UK Health Security Agency

COVID-19 Literature Digest – 08/01/2021

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 The reports include both preprints, which should be treated with caution as they are NOT peer-reviewed and may be subject to change, and also research that has been subject to peer review and wider scrutiny.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Report for 01.10.2021 (please note that papers that have **NOT been peer-reviewed** are highlighted in red).

Sections:

Serology and immunology

Publication Date	Title/URL	Journal / Article type	Digest
21.09.2021	Antibody titers and protection against a SARS-CoV-2 infection	J Infect / Article	• Examined antibody titers in 8,758 healthcare workers (HCWs) soon after the first epidemic wave had occurred in France (10.06.2020 to 10.07.2020); 4,811 (54.9%) had been given one (2,244; 46.6%) or two (2,567; 53.4%) doses of vaccine between January and April 15, 2021. • In this cohort, none of the two doses-vaccinated HCWs had an ELISA concentration below 141 BAU/ml one month after the second injection, unlike 79.3% of the HCWs three months after a natural infection.
27.09.2021	Multi-omics approach identifies novel age-, time- and treatment-related immunopathological signatures in MIS-C and pediatric COVID-19	medRxiv (non-peer reviewed) / Article	• Multi-omics was used to examine immunopathological signatures in children with COVID-19 (n=105) and MIS-C (n=76). • Paediatric COVID-19 (pCOVID-19) was characterised by enhanced type I IFN responses, and MIS-C by type II IFN- and NF-κB dependent responses, matrisome activation, and increased levels of Spike protein. • Reduced levels of IL-33 in pCOVID-19, and of CCL22 in MIS-C suggested suppression of Th2 responses. • Expansion of TRBV11-2 T-cell clonotypes in MIS-C was associated with inflammation and signatures of T-cell activation, and was reversed by glucocorticoids. • Association of MIS-C with combination of HLA A*02, B*35, C*04 alleles suggests genetic susceptibility; MIS-C B cells showed higher mutation load.
23.09.2021	Humoral and T-Cell Response to SARS-CoV-2 Vaccination in Patients With Multiple Sclerosis Treated With Ocrelizumab	JAMA Neurol / Brief report	• Of 72 patients with multiple sclerosis (MS) 49 were treated with ocrelizumab and 23 had not been treated for ≥6 months prior to vaccination. There were 40 healthy controls • Patients vaccinated ≥5 months after the last dose had a higher probability for positive serology response

			• A robust vaccine-specific T-cell and decreased humoral response was observed in patients with MS treated with ocrelizumab. • T-cell responses were detected in patients with either positive or negative humoral response, which may confer protection, even in the absence of antibody responses

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Vaccines

Publication Date	Title/URL	Journal / Article type	Digest
20.09.2021	COVID-19 Vaccines in Cancer Patients. Seropositivity and Safety. Systematic Review and Meta-Analysis	Vaccines (Basel) / Systematic review	• Systematic review included 6 studies (621 cancer patients and 256 controls). • Patients with solid tumours show adequate antibody responses to COVID-19 vaccines (>90%), though the antibody titers were significantly lower than those of healthy controls. • A significantly lower rate of seroconversion was registered in patients with hematologic malignancies. • COVID-19 vaccines showed a good safety profile; no grade 3-4 adverse events were registered.
11.09.2021	Varicella Zoster Virus Reactivation Following COVID-19 Vaccination: A Systematic Review of Case Reports	Vaccines (Basel) / Systematic review	• 12 articles included with 91 patients with herpes zoster (HZ) following COVID-19 vaccination. • Hypertension was the main comorbidity present in 18% of patients. 13% of patients (12/91) had an autoimmune condition, rheumatoid arthritis being the most common (4/12). 10% of patients (9/91) were receiving immunosuppressants. • Symptoms developed on average 5.8 days post-vaccination irrespective of dose. Treatment with oral valacyclovir as a monotherapy was employed in most patients (23/91). • This mild adverse event is still underreported and causality is not yet confirmed; however the increased awareness of clinicians and the early recognition of the disorder is important for the optimal management of these patients.
04.09.2021	Safety and Efficacy of COVID-19 Vaccines: A Systematic Review and Meta-Analysis of Different Vaccines at Phase 3	Vaccines (Basel) / Systematic review	• 12 reports on phase-3 clinical trials and observational studies were included in this review which found that the vaccines assessed are sufficiently safe and effective. • Whilst mRNA vaccines showed more relevance to serious adverse events than viral vector and inactivated vaccines, no solid evidence indicated that COVID-19 vaccines directly caused serious adverse events. • Serious metabolic, musculoskeletal, immune-system, and renal disorders were more common among recipients of inactivated vaccine, and serious gastrointestinal complications and infections were more common among recipients of viral vector and inactivated vaccine. The occurrence of serious vessel disorders was more frequent in mRNA vaccines.

