



UK Health
Security
Agency

COVID-19 Literature Digest – 19/11/2021

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 The reports include both preprints, which should be treated with caution as they are NOT peer-reviewed and may be subject to change, and also research that has been subject to peer review and wider scrutiny.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Report for 19.11.2021 (please note that papers that have **NOT been peer-reviewed** are highlighted in red).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
09.11.2021	Humoral and cellular immunogenicity to a second dose of COVID-19 vaccine BNT162b2 in people receiving methotrexate or targeted immunosuppression: a longitudinal cohort study	Lancet Rheumatol / Article	<ul style="list-style-type: none">• UK study with 67 psoriasis patients receiving methotrexate or targeted biological monotherapy and 15 healthy controls• All participants had detectable spike-specific antibodies following the second dose, and all groups demonstrated similar neutralising antibody titres against wild-type, alpha, and delta variants.• Whilst functional humoral immunity at 14 days following a second dose of BNT162b2 was not impaired by methotrexate or targeted biologics, a lower proportion of these participants (62% and 74% respectively) had detectable T-cell responses following the second vaccine dose, compared with 100% of controls• Linked comment: https://dx.doi.org/10.1016/s2665-9913(21)00360-x
13.11.2021	Persistence of anti-SARS-CoV-2 IgM in convalescent COVID-19 patients	J Infect / Letter	<ul style="list-style-type: none">• Immunoglobulin M (IgM) was tested in 473 convalescent individuals in Hubei, China following SARS-CoV-2 infection one year previously.• Of survivors, 23.9% were positive for anti-SARS-CoV-2 IgM; higher IgM titers detected in convalescent individuals with severe COVID-19.• Authors suggest IgM testing does not replace PCR testing in detecting acute SARS-CoV-2 infection and should not determine the need to quarantine.

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Vaccines

Publication Date	Title/URL	Journal / Article type	Digest
15.11.2021	Postvaccination SARS-CoV-2 infection among healthcare workers - A Systematic Review and meta-analysis	J Med Virol / Systematic review	<ul style="list-style-type: none"> • Systematic review up to August 2021 included 18 studies with 228,873 healthcare workers (HCWs). • Overall pooled proportion of COVID-19 infections among partially/fully vaccinated and unvaccinated HCWs was 2.1%. • Among partially vaccinated, fully vaccinated and unvaccinated HCWs, pooled proportion of COVID-19 infections was 2.3%, 1.3%, and 10.1%, respectively.
15.11.2021	Effectiveness of BNT162b2 (Comirnaty, Pfizer-BioNTech) COVID-19 booster vaccine against covid-19 related symptoms in England: test negative case-control study	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Vaccine effectiveness (VE) fell to 47.3 / 69.7 by 20+ weeks against Delta for two-dose ChAdOx1-S [AstraZeneca] / BNT162b2 [Pfizer] respectively. • 14 days after BNT162b2 booster: VE at 87.4 in ChAdOx1-S primary course group / 84.4 in BNT162b2 group. • Booster gave significant increased protection against symptomatic disease in over 50 year olds, irrespective of primary course received. • Associated commentary: https://www.bmj.com/content/375/bmj.n2814
11.11.2021	Efficacy, safety, and lot-to-lot immunogenicity of an inactivated SARS-CoV-2 vaccine (BBV152): interim results of a randomised, double-blind, controlled, phase 3 trial	Lancet / Article	<ul style="list-style-type: none"> • Phase 3 clinical trial of BBV152 COVID-19 vaccine: 24,419 participants received two doses of BBV152 (n = 12,221) or placebo (n = 12,198) between 16.11.2020 and 07.01.2021. • Overall vaccine efficacy of 77·8%. Efficacy against asymptomatic disease and severe symptomatic disease was 63·6% and 93·4%, respectively. • BBV152 conferred 65·2% protection against the SARS-CoV-2 Variant of Concern, B.1.617.2 [Delta]. Vaccination was well tolerated. • Preprint previously included. Linked editorial: https://dx.doi.org/10.1016/s0140-6736(21)02014-6
15.11.2021	Inactivated virus vaccine BBV152/Covaxin elicits robust cellular immune memory to SARS-CoV-2 and variants of concern	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Longitudinal study with 71 SARS-CoV-2 unexposed participants who received 2 doses of BBV152/Covaxin and 73 participants who had recovered from mild COVID-19 to determine the magnitude, quality and persistence of cellular and humoral memory responses up to 6 months after vaccination • The RBD-specific antibodies decline in the range of 3 to 10-fold against the SARS-CoV-2 variants in the order of alpha (B.1.1.7) >

