population, estimated increased risk of arterial thromboses and VTEs were 2.5% and 0.6% respectively 49 weeks after COVID-19 (corresponding to 7,197 and 3,517 additional events respectively after 1.4 million COVID-19 diagnoses). • Substantial increases in relative incidence of arterial thromboses and VTE events 1-2 weeks after COVID-19 diagnosis decline with time since diagnosis, although doubling of incidence of VTE events persisted up to 49 weeks after diagnosis.
24.11.2021	Severe COVID-19 induces molecular signatures of aging in the human brain	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Whole transcriptomic analysis of human frontal cortex in 12 COVID-19 cases plus age- and sex-matched uninfected controls. • COVID-19 induces profound changes in gene expression, despite absence of detectable virus in brain tissue. • Striking similarities between aged individuals / severe COVID-19 patients. • Individuals <65 years old exhibit profound transcriptomic changes not observed among older patients in cohort.
22.11.2021	Long-term sequelae are highly prevalent one year after hospitalization for severe COVID-19	Sci Rep / Article	<ul style="list-style-type: none"> • Prospective cohort study with 238 patients previously hospitalised for Covid-19 pneumonia in 2020 who underwent 4-month follow-up. • 200 participated in 12-months clinical assessment, including: pulmonary function tests with diffusing lung capacity for carbon monoxide (DLCO); post-traumatic stress (PTS) symptoms, motor function evaluation and chest Computed Tomography (CT). • Symptoms may persist up to 12 months after hospital discharge as a consequence of mental stress and organ damage. Altered respiratory

function secondary to structural lung damage and mental health sequelae persist over time in a significant proportion of patients.

- The recovery of motor function continues during the follow-up from 4 to 12 months. Female gender, arterial hypertension, chronic kidney disease and COPD may represent risk factors for persistent Covid-19 sequelae

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Epidemiology and clinical – risk factors

Publication Date	Title/URL	Journal / Article type	Digest
22.11.2021	SARS-CoV-2 Infection and COVID-19 Outcomes in Rheumatic Disease: A Systematic Literature Review And Meta-Analysis	Arthritis Rheumatol / Systematic review	<ul style="list-style-type: none"> • Systematic review including 100 observational studies and experimental trials published between 01.01.2019 – 13.02.2021. 54 studies had a low risk of bias. • The meta-analyses showed an increased prevalence of SARS-CoV-2 infection in people with rheumatic and musculoskeletal diseases (RMD) compared with the general population. • Odds of hospitalization, ICU admission, and mechanical ventilation were similar in patients with and without RMD, whereas odds of mortality was increased
15.11.2021	The Intersection Between HIV and COVID-19: Findings From the WHO Global Clinical Platform	SSRN (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Between January 2020-June 2021 clinical data from 338,566 hospitalised COVID-19 patients in 38 countries were reported to the WHO Clinical Platform; of 197,479 patients reporting HIV status, 16,955 were people living with HIV (PLHIV). • Analysis suggests PLHIV had 15% increased odds of severe/critical presentation (aOR=1.15) and were 38% more likely to die in-hospital (aHR=1.38). • Among PLHIV, being male, age 45-75 years, having chronic cardiac disease or hypertension increased odds of severe/critical COVID-19; male sex, age>18 years, having diabetes, hypertension, malignancy, TB, or chronic kidney disease increased risk of in-hospital mortality.
29.11.2021	Medium-term mortality after hip fractures and COVID-19: A prospective multi-centre UK study	Chin J Traumatol / Original article	<ul style="list-style-type: none"> • UK study between 01.03.2020 – 30.04.2020 included 746 patients, of which 87 (11.7%) tested positive for SARS-CoV-2. • Mortality rates at 30 and 120-day were significantly higher for COVID-19 positive patients relative to COVID-19 negative patients; however, mortality rates between 31 and 120-day were not significantly different, 16.1% and 9.4% respectively for COVID-19 positive and negative patients