			• Two mRNA vaccine doses conferred a lesser risk of SARS-COV-2 infection than did vaccination with viral vector and inactivated vaccines. All vaccines protected more against symptomatic than asymptomatic cases, but reduced the risk of severe SARS-COV-2 infection
26.09.2021	Effectiveness of COVID-19 vaccines against SARS-CoV-2 variants of concern: a systematic review and meta-analysis	medRxiv (non-peer reviewed) / Article	• Systematic review included 7 RCTs (51,169 participants), 10 cohort studies (14,385,909 participants) and 16 case-control studies (734,607 cases). Eight COVID-19 vaccines (mRNA-1273, BNT162b2, ChAdOx1, Ad26.COV2.S, NVX-CoV2373, BBV152, CoronaVac, and BBIBP-CorV) were included in the analysis. • Full vaccination was effective against Alpha, Beta/Gamma, and Delta variants, with vaccine effectiveness (VE) of 88.3%, 70.7%, and 71.6%, respectively; partial vaccination was less effective (VE of 59.0%, 49.3%, and 52.6%, respectively). • mRNA vaccines appear to have higher VE against VOC over non-mRNA vaccines.
25.09.2021	A systematic review of COVID-19 vaccine efficacy and effectiveness against SARS-CoV-2 infection and disease	medRxiv (non-peer reviewed) / Article	• Systematic review identified 58 real-world vaccine effectiveness studies covering five vaccines meeting the inclusion criteria: Pfizer-BioNTech, Moderna, Janssen, Oxford-AstraZeneca, and Sinovac. • Findings demonstrate robust evidence for the high vaccine efficacy/effectiveness ("VE") of COVID-19 vaccines: protection against severe infection or death was at least 80% and often close to 100%. • VE against symptomatic disease was heterogeneous between vaccine products/studies but almost always >65% and often >90%. • Most vaccines retained high levels of protection for most SARS-CoV-2 variants of concern, especially against severe outcomes; a few studies provided evidence of slight reductions in VE for infection or mild disease with the Beta (B.1.351) and Delta (B.1.617.2) strains. No included studies covered the Gamma (P.1) strain.
29.09.2021	mRNA vaccination in people over 80 years of age induces strong humoral immune responses against SARS-CoV-2 with cross neutralisation of P.1 Brazilian variant	Elife / Article	• UK study of serological and cellular response to spike protein in 100 people aged 80-96, two weeks after second BNT162b2 (Pfizer) vaccination. • All had antibody responses, with high titres in 98%. • Spike-specific cellular immune responses detectable in only 63%, correlated with humoral response. • Previous infection increased antibody responses after one vaccine; antibody and cellular responses remained 28-fold and 3-fold higher respectively after second. • mRNA vaccine delivers strong humoral immunity in people up to 96 years of age / retains broad efficacy against P.1 [Gamma] variant.
29.09.2021	The impact of SARS-CoV-2 vaccination on Alpha and Delta variant transmission	medRxiv (non-peer reviewed) / Article	• Observational cohort study of contacts of SARS-CoV-2-infected index cases using contact testing data from England: 51,798/139,164(37.2%) contacts tested were PCR-positive. • Two doses of BNT162b2 or ChAdOx1 vaccines in Alpha variant index cases independently reduced PCR-positivity in contacts (aOR vs. unvaccinated=0.18 and 0.37, respectively). • Delta variant attenuated vaccine-associated reductions in transmission: two BNT162b2 doses reduced Delta transmission (aOR=0.35), more than ChAdOx1 (aOR=0.64).