			<p>delta (B.1.617.2) > beta (B.1.351), with no observed impact of gamma (P.1) and kappa (B.1.617.1) variant. Vaccine-induced memory B cells are impacted by virus variants in the same order as antibodies.</p> <ul style="list-style-type: none"> • BBV152 induced a robust immune memory against spike and nucleoprotein that was comparable to that following SARS-CoV-2 infection for the levels of antibodies, memory B cells, and memory CD4+ T cells. Findings indicate that this response persists for at least six months
11.11.2021	Safety and immunogenicity of concomitant administration of COVID-19 vaccines (ChAdOx1 or BNT162b2) with seasonal influenza vaccines in adults in the UK (ComFluCOV): a multicentre, randomised, controlled, phase 4 trial	Lancet / Article	<ul style="list-style-type: none"> • Study included six cohorts of adults aged 18-64: (i) ChAdOx1 [AstraZeneca] plus cellular quadrivalent influenza vaccine (n=129), (ii) BNT162b2 [Pfizer] plus cellular quadrivalent influenza vaccine (n=139), (iii) ChAdOx1 plus MF59C adjuvanted, (iv) trivalent influenza vaccine (n=146), BNT162b2 plus MF59C adjuvanted, (v) trivalent influenza vaccine (n=79), (vi) ChAdOx1 plus recombinant quadrivalent influenza vaccine (n=128), (vi) BNT162b2 plus recombinant quadrivalent influenza vaccine (n=58) • 340 participants were assigned to concomitant administration of influenza and a second dose of COVID-19 vaccine at day 0 followed by placebo at day 21 • 339 participants were randomly assigned to concomitant administration of placebo and a second dose of COVID-19 vaccine at day 0 followed by influenza vaccine at day 21. • Concomitant vaccination with ChAdOx1 or BNT162b2 plus an age-appropriate influenza vaccine raises no safety concerns and preserves antibody responses to both vaccines.
17.11.2021	Safety, immunogenicity, and efficacy of a COVID-19 vaccine (NVX-CoV2373) co-administered with seasonal influenza vaccines: an exploratory substudy of a randomised, observer-blinded, placebo-controlled, phase 3 trial	Lancet Respir Med / Article	<ul style="list-style-type: none"> • Sub-study on influenza vaccine co-administration, conducted as part of phase 3 randomised trial of NVX-CoV2373 [Novavax] COVID-19 vaccine. • 431 participants randomised: 217 to NVX-CoV2373 plus influenza vaccine; 214 received placebo plus influenza vaccine. • Reactogenicity events more common in co-administration group included tenderness (70.1% vs 57.6%) or pain (39.7% vs 29.3%) at injection site; fatigue (27.7% vs 19.4%); muscle pain (28.3% vs 21.4%).

			<ul style="list-style-type: none"> • Rates of unsolicited adverse events (AEs), medically-attended AEs, and serious AEs were low and balanced between both groups. • Co-administration resulted in no change to influenza vaccine immune response; NVX-CoV2373 vaccine efficacy in sub-study was 87.5% vs. 89.8% in main study. • Preprint previously included.
09.11.2021	mRNA-1273 COVID-19 vaccination in patients receiving chemotherapy, immunotherapy, or chemoimmunotherapy for solid tumours: a prospective, multicentre, non-inferiority trial	Lancet Oncol / Article	<ul style="list-style-type: none"> • Four adult cohorts with a life expectancy of more than 12 months were enrolled between 17.02.2021 – 12.03.2021: individuals without cancer (cohort A [control cohort]), and patients with solid tumours, regardless of stage and histology, treated with immunotherapy (cohort B), chemotherapy (cohort C), or chemoimmunotherapy (cohort D). • The SARS-CoV-2-binding antibody response in each patient cohort was: 130 (99%) of 131 evaluable patients in cohort B, 223 (97%) of 229 evaluable patients in cohort C, and 143 (100%) of 143 evaluable patients in cohort D. These were all non-inferior to the control cohort A (100%) • The vaccine is safe in patients receiving these treatments. The minority of patients with an inadequate response after two vaccinations might benefit from a third vaccination.
18.11.2021	COVID-19 mRNA Vaccine Immunogenicity in Immunosuppressed Individuals	J Infect Dis / Article	<ul style="list-style-type: none"> • Cohort study of vaccinated adults (Pfizer/BioNTech or Moderna) without prior SARS-CoV-2 infection: included 61 participants on immunosuppressive (IS) therapy, and 21 controls • Findings suggest IS therapy reduced neutralising, binding, and non-neutralising antibody functions in addition to CD4 and CD8 T cell IFN-γ responses following COVID-19 mRNA vaccination compared to immunocompetent individuals. • IS therapy also reduced cross-reactivity against SARS-CoV-2 variants.