			<ul style="list-style-type: none"> • Findings indicate that hip fracture patients with concurrent COVID-19 infection have no significant difference in 120-day mortality, provided that they are alive at day-31 after injury.
23.11.2021	Was the risk of death among the population of teachers and other school workers in England and Wales due to COVID-19 and all causes higher than other occupations during the pandemic in 2020? An ecological study using routinely collected data on deaths from the Office for National Statistics	BMJ Open / Original research	<ul style="list-style-type: none"> • Analysis of national death registration data in England and Wales from the Office for National Statistics between 08.03.2020 – 28.12.2020 • Absolute mortality rates for deaths with COVID-19 were low among those working in schools (from 10 per 100 000 in female primary school teachers to 39 per 100 000 male secondary school teachers) relative to many other occupations. • Whilst primary school teachers had a lower risk, weak evidence was found that secondary school teachers had slightly higher risks of dying with COVID-19 compared with the average for all working-aged people. Stronger evidence was found of a higher risk compared with the average for all professionals. • Over all, school staff had COVID-19 mortality risks which were proportionate to their non-COVID-19 mortality risk.
15.11.2021	Long-term use of immunosuppressive medicines and in-hospital COVID-19 outcomes: a retrospective cohort study using data from the National COVID Cohort Collaborative	Lancet Rheumatol / Article	<ul style="list-style-type: none"> • 222,575 adults included in national US cohort study. The most common comorbidities were diabetes (23%), pulmonary disease (17%), and renal disease (13%). • 16,494 (7%) patients had long-term immunosuppression with medications for diverse conditions, including rheumatological disease (33%), solid organ transplant (26%), or cancer (22%). • Of the rheumatological, antineoplastic or antimetabolite therapies under investigation, only rituximab was associated with increases in in-hospital death. • Additional comment: https://dx.doi.org/10.1016/s2665-9913(21)00362-3
17.11.2021	Prognostic factors associated with COVID-19 related severity in sickle cell disease	Blood Cells Mol Dis / Article	<ul style="list-style-type: none"> • Retrospective analysis of 1098 patients with sickle cell disease (SCD) in a US health system from 01.03.2020 to 31.12.2020; in total, 3.3% of patients were diagnosed with COVID-19 • Overall rates: hospitalisation 80%; ICU admission 19%; cohort mortality 2.5%; in-hospital mortality 3.1%. • Multivariable analysis suggests hospitalisation risk decreased by 60% for every 1 g/dL increase in admission Hb • ICU admission risk increased by 84% as a health care worker; increased by 45% for every 1000/uL increase in admission immature granulocyte count; and decreased by 17% with hydroxyurea use.

20.11.2021	Blood Hemoglobin Substantially Modulates the Impact of Gender, Morbid Obesity, and Hyperglycemia on COVID-19 Death Risk: A Multicenter Study in Italy and Spain	Front Endocrinol (Lausanne) / Original research	<ul style="list-style-type: none"> • Multi-centre study with 3,065 consecutive patients used logistic regression analyses and machine learning (ML) algorithms to confirm that obesity and hyperglycemia were independent predictors of ICU admission. • Both extremes of BMI were associated with a poorer prognosis. • Hyperglycaemic and morbidly obese subjects with blood haemoglobin levels > median, had increased mortality risk, especially men, whose risk of mortality was increased 30 times compared with normoglycemic individuals or non-obese subjects • The protective effect of female sex was lost in subjects with increased haemoglobin levels.
24.11.2021	A Retrospective Analysis of COVID-19-infected Patients with Acute Hepatitis who Develop Acute Liver Failure in a Safety Net Hospital	BMJ Open Gastroenterol / Article	<ul style="list-style-type: none"> • In this single centre US study, 43 (6.9%) of 624 COVID-19-infected patients with concomitant acute hepatitis developed acute liver failure (ALF) during the course of their hospitalisation. Their mortality rate was 74.4% • The majority of patients with ALF were male (60.6%). Statistical analysis indicates that patients with ALF had a nearly four-fold higher odds of death in comparison to those without. • Findings suggest a significant association between mortality and the presence of ALF in patients infected with COVID-19.
23.11.2021	Risk of severe COVID-19 and mortality in patients with established chronic liver disease: a nationwide matched cohort study	BMC Gastroenterol / Article	<ul style="list-style-type: none"> • Nationwide cohort study of all Swedish adults with chronic liver disease (CLD) confirmed by liver biopsy between 1966 and 2017 (n = 42,320), who were alive on 01.02.2020 • Between 01.02.2020 - 31.07.2020, 161 (0.38%) CLD patients and 435 controls were hospitalised with COVID-19. Similar results were seen in patients with CLD due to alcohol use, non-alcoholic fatty liver disease, viral hepatitis, autoimmune hepatitis and other etiologies. • Patients with CLD in this national cohort had a higher risk of hospitalisation for COVID-19 compared to the general population, but they did not have an increased risk of developing severe COVID-19.
24.11.2021	Risks of SARS-CoV-2 Breakthrough Infection and Hospitalization in Fully Vaccinated Patients With Multiple Myeloma	JAMA Netw Open / Research letter	<ul style="list-style-type: none"> • US cohort study using deidentified electronic health records (EHR) of 507,288 patients who had been fully vaccinated between 01.12.2020-08.10.2021, and with no prior COVID-19 infection • Data was analysed to determine whether fully vaccinated patients with multiple myeloma (MM) had higher risk for breakthrough infections than individuals without cancer. • The overall risk of SARS-CoV-2 breakthrough infections was 15.4% in the MM population and 3.9% in the noncancer population. After propensity