			• Variation in viral load (Ct values) explained only a modest proportion of vaccine-associated transmission reductions. • Transmission reductions declined over time since second vaccination, for Delta reaching similar levels to unvaccinated individuals by 12 weeks for ChAdOx1 and attenuating substantially for BNT162b2; protection also declined in this period.
29.09.2021	COVID-19 hospital admissions and deaths after BNT162b2 and ChAdOx1 nCoV-19 vaccinations in 2.57 million people in Scotland (EAVE II): a prospective cohort study	Lancet Respir Med / Article	• Scottish study following up 2 572 008 individuals from receiving their first vaccination until admission to hospital for COVID-19, death, or end of study period. • Between 8.12.2020 - 18.04.2021: 841,090 (32·7%) received BNT162b2 [Pfizer] / 1,730,918 (67·3%) ChAdOx1 [AstraZeneca]. • 1196 (<0·1%) individuals were admitted to hospital or died due to COVID-19 ≥14 days after their first dose. • Severe COVID-19 associated with: older age (≥80 years), comorbidities, hospitalisation in previous 4 weeks, high-risk occupations, care home residence, socioeconomic deprivation, being male, being an ex-smoker. • COVID-19 infection before vaccination was protective. Linked comment: https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00413-6/fulltext
30.09.2021	Product-specific COVID-19 vaccine effectiveness against secondary infection in close contacts, Navarre, Spain, April to August 2021	Eurosurveillance / Rapid communication	• Cohort study of 30,240 adults who were close contacts of 12,263 COVID-19 index cases from April to August 2021 in Navarre, Spain. • COVID-19 vaccine effectiveness by product (two doses Comirnaty, Spikevax or Vaxzevria and one of Janssen), against infection ranged from 50% for Janssen to 86% for Vaxzevria-Comirnaty combination; among ≥ 60 year-olds, from 17% (−26 to 45) for Janssen to 68% (48 to 80) for Spikevax; and against hospitalisation from 74% for Janssen to > 90% for other products. • Two doses were highly effective against hospitalisation, but suboptimal for infection control.
27.09.2021	Effectiveness of BNT162b2 Vaccine in Adolescents during Outbreak of SARS-CoV-2 Delta Variant Infection, Israel, 2021	Emerg Infect Dis / Article	• Israeli study after BNT162b2 [Pfizer] vaccine approved for adolescents (12–15 year olds) in June 2021 as a 2-dose regimen / 21 days apart, shortly before B.1.617.2 (Delta) outbreak. • By 26.08.2021: 277,218 adolescents (46.1% of those eligible) had received 1 dose / 187,707 (31.2%) had received 2 dose. • Adjustments for sex and epidemiologic week for days 8–28 after the second dose combined demonstrated adjusted vaccine effectiveness of 91.5%
01.10.2021	Safety Monitoring of an Additional Dose of COVID-19 Vaccine - United States, August 12-September 19, 2021	MMWR Morb Mortal Wkly Rep / Article	• Among 12,591 participants who completed a health check-in survey (12.08.2021–19.09.2021) after all 3 doses of an mRNA COVID-19 vaccine, 79.4% and 74.1% reported local or systemic reactions, respectively, after the third dose; this compares to 77.6% and 76.5% after the second dose, respectively. • Suggests no unexpected patterns of adverse reactions after an additional dose of COVID-19 vaccine.
26.09.2021	Neutralizing efficacy of vaccines against the SARS-CoV-2 Mu variant	medRxiv (non-peer	• VLP (virus-like particle)-based rapid neutralisation test was conducted on post-vaccination sera collected from individuals one week after administration of the second dose of the BNT162b2 (Prizer-BioNTech) vaccine.

		reviewed) / Article	• Results suggest vaccine has 76% neutralising effectiveness against the Mu compared to 96% with original strain and that Mu, similar to the Delta variant, causes cell-to-cell fusion which can be an additional factor for the variant to escape vaccine-mediated humoral immunity.
29.09.2021	Initial Analysis of Viral Dynamics and Circulating Viral Variants During the mRNA-1273 Phase 3 COVE Trial	medRxiv (non-peer reviewed) / Article	• In the ongoing Coronavirus Efficacy (COVE) trial, mRNA-1273 (Moderna) vaccination significantly reduced SARS-CoV-2 viral copy number and associated Burden of Disease (BOD) and Burden of Infection (BOI). • Vaccine efficacies during the trial against SARS-CoV-2 variants circulating in the US were 82.4% for Epsilon and Gamma, and 81.2% for the Epsilon B.1.427 and B.1.429 variants

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Diagnostics and genomics

Publication Date	Title/URL	Journal / Article type	Digest
28.09.2021	Acceptability of and symptom findings from an online symptom check-in tool for COVID-19 outpatient follow-up among a predominantly healthcare worker population	BMJ Open / Original research	• Online symptom check-in tool for virtual disease triage among outpatients diagnosed with COVID-19 at Saint James's Hospital, Ireland. • Contact via text message with link to tool: high uptake (72%); over 800 responses from almost 300 unique participants (91% healthcare workers) during first wave. • Secondary aims: COVID-19 education, promotion of official information, analysis of reported symptomatology.
28.09.2021	Tiled-ClickSeq for targeted sequencing of complete coronavirus genomes with simultaneous capture of RNA recombination and minority variants	Elife / Article	• Tiled-ClickSeq provides a simple method for whole genome sequencing of virus isolates such as SARS-CoV-2 that can simultaneously map single-nucleotide variations, minority variants as well as recombination events.
01.10.2021	Emergence and spread of SARS-CoV-2 lineage B.1.620 with variant of concern-like mutations and deletions	Nat Commun / Article	• Describes a SARS-CoV-2 lineage carrying many mutations and deletions in the spike protein shared with widespread VOCs, including E484K, S477N and deletions HV69Δ, Y144Δ, and LLA241/243Δ. • Designated B.1.620, it is known to circulate in Lithuania and has been found in several European states (France, Germany, Spain, Belgium), but also in increasing numbers in Central African Republic. Travel records suggest a potential Central African origin of the lineage. • Preprint previously included
10.09.2021	Emergence and Spread of a B.1.1.28-Derived P.6 Lineage with Q675H and Q677H Spike Mutations in Uruguay	Viruses / Article	• The most prevalent viral variant during the first epidemic wave in Uruguay (December 2020–February 2021) was a B.1.1.28 sublineage carrying Spike mutations Q675H + Q677H, now designated as P.6.