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Diagnostics and genomics

Publication Date	Title/URL	Journal / Article type	Digest
14.11.2021	Whole blood-based measurement of SARS-CoV-2-specific T cells reveals asymptomatic infection and vaccine immunogenicity in healthy subjects and patients with solid organ cancers	Immunology / Article	<ul style="list-style-type: none"> • Study with 231 healthy donors and 68 cancer patients demonstrates the utility of a high-throughput, standardisable T cell immunoassay to accurately detect SARS-CoV-2-specific T cell responses associated with prior SARS-CoV-2 infection and/or vaccination • Highly significant differential SARS-CoV-2-specific T cell responses were seen amongst previously infected COVID-19-positive healthy donors in comparison to unknown / naïve individuals • Discrepancy in associations between SARS-CoV-2-specific T cell responses and symptom severity likely due to differences in sampling times; however T cell responses were still present and functional over this 3-6 month timeframe in nearly all SARS-CoV-2-infected convalescent and/or vaccinated participants, even in those up to 12 months post-infection
11.11.2021	Reducing false-positive SARS-CoV-2 diagnoses using long-range RT-qPCR	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Authors modified a commercial RT-qPCR kit to make it less sensitive to residual viral RNA genome fragments, reducing likelihood for false-positive results in recovered COVID-19 patients. • Able to distinguish between infectious and non-infectious samples; fewer positive results in samples >15 days after symptoms onset. • Method may improve test-to- release protocols, expand tools available for clinical testing, and help reduce hospital encumbrance.
12.11.2021	The challenge of SARS-CoV-2 environmental monitoring in schools using floors and portable HEPA filtration units: Fresh or relic RNA?	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • SARS-CoV-2 RNA monitored in five Californian schools (96 classrooms) via weekly surface-swab samples from classroom floors and/or portable high-efficiency particulate air (HEPA) units. • Twenty-two surfaces tested positive; HEPA filter swabs more sensitive than floor swabs. • No confirmed COVID-19 cases associated with classrooms yielding positive environmental samples; need to differentiate between fresh and relic SARS-CoV-2 RNA.

16.11.2021	Organ-specific genome diversity of replication-competent SARS-CoV-2	Nat Commun / Article	<ul style="list-style-type: none"> • Virological analysis of 13 postmortem COVID-19 cases demonstrates viremia and dissemination of infectious SARS-CoV-2 to multiple extrapulmonary organs including the heart, kidney, liver, and spleen. • Impaired antiviral response in immune-suppressed individuals enabled accelerated viral replication and multi-organ spread with organ-specific evolution. • Organ-specific SARS-CoV-2 genome diversity found in an immunocompromised patient with long-term COVID-19; variants with hallmark mutations of Alpha, Beta, and Gamma VOCs were identified in multiple organs of a patient who died long before the reported emergence of these variants. • Whilst immunocompetent patients who mount an adequate antiviral response may clear the virus in the lungs and plasma and survive the initial phase of the disease, secondary (extra)pulmonary manifestations due to SARS-CoV-2 infection may still result in death later on.
12.11.2021	#COVIDisAirborne: AI-Enabled Multiscale Computational Microscopy of Delta SARS-CoV-2 in a Respiratory Aerosol	bioRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Authors provide atomic-level views of SARS-CoV-2 virus within a respiratory aerosol. • Present a significantly enhanced all-atom model and simulation of the SARS-CoV-2 Delta virion. • Evidence how changes in pH may alter dynamics and allosteric communication pathways in key functional regions of Delta spike protein.
18.11.2021	COVID-19 targets human adrenal glands	Lancet Diabetes Endocrinol / Correspondence	<ul style="list-style-type: none"> • Authors investigate whether adrenal vascular cells are direct targets of SARS-CoV-2. • SARS-CoV-2 spike protein in adrenocortical cells in 18 (45%) of 40 adrenal gland tissues. • SARS-CoV-2 mRNA detected using in situ hybridisation in 18/40 (45%) adrenal tissues. • Concordance rate between immunohistochemistry and ISH methods was 90% (36/40). • Adrenal gland is a prominent target for the viral infection and ensuing cellular damage, which could trigger a predisposition for adrenal dysfunction.

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Epidemiology and clinical - children and pregnancy

Publication Date	Title/URL	Journal / Article type	Digest
13.11.2021	Immunocompromised children and young people are at no increased risk of severe COVID-19	J Infect / Article	<ul style="list-style-type: none"> • From March 2020 – 2021 weekly questionnaires were sent to immunocompromised UK paediatric patients or their parents (1527 participants from 46 hospitals) • No COVID-19 cases reported until the end of September 2020. From 28.09.2020 through March 2021 a total of 38 COVID-19 infections were reported; four were admitted to hospital; none had severe COVID-19. • Increasing age and worsening symptoms (fever, cough, or sore throat) increased reporting of COVID-19 infection. • Serology data included 452 unvaccinated participants. Detectable antibodies found in 9 of 18 (50%) in those reporting prior infection, and in 32 of 434 (7.4%) of those with no prior report of infection.

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Epidemiology and clinical - long-term complications / sequelae

Publication Date	Title/URL	Journal / Article type	Digest
15.11.2021	Global Prevalence of Post-Acute Sequelae of COVID-19 (PASC) or Long COVID: A Meta-Analysis and Systematic Review	medRxiv (non-peer reviewed) / Systematic Review	<ul style="list-style-type: none"> • Systematic review; prevalence of long COVID (ailments persisting ≥ 28 days after diagnosis or recovery) / geographic heterogeneities. • Search until 12.08.2021; 40 studies included. • Meta-analysis suggest that worldwide PASC comprises a significant fraction (0.43) of COVID-19 tested positive cases and more than half of hospitalized COVID-19 cases. • Geographic differences appear to exist, lowest to highest PASC prevalence observed for North America to Asia (Africa and Australia data largely absent) • Stratifying PASC by race-ethnicity is a noteworthy gap in the literature. Few children were included in the underlying sample.