score matching for demographics, adverse socioeconomic determinants of health, transplant procedures, comorbidities, vaccine types, and medications, patients with MM remained at significantly increased risk for breakthrough infections compared with matched patients without cancer

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Epidemiology and clinical – other

Publication Date	Title/URL	Journal / Article type	Digest
22.11.2021	Prospective validation of the 4C prognostic models for adults hospitalised with COVID-19 using the ISARIC WHO Clinical Characterisation Protocol	Thorax / Original research	<ul style="list-style-type: none"> • Prospective observational cohort study across 306 UK hospitals with 76,588 adult participants (age ≥18 years) with confirmed or highly suspected COVID-19 recruited between 27.08.2020 - 17.02.2021. • 27,352 (37.4%) participants deteriorated and 12,581 (17.4%) died. 4C risk stratification models for deterioration and mortality demonstrate consistent performance to predict clinical deterioration and mortality in a large prospective second wave validation cohort of UK patients.
23.11.2021	Ten months of temporal variation in the clinical journey of hospitalised patients with COVID-19: an observational cohort	Elife / Article	<ul style="list-style-type: none"> • Examines trends in a large international cohort of 142,540 patients hospitalised with COVID-19 at 620 sites in 47 countries [March to December 2020] • Time from onset to admission showed rapid decline during the first months of the pandemic followed by peaks during August/September and December • From June to August ICU/HDU [high density unit] admission was more frequent, possibly reflecting delayed presentation in Northern Hemisphere countries following return from holidays. • Hospital case fatality ratios decreased from 0.35 in March to 0.21 by mid-2020, increasing again to 0.29 in December; this broadly follows the pandemic waves and therefore the number of admissions. • Raw numbers for overall hospital stay showed little variation, but a clear decline in time to discharge for ICU/HDU survivors.

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Infection control / non-pharmaceutical interventions