			• More efficient dissemination of lineage P.6 and presence of mutations (Q675H and Q677H) in the proximity of the key cleavage site at the S1/S2 boundary suggest P.6 may be more transmissible. • Although P.1 replaced P.6 as the dominant lineage in Uruguay since April 2021, monitoring of Q675H + Q677H in VOCs should be of worldwide interest.
29.09.2021	The role of viral genomics in understanding COVID-19 outbreaks in long-term care facilities	Lancet Microbe / Review	• Authors reviewed all genomic epidemiology studies on COVID-19 in long-term care facilities (LTCFs). • Staff and residents usually infected with identical / near identical SARS-CoV-2 genomes. • Outbreaks: (i) usually involved one predominant cluster, same lineages persisted in LTCFs despite infection control measures. (ii) commonly due to single or few introductions followed by a spread (versus series of seeding events from community into LTCFs).
29.09.2021	Interventions to Disrupt Coronavirus Disease Transmission at a University, Wisconsin, USA, August-October 2020	Emerg Infect Dis / Article	• COVID-19 outbreak at US university. Aug - Oct 2020, 3,485 students, including 856/6,162 students living in dormitories, tested positive. • Multiple prevention efforts, including quarantining 2 dormitories. • Genomic surveillance provided more comprehensive understanding of transmission dynamics both in specific outbreak settings and in general population. • Universities and health departments can use tools to monitor spillover into community / inform campus and community mitigation efforts.
28.09.2021	Large-scale analysis of SARS-CoV-2 spike-glycoprotein mutants demonstrates the need for continuous screening of virus isolates	PLoS One / Article	• In an analysis of 1,036,030 SARS-CoV-2 genome assemblies and 30,806 NGS datasets from GISAID and European Nucleotide Archive (ENA) focusing on non-synonymous mutations in the spike protein, only around 2.5% of the samples contained the wild-type spike protein with no variation from the reference. • Among the spike protein mutants, a low mutation rate was observed, but the mean and median number of spike protein mutations per sample increased over time. • Of the 5,472 distinct variants found, most were recurrent, but only 21 and 14 recurrent variants were found in at least 1% of the mutant genome assemblies and NGS samples, respectively. • The observation of high-confidence subclonal variants in about 2.6% of the NGS data sets with mutant spike protein might indicate co-infection with various SARS-CoV-2 strains and/or intra-host evolution. Some variants may also have an effect on antibody binding or T-cell recognition.
20.09.2021	Building knowledge of university campus population dynamics to enhance near-to-source sewage surveillance for SARS-CoV-2 detection	Sci Total Environ / Article	• Study investigates methods to account for variation in upstream populations at a site with highly transient footfall, providing a better understanding of the impact of variable populations on the SARS-CoV-2 trends provided by wastewater-based epidemiology (WBE). • The potential for complementary data, such as flush count data, to estimate the occupancy of different buildings in within the near-to-source site population is also explored, and potential concerns arising due to the presence of heavily diluted samples during wet weather are addressed.

			• Population normalisation, using either ammoniacal nitrogen or orthophosphate, is considered critical for providing a comprehensive understanding of the results from WBE when population size is highly variable.

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Epidemiology and clinical - children and pregnancy

Publication Date	Title/URL	Journal / Article type	Digest
20.09.2021	Vertical Transmission of SARS-CoV-2: A Systematic Review of Systematic Reviews	Viruses / Systematic review	• 69 studies included to investigate whether there is adequate evidence supporting the possibility of vertical transmission of SARS-CoV-2 and to ascertain the possibility of mother-to-child transmission of SARS-CoV-2 during pregnancy • Most (>70%) of the mother-to-child infection was likely due to environmental exposure, although about 20% was attributable to potential vertical transmission of SARS-CoV-2. • SARS-CoV-2 could be potentially transmitted vertically. The mode of delivery for women infected with SARS-CoV-2 did not appear to increase or decrease the risk of COVID-19 infection for newborns but likely increased the risk for direct and indirect adverse health outcomes. • Maternal death rates were significantly higher in pregnant woman infected with COVID-19 than those without. Prospective studies are needed to clarify the actual risk of SARS-CoV-2 mother-to-child infection and identify the optimal prevention and control strategies.
13.09.2021	COVID-19 and maternity care in South East London: shared working and learning initiative	BMJ Open Qual / Quality improvement report	• South East London Local Maternity System adapted to respond to clinicians managing pregnant women during pandemic via COVID-19 huddles. • This collaborative network approach provides support and safe space for maternity multidisciplinary team across the sector and beyond.
30.09.2021	Robust innate responses to SARS-CoV-2 in children resolve faster than in adults without compromising adaptive immunity	Cell Rep / Article	• Longitudinal analysis of early innate responses in children and adults with mild infection within household clusters. 46 participants, of which 37 had SARS-CoV-2 infection (21 adults / 16 children, aged 0.8 -16 years). • Innate response against SARS-CoV-2 is robust in children despite limited symptoms. • Resolution of inflammation and onset of B cell response occur faster. • Antibody response is not compromised by the shorter antiviral inflammatory response. • Children's better early control of inflammation may be key for rapidly controlling infection and limiting disease course.