13.11.2021	Post-COVID-19 assessment in a specialist clinical service: a 12-month, single-centre, prospective study in 1325 individuals	BMJ Open Respir Res / Article	<ul style="list-style-type: none"> • First UK dedicated post-COVID-19 clinical service to include hospitalised and non-hospitalised patients. • 1325 individuals, assessed April 2020 - April 2021, compared by referral route: post-hospitalised (PH), non-hospitalised (NH) and post-emergency department (PED). • Findings include: (i) significant functional impairment across all patient groups, particularly NH individuals; (ii) need for multidisciplinary, structured assessment following SARS-CoV-2 infection in all patient groups, (iii) high burden of specialist input, onward therapy and psychology support; (iv) potential inequitable access to post-COVID-19 care.
13.11.2021	SARS-CoV-2 infection is associated with an increased risk of idiopathic acute pancreatitis but not pancreatic exocrine insufficiency or diabetes: long-term results of the COVIDPAN study	Gut / Letter	<ul style="list-style-type: none"> • 12-month follow-up of 1476 patients with acute pancreatitis (AP), of whom 118 were SARS-CoV-2 positive, to establish an aetiology for AP and development of diabetes mellitus (DM) • Patients who were SARS-CoV-2 positive were more likely to have idiopathic AP (34.7% vs 13.9%) with over five times increased risk after adjusting for age, smoking status, body mass index and ethnicity. These findings raise speculation that SARS-CoV-2 may cause AP • Previous research: https://gut.bmj.com/content/70/6/1061
12.11.2021	Burdens of post-acute sequelae of COVID-19 by severity of acute infection, demographics and health status	Nat Commun / Article	<ul style="list-style-type: none"> • Cohort of 181,384 people with COVID-19 and 4,397,509 non-infected controls from the healthcare databases of the US Department of Veterans Affairs • Overall burden of post-acute sequelae of COVID-19 (PASC) beyond the first 30 days of illness is estimated to be 7%, (4.4%, 21.7%, and 36.5% among non-hospitalized, hospitalized, and those admitted to ICU respectively) • PASC is a complex multifaceted non-monolithic entity that may manifest differently in various population groups.
15.11.2021	From Online Data Collection to Identification of Disease Mechanisms: The IL-1β, IL-6 and TNF-α Cytokine Triad Is Associated With Post-Acute Sequelae of COVID-19 in a Digital Research Cohort	SSRN (non-peer reviewed) / Article	<ul style="list-style-type: none"> • German ongoing digital clinical trial with biobanking; of first 318 participants, 258 on average eight months after mostly mild infection. Long COVID (PASC) reported in 67.8% of cases . • IL-1β, IL-6 and TNF-α represented a triad cytokine signature associated with PASC. • Blood profiling and single-cell data from early infection indicated that these cytokines are induced in COVID-19 lung pro-inflammatory macrophages creating a feedback loop that may trigger their long-term activation.

			<ul style="list-style-type: none"> • Authors provide evidence for a long-lasting cytokine signature potentially underlying many of the clinical symptoms of PASC that may be driven by macrophage primed during acute infection.
17.11.2021	Reduced Incidence of Long-COVID Symptoms Related to Administration of COVID-19 Vaccines Both Before COVID-19 Diagnosis and Up to 12 Weeks After	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • US retrospective analysis of 240,648 COVID-19-infected persons to identify factors influencing development / progression of long-COVID. • Patients who had at least one vaccine dose prior to their COVID-19 diagnosis: 7-10 times less likely to report two or more long-COVID symptoms compared to unvaccinated patients. • Unvaccinated patients who received first vaccination (i) within four weeks of SARS-CoV-2 infection: 4-6 times less likely to report multiple long-COVID symptoms; (ii) 4-8 weeks after diagnosis: 3 times less likely to report multiple long-COVID symptoms compared to those who remained unvaccinated. • Supports COVID-19 vaccination being protective against long-COVID, even if vaccination up to 12 weeks after COVID-19 diagnosis.

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Epidemiology and clinical – risk factors

Publication Date	Title/URL	Journal / Article type	Digest
10.11.2021	Key findings from the UKCCMP cohort of 877 patients with haematological malignancy and COVID-19: disease control as an important factor relative to recent chemotherapy or anti-CD20 therapy	Br J Haematol / Article	<ul style="list-style-type: none"> • Prospective observational study included 877 unvaccinated UK patients with SARS-CoV-2 infection and active haematological cancer. • In multivariate analysis the highest mortality was in patients with acute leukaemia (odds ratio [OR] = 1.73) and myeloma (OR 1.3). • Having uncontrolled cancer (newly diagnosed awaiting treatment as well as relapsed or progressive disease) was associated with increased mortality (OR = 2.45), as was receiving second or beyond line of treatment (OR = 1.7). • No association between recent cytotoxic chemotherapy or anti-CD19/anti-CD20 treatment and increased risk of death (within limitations of the cohort size).