Publication Date	Title/URL	Journal / Article type	Digest
15.11.2021	Effectiveness of 3 Versus 6 ft of Physical Distancing for Controlling Spread of Coronavirus Disease 2019 Among Primary and Secondary Students and Staff: A Retrospective, Statewide Cohort Study	Clinical Infectious Diseases / Article	<ul style="list-style-type: none"> • Compares cases of SARS-CoV-2 among public schools in 251 districts in Massachusetts, USA (537,336 students and 99,390 staff during the study) with different physical distancing requirements; masking policy also varied, although the majority required universal masking for students in grades 2 and higher. • Student case rates were similar in the 242 districts with ≥ 3 versus ≥ 6 ft of physical distancing between students (IRR, 0.891); results were similar after adjustment for community incidence (adjusted IRR 0.904). • Cases among school staff in districts with ≥ 3 versus ≥ 6 ft of physical distancing were also similar (IRR, 1.015). • Suggests lower physical distancing requirements could be adopted in school settings with masking mandates.
18.11.2021	The Association of COVID-19 Incidence with Sport and Face Mask Use in United States High School Athletes	J Athl Train / Article	<ul style="list-style-type: none"> • Descriptive epidemiology study of 991 US schools which had restarted sports in Autumn 2020 (152,484 athletes on 5,854 teams). • In total 2,565 COVID-19 cases were reported [1,682 cases per 100,000 athletes, and 24.6 cases per 100,000 player-days.] • Mixed effects modelling found COVID-19 incidence was lower among outdoor versus indoor sports (incidence rate ratio [IRR]=0.54) and non-contact versus contact sports (IRR=0.78), but not team versus individual sports (IRR=0.96). • Face mask use was associated with decreased incidence in girls' volleyball (IRR=0.53), boys' basketball (IRR=0.53) and girls' basketball (IRR=0.36).

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Transmission

Publication Date	Title/URL	Journal / Article type	Digest
15.11.2021	Wastewater surveillance to infer COVID-19 transmission: A systematic review	Sci Total Environ / Systematic review	<ul style="list-style-type: none"> • Systematic review included 92 studies up to 31.07.2021 with findings from 34 countries and a total of 26,197 samples • Positive samples were detected in various settings – wastewater treatment plants, parts of the sewage system, hospitals, rivers, aircrafts and airport.

			<ul style="list-style-type: none"> • Overall sample positivity was moderate at 29.2% in all examined settings with the spike (S) gene having maximum rate of positive detections and nucleocapsid (N) gene being the most targeted. • Studies included typically reported anticipation of COVID-19 cases 16 days prior to clinical detection (≤ 10 days; 24 studies, ≥ 14 days; 8 studies). Wastewater surveillance cannot replace large-scale diagnostic testing, but it can complement clinical surveillance by providing early signs of potential transmission for more active public health responses.
22.11.2021	The role of multi-generational household clusters in COVID-19 in England	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • 1,980,527 (54.3%) of English COVID-19 cases 01.04.2020 - 20.05.2021 occurred in residential clusters; 1.5% of these were multi-generational households (at least three different generations resident in same property). • Multi-generational households formed larger clusters than non-multi-generational clusters (median cluster size 6 vs. 3); were more common: in areas of higher population density, higher relative deprivation, among households of non-White ethnicity. • A minority of COVID-19 clusters occurred in multi-generational households.
22.11.2021	COVID-19 Nosocomial Transmission Dynamics, a Retrospective Cohort Study of Two Healthcare Associated Clusters in a District Hospital in England during March and April 2020	Infect Control Hosp Epidemiol / Article	<ul style="list-style-type: none"> • Retrospective cohort study of 153 patients (65 being COVID-19 patients [45 healthcare-associated]) examined transmission dynamics of SARS-CoV-2 in a hospital outbreak • Exposure to a COVID-19 patient with respiratory symptoms was associated with healthcare-associated infection irrespective of proximity (aOR 3.81), non-respiratory exposure was only significant within 2.5m (aOR 5.21). • A small increase in risk ratio was observed for exposure to a respiratory patient for >1 day compared to 1 day from 2.04 to 2.36.
23.11.2021	Adaptation, spread and transmission of SARS-CoV-2 in farmed minks and associated humans in the Netherlands	Nat Commun / Article	<ul style="list-style-type: none"> • Authors use sequence data with Bayesian phylodynamic methods to explore SARS-CoV-2 transmission in minks and humans on farms. • High number of farm infections (68/126) in minks and farm workers ($>50\%$ of farms) were detected, with limited community spread. 3/5 initial introductions of SARS-CoV-2 led to subsequent spread between mink farms until November 2020. • The findings of high numbers of SARS-CoV-2 infections in mink farms, the specific amino acid changes in the spike regions, and the potential for emergent variants to affect the virus' host range indicate the need for continuous surveillance of the human-animal interface