27.09.2021	Characteristics of children admitted to hospital with acute SARS-CoV-2 infection in Canada in 2020	CMAJ / Article	• National prospective study in Canada: among 264 hospital admissions involving children with SARS-CoV-2 infection (8 Apr. to 31 Dec. 2020), 150 (56.8%) admissions were related to COVID-19 and 100 (37.9%) were incidental infections (admissions for other reasons and found to be positive for SARS-CoV-2 on screening). Infants (37.3%) and adolescents (29.6%) represented most cases. • Among hospital admissions related to COVID-19, 52 (34.7%) had critical disease, of which 42 (28.0%) required any form of respiratory or hemodynamic support, and 59 (39.3%) had at least 1 underlying comorbidity. • Children with obesity, chronic neurologic conditions or chronic lung disease other than asthma were more likely to have severe or critical COVID-19.
27.09.2021	Willingness of children and adolescents to have a COVID-19 vaccination: Results of a large whole schools survey in England	EClinicalMedicine	• OxWell Student Survey: 27,910 students from 180 schools in England between 14th May and 21st July 2021 • In total, 13984 (50.1%) would opt-in to vaccination, 10322 (37.0%) were undecided, and 3604 (12.9%) would opt-out; younger age groups were less likely to opt-in compared to 17-year-olds (77.8%) • Students who were 'opt-out' or 'undecided' (a combined 'vaccine hesitant' group) were more likely to come from deprived socioeconomic contexts, smoke or vape, spend longer on social media, and feel that they did not belong in their school community, but had lower levels of anxiety and depression. • 'Opt-out' students had higher reported confirmed or probable previous COVID-19 infection than the 'opt-in' group.

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Epidemiology and clinical - long-term complications / sequelae

Publication Date	Title/URL	Journal / Article type	Digest
29.09.2021	Characterising long COVID: a living systematic review	BMJ Glob Health / Systematic Review	• Living systematic review, to 17.03.2021. Included 39 studies (32 cohort, 6 cross-sectional, 1 case-control) incorporating 10,951 mostly adult participants. • Most studies showed high or moderate risk of bias; the nature of studies precludes a precise case definition or risk evaluation. • Weakness (41%), general malaise (33%), fatigue (31%), concentration impairment (26%) and breathlessness (25%) most common symptoms. • Previously included as a preprint.
27.09.2021	Evolving phenotypes of non-hospitalized patients that indicate long COVID	BMC Med / Research article	• Retrospective electronic health record (EHR) cohort study with 96,025 patients, evaluating post-test phenotypes in two temporal windows at 3–6 and 6–9 months from 03.2020 to 06.2021

			• MLHO, a computational framework, identified 41 phenotypes in different age/gender groups and/or time windows as positively associated with a past positive COVID-19 test. • Study confirms many of the long COVID symptoms and suggests that a variety of new diagnoses, including new diabetes mellitus and neurological disorder diagnoses, are more common among those with a history of COVID-19 than those without the infection. •>63% of post-acute sequelae of COVID-19 (PASC) phenotypes were observed in patients <65 years of age
29.09.2021	Retinal vessels modifications in acute and post-COVID-19	Sci Rep / Article	• Study with 59 eyes from 32 COVID-19 patients and 80 eyes from 53 unexposed subjects found retinal arteries diameter was increased in patients with acute COVID-19 compared to those unexposed to the virus and the difference in arteries diameter was statistically significant between severe cases and unexposed subjects. • COVID-19 can induce important changes to the retinal vasculature during the acute phase of the disease, including microvascular infarcts and major arteries and veins dilation. Whilst most of these changes disappear after 6 months, patients who suffered from severe COVID-19 show persistent dilation of retinal vessels after the normalization of their systemic inflammatory parameters
23.09.2021	Guillain-Barré syndrome after SARS-CoV-2 infection in an international prospective cohort study	Brain / Article	• A confirmed or probable preceding SARS-CoV-2 infection were observed in 11 (22%) Guillain-Barré syndrome (GBS) patients during the first months of the pandemic in the context of a large, international, prospective cohort study. • These patients shared similar features, as they frequently had a sensorimotor phenotype with facial palsy and significantly more often had a demyelinating subtype compared with both the other patients included in the same time window as well as historical control patients. • There was no increase in inclusion rate in International GBS Outcome Study (IGOS), suggesting that a strong association between SARS-CoV-2 and GBS is unlikely; however SARS-CoV-2 may be an occasional trigger for GBS.
27.09.2021	Prevalence, Symptoms and Duration of Post Acute Effects in SARS-CoV-2 Positive Children – a Nationwide Cohort Study	Research Square (non-peer reviewed) / Article	• Nationwide cohort study of 37,522 Danish children (0-17 years) with RT-PCR verified SARS-CoV-2 infection and a control group of 78,037 randomly selected children, surveyed from 24 March to 9 May 2021. • Long COVID symptoms were reported by 12-51% of SARS-CoV-2 infected children; in the majority symptoms resolved within 1-5 months. • Statistically significant symptoms of Long COVID among pre-school children included fatigue (Risk Difference (RD) 0.05), loss of smell (RD 0.01), loss of taste (RD 0.01) and muscle weakness (RD 0.01). • Among school children the most significant symptoms were loss of smell (RD 0.12), loss of taste (RD 0.10), fatigue (RD 0.05), respiratory problems (RD 0.03), dizziness (RD 0.02), muscle weakness (RD 0.02), and chest pain (RD 0.01).
29.09.2021	Efficacy of COVID-19 Vaccination on the Symptoms of Patients With Long COVID: A Target Trial Emulation Using Data From the ComPaRe e-Cohort in France.	SSRN (non-peer reviewed) / Article	• Study using ComPaRe long COVID cohort data for 910 patients with persistent symptoms: 455 vaccinated matched to 455 control. • By 120 days: vaccination reduced long COVID symptoms; doubled rate of patients in complete remission; reduced disease impact.