15.11.2021	Characteristics, Comorbidities, and Outcomes of SARS-CoV-2 Infection in Patients with Autoimmune Conditions Treated with Systemic Therapies: a Population-based Study	J Rheumatol / Article	<ul style="list-style-type: none"> • Retrospective cohort study (01.02.2020 to 09.12.2020) included 315,101 COVID-19 patients in the US. • Adjusting for demographics, COVID-19 patients with rheumatoid arthritis (RA, n=2,306) had increased risk of hospitalisation (odds ratio 1.54) and in-hospital death (1.61), compared with comparator cohort (n=311,563). • Increased risk was also observed when adjusted for demographics plus comorbidities (hospitalisation 1.25, in-hospital death 1.35). • Risk of hospitalisation was lower in COVID-19 patients with RA receiving tumour necrosis factor inhibitors (TNFi) vs non-TNFi biologics (0.32) and the comparator cohort (0.77). • Risk of hospitalisation due to COVID-19 was similar between patients receiving tofacitinib and the comparator cohort.
16.11.2021	Mortality Risk Among Patients With COVID-19 Prescribed Selective Serotonin Reuptake Inhibitor Antidepressants	JAMA Netw Open / Original investigation	<ul style="list-style-type: none"> • US Cohort Study of patients with a positive SARS-CoV-2 diagnosis (n=83,584) of which 3401 were prescribed selective serotonin reuptake inhibitors (SSRIs) • Findings suggest SSRIs may be linked to reduced COVID-19 severity and relative risk of mortality Invited commentary: 10.1001/jamanetworkopen.2021.36510
11.11.2021	Case-control study to estimate odds of death within 28 days of positive test for SARS-CoV-2 prior to vaccination for residents of long-term care facilities in England, 2020-2021	J Epidemiol Community Health / Article	<ul style="list-style-type: none"> • Examined a random sample of people in England who died (n=6000) or did not die (n=36,000) within 28 days of a positive SARS-CoV-2 test between March 2020 and January 2021. • Multivariable analysis found an interaction effect between age and residence type determined the outcome. • Compared with a 60-year-old person not living in a long-term care facility (LTCF), the adjusted OR (aOR) for same-aged persons living in residential and nursing LTCFs was 1.77 and 3.95, respectively; at 90 years of age, aORs were 0.87 and 0.74, respectively. • The model had an overall accuracy of 94.2% when applied to the full dataset of 2,978,800 patients.
31.11.2021	COVID-19 in Children with Down Syndrome: Data from the Trisomy 21 Research Society Survey	J Clin Med / Article	<ul style="list-style-type: none"> • Retrospective cohort study of 328 paediatric COVID-19 patients with Down syndrome (DS) and 224 controls: in the DS group significant risk factors for hospitalisation included older age, obesity, and epilepsy, while significant risk factors for acute respiratory distress syndrome included age and thyroid disorder.

			<ul style="list-style-type: none"> • Hospitalised COVID-19 patients with DS (n=127) had higher incidence of cough, fever, nasal signs and shortness of breath compared with controls. • Hospitalised children with DS (especially those from low-to-middle-income countries) had higher prevalence of COVID-19-related complications (pneumonia, ARDS, acute renal failure) compared with controls • Preprint previously included
16.11.2021	COVID-19 in breast cancer patients: a subanalysis of the OnCovid registry	Ther Adv Med Oncol / Article	<ul style="list-style-type: none"> • Cross-European study with 415 participants with both COVID-19 and breast cancer diagnoses • Findings show that breast cancer patients appear to have lower SARS-CoV-2 complications and mortality rate compared to other cancer patients • Cancer treatment isn't impacted by COVID-19 complications
13.11.2021	Chronic diseases associated with increased likelihood of hospitalization and mortality in 68,913 COVID-19 confirmed cases in Spain: A population-based cohort study	PLoS One / Research article	<ul style="list-style-type: none"> • Retrospective, observational study in an open cohort analysing all 68,913 individuals (mean age 44.4 years, 53.2% women) with SARS-CoV-2 infection over 30 days or until death within the period 15.06.2020 - 19.12.2020 using exhaustive electronic health registries. • Multivariate logistic regression was used to analyse the association between each chronic disease and severe infection, based on hospitalization and all-cause mortality. • In addition to old age and the presence of specific cardiovascular and metabolic conditions, which consistently increased the risk of severe SARS-CoV-2 infections in men and women, results also reveal sex differences in certain disorders, such as neoplasms and acute cerebrovascular disease in men or thyroid disorders and hepatic steatosis in women
16.11.2021	Outcomes of COVID-19 in patients with primary systemic vasculitis or polymyalgia rheumatica from the COVID-19 Global Rheumatology Alliance physician registry: a retrospective cohort study	Lancet Rheumatol / Article	<ul style="list-style-type: none"> • International cohort study between 12.03.2020 – 12.04.2021 found patients with primary systemic vasculitis or polymyalgia rheumatica experienced high rates of severe COVID-19 outcomes, particularly in patients with giant cell arteritis and ANCA-associated vasculitis • Of 1020 with outcome data 512 (50.2%) were not hospitalised, 114 (11.2%) were hospitalised and did not receive supplemental oxygen, 239 (23.4%) were hospitalised and received ventilation or supplemental oxygen, and 155 (15.2%) died.