Treatment

Publication Date	Title/URL	Journal / Article type	Digest
23.11.2021	Efficacy of subcutaneous interferon-beta in COVID-19: a meta-analysis and systematic review	J Community Hosp Intern Med Perspect / Systematic review	<ul style="list-style-type: none"> • Search from 01.04.2021 - 28.02.2021 found 7 studies (n=6078) eligible for inclusion in the systematic review and meta-analysis. • Meta-analysis shows that there is no significant difference in 28-day mortality between the interferon-beta intervention (IFN-beta) group compared to controls. • Limitations, such as the possible confounding effects of concomitant medication, are acknowledged, however the findings support the withdrawal of IFN-beta treatment in COVID-19
20.11.2021	Association between convalescent plasma treatment and mortality in COVID-19: a collaborative systematic review and meta-analysis of randomized clinical trials	BMC Infect Dis / Systematic review	<ul style="list-style-type: none"> • Systematic review of 33 trials (n=16,477) up to 08.04.2021. Of 8495 patients treated with convalescent plasma (CP), 23% died; of 7982 controls, 24% died. • CP treatment did not reduce all-cause mortality in COVID-19 patients. Findings provide strong evidence that CP should not be used outside of randomised trials.
18.11.2021	New analyses of two AZD7442 COVID-19 Phase III trials in high-risk populations confirm robust efficacy and long-term prevention	AstraZeneca (non-peer reviewed) / Press Release	<ul style="list-style-type: none"> • Reports data from two Phase III trials of a one-time intramuscular (IM) dose of the long-acting antibody combination AZD7442 • Six-month analysis of the ongoing PROVENT trial found one 300mg IM dose of AZD7442 reduced the risk of developing symptomatic COVID-19 compared to placebo by 83%. • Exploratory analysis of the TACKLE outpatient treatment trial [featuring patients with mild-to-moderate COVID-19] showed that in patients who had been symptomatic for ≤ 3 days at time of treatment, one 600mg IM dose reduced risk of developing severe COVID-19 or death (from any cause) by 88% compared to placebo group. • AZD7442 generally well tolerated in both studies.
17.11.2021	Aspirin in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial	Lancet / Article	<ul style="list-style-type: none"> • In a randomised controlled trial 7351 hospitalised COVID-19 patients were allocated to receive aspirin (150mg aspirin 1/day) and 7541 patients to receive usual care alone; 1222 (17%) patients allocated to aspirin and 1299 (17%) patients allocated to usual care died within 28 days. • Patients allocated to aspirin had a slightly shorter duration of hospitalisation (median 8 days vs. 9 days) and a slightly higher proportion were discharged alive within 28 days (75% vs. 74%). There was no

			<p>significant difference in the proportion meeting composite endpoint of invasive mechanical ventilation or death (21% vs. 22%).</p> <ul style="list-style-type: none"> • Aspirin use was associated with an absolute reduction in thrombotic events of 0.6% and an absolute increase in clinically significant bleeding of 0.6%. • Preprint previously included • Added comment: https://dx.doi.org/10.1016/s0140-6736(21)01906-1
22.11.2021	Efficacy of Inhaled Ciclesonide for Outpatient Treatment of Adolescents and Adults With Symptomatic COVID-19: A Randomized Clinical Trial	JAMA Intern Med / Original investigation	<ul style="list-style-type: none"> • US phase 3 randomized clinical trial: inhaled corticosteroids and treatment of mild to moderate disease. • 400 outpatients with symptomatic COVID-19 received ciclesonide MDI (total daily dose, 640 µg) or placebo for 30 days. • No difference in resolution of all symptoms by day 30. • Treatment group had fewer subsequent emergency department visits or hospital admissions for reasons related to COVID-19.
22.11.2021	Favipiravir for treatment of outpatients with asymptomatic or uncomplicated COVID-19: a double-blind randomized, placebo-controlled, phase 2 trial	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • US Phase 2 randomized controlled trial of favipiravir in asymptomatic / mildly symptomatic adults. • 149 outpatients 1:1 randomized: favipiravir (1800 mg BID Day 1, 800mg BID Days 2–10) / placebo. • No difference in time to shedding cessation or symptom resolution.