			• COVID-19 vaccination lowers severity and life impact of long COVID at 120 days among patients with persistent symptoms.

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Epidemiology and clinical – risk factors

Publication Date	Title/URL	Journal / Article type	Digest
00.08.2021	Excess deaths from COVID-19 and other causes by region, neighbourhood deprivation level and place of death during the first 30 weeks of the pandemic in England and Wales: A retrospective registry study	Lancet Reg Health Eur / Research paper	• Analysis of national statistics estimates 62,321 excess deaths in England and Wales in the first 30 weeks of the COVID-19 pandemic: 46,221 attributable to respiratory causes, including COVID-19. • Rates of all-cause excess mortality varied by region and level of deprivation (e.g. 93 per 100,000 in the most affluent fifth of areas to 124 per 100,000 in the most deprived). • The most deprived areas had highest rates of death attributable to COVID-19 and other indirect deaths; no socioeconomic gradient found for excess deaths from cardiovascular disease, diabetes, and cancer.
25.09.2021	COVID-19 mortality risk correlates inversely with vitamin D3 status, and a mortality rate close to zero could theoretically be achieved at 50 ng/ml 25(OH)D3: Results of a systematic review and meta-analysis	medRxiv (non-peer reviewed) / Article	• Systematic review (1 population study and 7 clinical studies) found a negative Pearson correlation of vitamin D3 levels and mortality risk (r(17)=-.4154 / r(13)=-.4886). • For the combined data, median D3 levels were 23.2 ng/ml (17.4 – 26.8), and a significant Pearson correlation was observed (r(32)=-.3989). • Overall, findings suggest low D3 is a predictor rather than a side effect of the infection. • Regression suggests a theoretical point of zero mortality at approximately 50 ng/ml D3.
23.09.2021	Association of Disease-Modifying Treatment and Anti-CD20 Infusion Timing With Humoral Response to 2 SARS-CoV-2 Vaccines in Patients With Multiple Sclerosis	JAMA Neurol / Research Letter	• Cohort study of 120 vaccinated Swiss multiple sclerosis (MS) patients found humoral response against SARS-CoV-2 at 1 month after vaccination was appropriate under treatment with cladribine and teriflunomide and diminished/absent under treatment with anti-CD20 therapies and S1P modulators. • Delaying anti-CD20 infusions by 3 to 6 months before vaccination could, however, increase the probability of developing appropriate humoral responses.
27.09.2021	Smoking and COVID-19 outcomes: an observational and Mendelian randomisation study using the UK Biobank cohort	Thorax / Article	• In this study with 421,469 participants, 1649 confirmed infections, 968 COVID-19-related hospitalisations and 444 COVID-19-related deaths, current smokers had higher risks of hospitalisation compared with those who had never smoked.

			• Overall, the congruence of observational analyses indicating associations with recent smoking behaviours and meta-regression analyses indicating associations with lifelong predisposition to smoking and smoking heaviness support a causal effect of smoking on COVID-19 severity.

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Epidemiology and clinical – other

Publication Date	Title/URL	Journal / Article type	Digest
26.09.2021	Quantifying impacts of the COVID-19 pandemic through life-expectancy losses: a population-level study of 29 countries	Int J Epidemiol / Article	• Authors calculated life expectancy tables for 29 countries during 2015-2020; included most European countries, Chile and USA. • Life expectancy at birth declined from 2019 to 2020 in 27 of 29 countries. • Largest losses in life expectancy during 2020 were in males from USA (2.2 years) and Lithuania (1.7 years); reductions of over one year documented in 11 countries for males and 8 for females. • Reductions mostly attributable to increased mortality above age 60 years and to official COVID-19 deaths.
27.09.2021	Area level deprivation and monthly COVID-19 cases: The impact of government policy in England	Soc Sci Med / Article	• Area level deprivation was significantly associated with COVID-19 cases from March 2020; linked to the premature easing of national restrictions in July 2020 when cases were still high in the most deprived areas in England and subsequent economic policies, such as 'Eat Out, To Help Out' to stimulate the retail and hospitality sectors exacerbated this trend. • Local lockdowns from July 2020 and the introduction of a regional tiered system in the North and Midlands of the country were introduced to contain the disease while minimising the severe economic effect. • Whilst these measures were taken without wider socio-economic considerations, they inadvertently reversed the previously observed relationship between area level deprivation on COVID-19 cases at the Middle Super Output Area (MSOA) level in England.