		<ul style="list-style-type: none"> • Severe outcomes were associated with variable and largely unmodifiable risk factors, including age, sex, comorbidities, and treatments, including high-dose glucocorticoids. • Patients with COVID-19 submitted to the registry later in the analysis period (01.10.2020 - 12.04.2021) had a lower rate of poor outcomes than those submitted earlier in the analysis period (on or before 15.06.2020). • Linked comment: https://www.sciencedirect.com/science/article/pii/S266599132100357X?via%3Dihub
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Epidemiology and clinical – other

Publication Date	Title/URL	Journal / Article type	Digest
18.11.2021	Changes in COVID-19 outbreak severity and duration in long-term care facilities following vaccine introduction, England, November 2020 to June 2021	Euro Surveill	<ul style="list-style-type: none"> • Describes characteristics of COVID-19 outbreaks in 330 long-term care facilities (LTCF) in England between November 2020 and June 2021. • As vaccine coverage in LTCF increased and national incidence declined, total number of outbreaks and outbreak severity decreased across LTCF. • Number of infected cases per outbreak decreased by 80.6%, while proportion of outbreaks affecting staff only increased.
12.11.2021	Management of a large outbreak of COVID-19 at a British Army training centre: lessons for the future	BMJ Mil Health / Article	<ul style="list-style-type: none"> • Narrative review of an outbreak (185 cases, 15% total population) at Royal Military Academy Sandhurst (RMAS) in January–March 2021. • Key lessons learnt include importance of multidisciplinary working, utility of sync matrices to monitor outbreaks in real time, timing of high-risk training activities, infrastructure, use of LFDs.
27.10.2021	Infection of Brain Pericytes Underlying Neuropathology of COVID-19 Patients	Int J Mol Sci / Article	<ul style="list-style-type: none"> • 6 COVID-19 patients and 7 healthy controls included in an autoptic study that used immunostaining of human brains to demonstrate that expression of the SARS-CoV-2 receptor ACE2 is restricted to a subset of neurovascular pericytes.

			<ul style="list-style-type: none"> • Neurological symptoms were exclusive to, and ubiquitous in, patients that exhibited moderate to high ACE2 expression in perivascular cells. • Cerebrospinal fluid from an additional 8 COVID-19 patients and 8 controls. Significantly lower levels of the pericyte marker PDGFRβ were observed in SARS-CoV-2-infected cases, indicative of disrupted pericyte homeostasis. • Pericyte infection by SARS-CoV-2 underlies virus entry into the privileged central nervous system space, as well as neurological symptomatology due to perivascular inflammation and a locally compromised blood–brain barrier.
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Infection control / non-pharmaceutical interventions

Publication Date	Title/URL	Journal / Article type	Digest
18.11.2021	Effectiveness of public health measures in reducing the incidence of covid-19, SARS-CoV-2 transmission, and covid-19 mortality: systematic review and meta-analysis	BMJ / Systematic review	<ul style="list-style-type: none"> • Systematic review with 72 studies: 35 evaluated individual public health measures (34 observational studies and 1 RCT) / 37 assessed a “package of interventions.” • Eight studies included in meta-analysis: reduction in COVID-19 incidence associated with handwashing, mask wearing, and physical distancing. Other measures not included due to heterogeneity of studies. • Pooled analysis suggested 53% reduction in covid-19 incidence for both handwashing and mask wearing, 25% for social distancing. • Limitations include lack of high quality evidence. • Associated editorials: https://www.bmj.com/content/375/bmj.n2729 ; https://doi.org/10.1136/bmj.n2812
11.11.2021	Effectiveness of non-pharmaceutical measures (NPIs) on COVID-19 in Europe: A systematic literature review	medRxiv (non-peer reviewed) / Systematic Review	<ul style="list-style-type: none"> • Systematic review focusing on community (meso-level) / society (macro-level) level non-pharmaceutical interventions (NPIs) in Europe during first wave. Search up to 15.04.2021. • 45 studies included (30 modelling studies, 13 observational, one quasi-experimental and one experimental).