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Modelling

Publication Date	Title/URL	Journal / Article type	Digest
22.11.2021	Behaviour, booster vaccines and waning vaccine protection: modelling the medium-term dynamics of SARS-CoV-2 transmission in England	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Using a model fitted to 18 months of epidemiological data, authors project potential dynamics of SARS-CoV-2 transmission in England to September 2022. • Key uncertainties considered include behavioural change, waning vaccine protection, vaccination strategies, reintroduction of public health and social measures. • Widespread booster vaccinations or reimposition of mild public health and social measures (e.g. work-from-home policies) could largely mitigate wave of COVID-19 transmission projected to occur in England in Spring/Summer 2022.
24.11.2021	Growth, reproduction numbers and factors affecting the spread of SARS-	BMJ Open / Original research	<ul style="list-style-type: none"> • Modelling for England (October 2020 to July 2021); observed replacement of B.1.1.7 (Alpha) by the B.1.617.2 (Delta) variant.

	CoV-2 novel variants of concern in the UK from October 2020 to July 2021: a modelling analysis		<ul style="list-style-type: none"> • Exponential growth initially detected in the youngest age groups, although now observed across all ages; doubling time of 10.7 days and 8 days for cases and hospitalisations, respectively. • Growth in cases first detected in Indian ethnicity group in late February, with a peak of 0.06 in the instantaneous growth rate, but now maintained by white ethnicity groups, with doubling time of 6.8 days. • Rt analysis indicates a reproduction number advantage of 0.45 for B.1.617.2 relative to B.1.1.7, with the Rt value peaking at 1.85 for B.1.617.2.
25.11.2021	Estimated number of deaths directly averted in people 60 years and older as a result of COVID-19 vaccination in the WHO European Region, December 2020 to November 2021	Euro Surveill / Rapid Communication	<ul style="list-style-type: none"> • Modelling for the World Health Organization European Region using weekly data from 33 countries [December 2020 to November 2021] estimates that COVID-19 vaccination averted 469,186 deaths in people aged ≥ 60 years (51% of 911,302 expected deaths) • Impact by country ranged from 6–93%; largest when implementation was early.

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Overviews, comments and editorials

Publication Date	Title/URL	Journal / Article type
24.11.2021	A Possible Role for Anti-idiotypic Antibodies in SARS-CoV-2 Infection and Vaccination	N Engl J Med / Clinical Implications of Basic Research
24.11.2021	COVID-19 Vaccine Makers Plan for Annual Boosters, but It's Not Clear They'll Be Needed	JAMA / Medical News & Perspectives
22.11.2021	COVID-19: Using high-throughput flow cytometry to dissect clinical heterogeneity	Cytometry A / Review
25.11.2021	Heavily mutated coronavirus variant puts scientists on alert	Nature / News
23.11.2021	Emerging SARS-CoV-2 variants can potentially break set epidemiological barriers in COVID-19	J Med Virol / Review
23.11.2021	The experiences of 33 national COVID-19 dashboard teams during the first year of the pandemic in the WHO European Region: a qualitative study	medRxiv (non-peer reviewed) / Article
22.11.2021	Understanding and tracking the impact of long COVID in the United Kingdom	Nat Med / Correspondence
03.11.2021	COVID-19 infection and body weight: A deleterious liaison in a J-curve relationship	Obes Res Clin Pract / Review

20.11.2021	Rapid evidence review to inform safe return to campus in the context of coronavirus disease 2019 (COVID-19)	Wellcome Open Res / Review
24.11.2021	Nasal therapy-The missing link in optimising strategies to improve prevention and treatment of COVID-19	PLoS Pathog / Opinion
23.11.2021	Challenges in simulating and modeling the airborne virus transmission: A state-of-the-art review	Phys Fluids (1994) / Review

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