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Infection control / non-pharmaceutical interventions

Publication Date	Title/URL	Journal / Article type	Digest

30.09.2021	Strategies to reduce the risk of SARS-CoV-2 importation from international travellers: modelling estimations for the United Kingdom, July 2020	Eurosurveillance	• Simulation modelling examined air travellers arriving in the United Kingdom from the European Union or the United States • Quarantine upon arrival with a PCR test on day 7 plus a 1-day delay for results can reduce the number of infectious arriving travellers released into the community by a median 94% compared with no quarantine/no test scenario; similar to that achieved by a 14-day quarantine period (median > 99%). • Even shorter quarantine periods can prevent a substantial amount of transmission; all strategies in which travellers spend at least 5 days (mean incubation period) in quarantine and have at least one negative test before release are highly effective (median reduction 89%).
28.09.2021	Non-Pharmaceutical Interventions and COVID-19 Burden in the United States	medRxiv (non-peer reviewed) / Article	• Modelling for the US suggests the odds of a decrease in COVID-19 case velocity were significantly elevated for several non-pharmaceutical interventions (NPIs) including: stay at home orders (OR 2.02); indoor dining ban (OR 1.62); public mask mandate (OR 2.18); and severe gathering ban (OR 1.68). • In mutually adjusted models, odds remained elevated for stay at home (AOR 1.47) and public mask mandate (AOR = 2.27). • Stay at home (OR 2.00; AOR 1.89) was also associated with greater likelihood of decrease in death velocity in unadjusted and adjusted models.

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Transmission

Publication Date	Title/URL	Journal / Article type	Digest
27.09.2021	Quantifying the relationship between SARS-CoV-2 viral load and infectiousness	Elife / Article	• Cohort study of 259 index cases and 582 high-risk contacts: the effect of viral load was larger in household contacts than in non-household contacts: transmission probability as large as 48% when viral load greater than 1010 copies per mL. • Transmission probability peaked at symptom onset, with a mean probability of transmission of 29%, with large individual variations. • Modelling predicts larger viral load levels could lead to relative increase in probability of transmission: 24% to 58% in household contacts, and 15% to 39% in non-household contacts.
27.09.2021	Risk Assessment of COVID Infection by Respiratory Droplets from Cough for Various Ventilation Scenarios Inside an Elevator: An OpenFOAM based CFD Analysis	ArXiv (non-peer reviewed) / Article	• Simulation results show that in an elevator without forced air circulation a significantly large percentage of droplets remain suspended in the risky height zone (0.8m to 1.8m).

			• With forced circulation a reduced percentage of droplets remain suspended, instead sticking to elevator surfaces or escaping. • In all the ventilation scenarios a maximum of 29.68% and minimum of 0% of droplets remain suspended in the air; without forced circulation the corresponding percentage is 42.01%.

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Treatment

Publication Date	Title/URL	Journal / Article type	Digest
23.09.2021	Antibody and cellular therapies for treatment of covid-19: a living systematic review and network meta-analysis	BMJ / Research	• Systematic review up to 21.07.2021 identified 47 trials • Patients with non-severe disease randomised to antiviral monoclonal antibodies had lower risk of hospitalisation than placebo groups: casirivimab-imdevimab (odds ratio (OR) 0.29; risk difference (RD) -4.2%; moderate certainty), bamlanivimab (OR 0.24; RD -4.1%; low certainty), bamlanivimab-etesevimab (OR 0.31; RD -3.8%; low certainty), and sotrovimab (OR 0.17; RD -4.8%; low certainty). • No notable difference between monoclonal antibodies.
24.09.2021	Beneficial and Harmful Outcomes of Tocilizumab in Severe COVID-19: A Systematic Review and Meta-Analysis	Pharmacotherapy / Systematic review	• 64 studies included, with a total of 20,616 hospitalised patients. • 7,668 patients received tocilizumab (TCZ) in addition to standard of care (SOC), including 1,915 patients admitted to intensive care units (ICU) with reported mortality. 12,948 patients received SOC only, including 4,410 patients admitted to ICU with reported mortality. • TCZ prevented mortality in patients hospitalized for COVID-19, was more beneficial in patients receiving concomitant corticosteroids and when TCZ administration occurred within the first 10 days after symptom onset
27.09.2021	Efficacy and safety of ivermectin for the treatment of COVID-19: A systematic review and meta-analysis	Qjm / Systematic review	• Three observational studies and 14 randomised controlled trials (RCTs), were included. Based on meta-analysis of RCTs, the use of ivermectin was not associated with reduction in time to viral clearance, duration of hospitalization, incidence of mortality and incidence of mechanical ventilation. • Ivermectin use was not associated with increased odds of adverse events or serious adverse events based on moderate quality of evidence from RCTs; however, due to lack of evidence as to its efficacy, it not recommended for treatment of COVID-19 beyond the context of clinical trials.
29.09.2021	REGEN-COV Antibody Combination and Outcomes in Outpatients with Covid-19	N Engl J Med	• Phase 3 of an adaptive trial, with 4,057 patients included in the final analysis were randomly assigned to receive various doses of intravenous REGEN-COV or placebo. • Covid-19–related hospitalization or death from any cause occurred in 18 of 1355 patients in the REGEN-COV 2400-mg group (1.3%) and in 62 of 1341 patients in the placebo group (4.6%); these