			<ul style="list-style-type: none"> • Despite heterogeneity across studies, NPIs are effective in reducing SARS-CoV-2 transmission rates / COVID-19 hospitalisation rates and deaths in European Region.
16.11.2021	Efficacy of FFP3 respirators for prevention of SARS-CoV-2 infection in healthcare workers	Elife / Article	<ul style="list-style-type: none"> • Authors use observational data and modelling to analyse infection rates amongst UK healthcare workers (HCWs) working on 'red' (COVID-19) and 'green' (non-COVID-19) wards during the second wave of the pandemic. • Whilst using fluid resistant surgical masks (FRSMs), HCWs on red wards faced an approximately 31-fold (and at least 5-fold) increased risk of direct, ward-based infection. • After changing to FFP3 respirators, this risk was significantly reduced (52-100% protection).
16.11.2021	Comparative Effectiveness of an Automated Text Messaging Service for Monitoring COVID-19 at Home	Ann Intern Med / Article	<ul style="list-style-type: none"> • US retrospective study examining text message–based remote monitoring service for 3488 patients diagnosed with COVID-19. • Group received twice-daily, automated text message check-ins, from 23.03.2020 – 30.11.2020. (4377 in usual care control group). • Reduced mortality by 1.8 fewer per 1000 compared to standard care • Associated editorial: https://doi.org/10.7326/M21-4273
12.11.2021	Using high-resolution contact networks to evaluate SARS-CoV-2 transmission and control in large-scale multi-day events	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Authors combined high-resolution data on contacts among passengers and crew on cruise ships with network transmission models, to see how social contacts influence interventions needed. • Passengers had a median of 20 (IQR 10–36) unique close contacts per day; over 60% of their contact episodes were made in dining or sports areas where mask wearing is typically limited. • Simulated outbreaks showed larger effect of vaccination coverage and rapid antigen tests than mask mandates alone; combined interventions are required.

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Treatment

Publication Date	Title/URL	Journal / Article type	Digest
17.11.2021	Azithromycin in patients with COVID-19: a systematic review and meta-analysis	J Antimicrob Chemother / Systematic Review	<ul style="list-style-type: none"> • Systematic review up to 5 July 2021 included 16 studies (5 RCTs and 11 observational studies) with a total of 22,984 patients. • Meta-analysis found no difference in mortality for those treated with or without azithromycin, in observational studies [OR: 0.90], RCTs [OR: 0.97] or when both types of studies were pooled together [overall OR: 0.95]. • Individual studies reported no significant difference for those treated with or without azithromycin in need for hospital admission, time to admission, clinical severity, need for intensive care, or adverse effects. • Findings do not support use of azithromycin in COVID-19 management.
14.11.2021	The Use of Tocilizumab in Patients with COVID-19: A Systematic Review, Meta-Analysis and Trial Sequential Analysis of Randomized Controlled Studies	J Clin Med / Systematic review	<ul style="list-style-type: none"> • Systematic review of 11 randomised controlled trials (RCTs) up to 30.04.2021 with a total of 3358 patients treated with tocilizumab (TCZ) • Meta-analysis confirms the value of TCZ in ameliorating the overall survival of COVID-19 patients, especially when burdened by severe or critical disease • Limitations are identified, including the omission of secondary outcomes and meta-regression. The need for further RCTs to confirm these conclusions was maintained.
11.11.2021	Tenofovir Disoproxil Fumarate and severity of COVID-19 in people with HIV infection	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Authors studied 51,558 HIV-positive individuals on antiretroviral therapy (ART) in 2020 at 69 HIV clinics in Spain. • 48-week risks compared for: (i) 11.9% individuals receiving tenofovir disoproxil fumarate (TDF)/emtricitabine (FTC), (ii) 39.6% on tenofovir alafenamide (TAF)/ FTC, (iii) 26.6% on abacavir (ABC)/lamivudine (3TC), (iv) 21.8% other regimes • Compared with other antiretrovirals, TDF/FTC lowers COVID-19 severity among HIV-positive individuals with virological control. • This protective effect may be restricted to individuals aged 50 years and older.
16.11.2021	Post-exposure Lopinavir-Ritonavir Prophylaxis versus Surveillance for Individuals Exposed to	EClinicalMedicine / Article	<ul style="list-style-type: none"> • Of 319 participants, 209 were randomised to lopinavir-ritonavir post-exposure prophylaxis (LPV/r PEP)

	SARS-CoV-2: The COPEP Pragmatic Open-Label, Cluster Randomized Trial		<ul style="list-style-type: none"> • During 21-day follow-up, 35/209 (16.7%) in the LPV/r group developed COVID-19 compared with 13/109 (11.9%) in the surveillance group. In primary endpoint analysis, adjusted for baseline imbalance, the hazard ratio for developing COVID-19 in the LPV/r group vs surveillance was 0.60. • Only weak evidence was found in favour of LPV/r as prophylactic treatment for those in close contact with SARS-CoV-2. The point estimate of the effect after adjustment for baseline imbalances showed a statistically non-significant trend towards protection in the LPV/r treated group in some but not all analyses.
13.11.2021	Association Between Androgen Deprivation Therapy and Mortality Among Patients With Prostate Cancer and COVID-19	JAMA Netw Open / Original investigation	<ul style="list-style-type: none"> • Cohort study with 1106 patients between 17.03.2020-11.02.2021 found no statistically significant difference in the rates of all-cause mortality among men with prostate cancer receiving androgen deprivation therapy (ADT) (15%) compared to those who were not (14%) • Findings indicate that the use of ADT is not associated with a decreased mortality from SARS-CoV-2