			outcomes occurred in 7 of 736 patients in the REGEN-COV 1200-mg group (1.0%) and in 24 of 748 patients in the placebo group who underwent randomization concurrently (3.2%). • Median time to resolution of symptoms was 4 days shorter with each REGEN-COV dose than with placebo (10 days vs. 14 days) REGEN-COV was efficacious across various subgroups, including patients who were SARS-CoV-2 serum antibody–positive at baseline. Both REGEN-COV doses reduced viral load faster than placebo • Serious adverse events occurred more frequently in the placebo group (4.0%) than in the 1200-mg group (1.1%) and the 2400-mg group (1.3%). Infusion-related reactions of grade 2 or higher occurred in less than 0.3% of the patients in all groups.
29.09.2021	Extracorporeal membrane oxygenation for COVID-19: evolving outcomes from the international Extracorporeal Life Support Organization Registry	Lancet / Article	• Study of 4812 COVID-19 patients from 349 sites in 41 countries: over 2020, mortality after extracorporeal membrane oxygenation (ECMO) support increased by about 15%. Median duration of ECMO support increased by 6 days. • Compared with earlier in pandemic, patients who received ECMO after 01.05.2020 were more commonly treated with corticosteroids. • Factors appearing to affect outcomes include: (i) patients receiving ECMO after May 1 had higher likelihood of treatment-refractory disease despite similar conventional risk factors; (ii) centres with less experience providing ECMO support for COVID-19 were more likely to have a higher mortality rate.
30.09.2021	Outpatient and inpatient anticoagulation therapy and the risk for hospital admission and death among COVID-19 patients	EClinicalMedicine / Research Paper	• U.S prospective cohort study, 04.03.2020 - 27.08.2020, of all COVID-19 patients over 18 years old among 12 hospitals and 60 outpatient clinics. • Outpatients with COVID-19 who were on outpatient anticoagulation at the time of diagnosis (160 of 5597, 2.9%) experienced a 43% reduced risk of hospitalization. • Failure to initiate anticoagulation upon hospitalization or maintaining outpatient anticoagulation in hospitalized COVID-19 patients associated with increased mortality risk.

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Modelling

Publication Date	Title/URL	Journal / Article type	Digest
22.09.2021	Development of a model-inference system for estimating epidemiological characteristics of SARS-CoV-2 variants of concern	Nat Commun / Article	• Validation of a model which accounts for population susceptibility, disease seasonality, NPIs, and vaccination. Use of independent data indicates that the model-inference system is able to closely capture pandemic dynamics, accurately estimate cumulative infection rates and closely matches available epidemiological data

			• Modelling used to estimate that B.1.1.7 has a 46.6% transmissibility increase but nominal immune escape from protection induced by prior wild-type infection; B.1.351 has a 32.4% increase and 61.3% immune escape; and P.1 has a 43.3% transmissibility increase and 52.5% immune escape.

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Guidance and consensus statements

Publication Date	Title/URL	Journal / Article type
24.09.2021	Use of Pfizer-BioNTech COVID-19 Vaccine in Persons Aged ≥16 Years: Recommendations of the Advisory Committee on Immunization Practices - United States, September 2021	MMWR Morb Mortal Wkly Rep / Guidance statement

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Overviews, comments and editorials

Publication Date	Title/URL	Journal / Article type
28.09.2021	Cheap and Commonplace: Making the Case for BCG and γδ T Cells in COVID-19	Front Immunol / Perspective
27.09.2021	COVID-19 vaccination in kidney transplant recipients	Nat Rev Nephrol / Comment
30.09.2021	Neuropsychiatric manifestations of COVID-19, potential neurotropic mechanisms, and therapeutic interventions	Translational Psychiatry / Review Article
27.09.2021	Covid-19: England sees biggest fall in life expectancy since records began in wake of pandemic	BMJ / News
23.09.2021	Combination therapies for COVID-19: an overview of the clinical trials landscape	Br J Clin Pharmacol / Review Article
29.09.2021	Following the science? Views from scientists on government advisory boards during the COVID-19 pandemic: a qualitative interview study in five European countries	BMJ Glob Health / Article
27.09.2021	Commentary on the use of the reproduction number R during the COVID-19 pandemic	Stat Methods Med Res / Comment

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