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Modelling

Publication Date	Title/URL	Journal / Article type	Digest
16.11.2021	Vaccination against COVID-19 and society's return to normality in England: a modelling study of impacts of different types of naturally acquired and vaccine-induced immunity	BMJ Open / Article	<ul style="list-style-type: none"> • Modelling suggests that in an optimistic scenario (vaccine efficacy 85%, vaccine-induced immunity ≥ 182 days, and $\geq 60\%$ reduction in reinfectivity), annual mass vaccination programmes can prevent further COVID-19 outbreaks in England; estimated cumulative COVID-19 deaths 130,000 to 150,000 by the end of 2024. • Under a pessimistic scenario (vaccine efficacy 62.5%, natural/vaccine immunity 365/182 days, and 30% reduction in reinfectivity), total number of COVID-19 deaths may be up to 431,000. • More frequent revaccinations are associated with lower total numbers and lower peaks of daily COVID-19 deaths.

15.11.2021	External validation of the QCovid risk prediction algorithm for risk of COVID-19 hospitalisation and mortality in adults: national validation cohort study in Scotland	Thorax / Article	<ul style="list-style-type: none"> Assesses performance of QCovid algorithm [version 1] in predicting COVID-19 hospitalisations and deaths using a Scottish dataset (5,384,819 individuals) for two time periods matching the original study in England. QCovid showed good calibration in the first period, but systematic overestimation of risk in the second period, prior to temporal recalibration. Harrell's C in the first period: i) deaths in females (0.95) and males (0.93); ii) hospitalisations in females (0.81) and males (0.82). Associated editorial: https://thorax.bmj.com/content/early/2021/11/14/thoraxjnl-2021-218169
10.11.2021	Unexposed populations and potential COVID-19 burden in European countries	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> Authors estimate proportion of population in 19 European countries that has acquired immunity to severe disease through infection or vaccination to estimate potential remaining COVID-19 burden. Suggest many countries face a substantial burden of hospitalisations and deaths, particularly those with lower vaccine coverage, less historical transmission, and/or older populations.

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Guidance and consensus statements

Publication Date	Title/URL	Journal / Article type
10.11.2021	Infection control in the intensive care unit: expert consensus statements for SARS-CoV-2 using a Delphi method	Lancet Infect Dis / Review

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Overviews, comments and editorials

Publication Date	Title/URL	Journal / Article type
14.11.2021	ACE2 and Innate Immunity in the Regulation of SARS-CoV-2-Induced Acute Lung Injury: A Review	Int J Mol Sci / Review
16.11.2021	SARS-CoV2 Infection and the Importance of Potassium Balance	Front Med (Lausanne) / Perspective
13.11.2021	Boosting immunity to COVID-19 vaccines	Nat Med / Article
26.10.2021	Comparing COVID-19 vaccines for their characteristics, efficacy and effectiveness against SARS-CoV-2 and variants of concern: A narrative review	Clin Microbiol Infect / Narrative review
10.11.2021	The influence of interval between doses on response to vaccines	Vaccine / Article
14.11.2021	A Review on the Role of Stem Cells against SARS-CoV-2 in Children and Pregnant Women	Int J Mol Sci / Review
14.11.2021	An Insight into the Role of Postmortem Immunohistochemistry in the Comprehension of the Inflammatory Pathophysiology of COVID-19 Disease and Vaccine-Related Thrombotic Adverse Events: A Narrative Review	Int J Mol Sci / Review
16.11.2021	The Spectrum of Manifestations of Severe Acute Respiratory Syndrome-Coronavirus 2 (SARS-CoV2) Infection in Children: What We Can Learn From Multisystem Inflammatory Syndrome in Children (MIS-C)	Front Med (Lausanne) / Review
15.11.2021	Maternal COVID-19 leaves a lasting immunological impression on the fetus	Nat Immunol / News and views
18.11.2021	Counting the neurological cost of COVID-19	Nature Reviews Neurology / News & Views
13.11.2021	Revisiting COVID-19 policies: 10 evidence-based recommendations for where to go from here	BMC Public Health / Review
08.11.2021	How an outbreak became a pandemic: a chronological analysis of crucial junctures and international obligations in the early months of the COVID-19 pandemic	Lancet / Health Policy
19.11.2021	COVID-19-associated mucormycosis: Evidence-based critical review of an emerging infection burden during the pandemic's second wave in India	PLoS Negl Trop Dis / Review
10.11.2021	Coughs and sneezes spread diseases: but do 'aerosol generating' procedures?	Thorax / Editorial

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