



UK Health  
Security  
Agency

## COVID-19 Literature Digest – 29/10/2021

Dear all,

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

UKHSA's COVID-19 Literature Digest has been produced since February 2020. A selection of our previous Digests [can be found here](#). This resource aims to highlight a small selection of recent COVID-19 papers that are relevant to UK settings, contain new data, insights or emerging trends. The Digest Team generate a report once per week (Fri). The reports include both preprints, which should be treated with caution as they are NOT peer-reviewed and may be subject to change, and also research that has been subject to peer review and wider scrutiny. The Digest is very rapidly produced and does not claim to be a perfect product; the inclusion or omission of a publication should not be viewed as an endorsement or rejection by UKHSA. We do not accept responsibility for the availability, reliability or content of the items included in this resource.

To join our email distribution list, or to be removed, please send a request to [COVID.LitDigest@phe.gov.uk](mailto:COVID.LitDigest@phe.gov.uk). If you are interested in papers relating to behaviour and social science please contact [COVID19.behaviouralscience@phe.gov.uk](mailto: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**Report for 29.10.2021** (please note that papers that have **NOT been peer-reviewed** are highlighted in red).

Sections:

[Serology and immunology](#)

[Vaccines](#)

[Diagnostics and genomics](#)

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

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

[Epidemiology and clinical - risk factors](#)

[Epidemiology and clinical - other](#)

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

[Transmission](#)

[Treatment](#)

[Modelling](#)

[Guidance and consensus statements \(no digest\)](#)

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

### Serology and immunology

Publication Date	Title/URL	Journal / Article type	Digest
19.10.2021	<a href="#">SARS-CoV-2 Reinfection Is a New Challenge for the Effectiveness of Global Vaccination Campaign: A Systematic Review of Cases Reported in Literature</a>	Int J Environ Res Public Health / Systematic review	<ul style="list-style-type: none"><li>• Systematic Review of reinfection cases; search up to July 2021. 117 papers included.</li><li>• Severity of reinfection episode was more severe in 92/260 (35.3%) with death on average.</li><li>• Detection of different clades or lineages by genome sequencing between initial infection and reinfection in 52/260 (20%) cases.</li><li>• (Note search end date in relation to reinfections)</li></ul>
21.10.2021	<a href="#">Meta-analysis of COVID-19 single-cell studies confirms eight key immune responses</a>	Sci Rep / Article	<ul style="list-style-type: none"><li>• Re-analyses data from several single-cell RNA sequencing (scRNA-seq) studies associated with COVID-19 infection; validated 8 of the 20 published results across multiple datasets.</li><li>• Found a consistent decrease in T-cells with increasing COVID-19 infection severity. Interferon signal pathways, presence of expanded B-cell clones in COVID-19 patients, and increased expression of T-cells in T-cell clonal expansion.</li><li>• Suggests conclusions drawn from scRNA-seq data analysis of small cohorts of COVID-19 patients should be treated with some caution.</li></ul>

[Back to menu](#)

### Vaccines

Publication Date	Title/URL	Journal / Article type	Digest
29.09.2021	<a href="#">Safety, Immunogenicity, and Efficacy of COVID-19 Vaccines in Children and Adolescents: A Systematic Review</a>	Vaccines / Systematic Review	<ul style="list-style-type: none"><li>• Systematic review including 8 published (n=2852 children or adolescents) and 28 pre-published studies.</li><li>• Results showed that selected COVID-19 vaccines had a good safety profile in children and adolescents, with mostly mild and moderate adverse effects, including injection site pain, fatigue, headache, and fever. A few cases of myocarditis and pericarditis were also reported.</li></ul>

			<ul style="list-style-type: none"> <li>• Authors conclude that some COVID-19 vaccines have potential protective effects but awareness is needed to monitor possible adverse effects after injection, especially pericarditis</li> <li>• Preprint previously included</li> </ul>
22.10.2021	<a href="#">REACT-1 study round 14: High and increasing prevalence of SARS-CoV-2 infection among school-aged children during September 2021 and vaccine effectiveness against infection in England</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• 100,527 participants aged 5-17 provided a wet swab with a valid result from RT-qPCR SARS-CoV-2 positive</li> <li>• In September 2021, the start of the school term, infections were increasing exponentially. During the same period, a decreasing prevalence was observed among adults aged 18-64</li> <li>• Swab-positivity among unvaccinated individuals remains 3-4 times higher than in vaccinated individuals, however data also indicates that breakthrough infections following two-dose vaccination are sustained up to 6 months</li> </ul>
28.10.2021	<a href="#">Characteristics and risk of COVID-19-related death in fully vaccinated people in Scotland</a>	Lancet / Correspondence	<ul style="list-style-type: none"> <li>• Of vaccine-eligible Scottish population aged 65–79, death rate per 10,000 person-years was 4.2 for unvaccinated individuals / 4.2 for fully vaccinated.</li> <li>• Most marked in over 80s: 4.0 deaths for fully vaccinated vs 420.1 deaths for unvaccinated</li> <li>• 236 deaths in fully vaccinated people were recorded. Most older than 75 years with 106/236 deaths were viral sequenced: 5 from Alpha / 101 Delta variant.</li> </ul>
25.10.2021	<a href="#">Moderna Announces Positive Top Line Data from Phase 2/3 Study of COVID-19 Vaccine in Children 6 to 11 Years of Age</a>	Moderna (non-peer reviewed) / News	<ul style="list-style-type: none"> <li>• In a cohort of 4,753 children and adolescents (aged 6 to less than 12 years) two doses of mRNA-1273 (Moderna) were generally well tolerated and showed robust neutralising antibody responses</li> <li>• SARS-CoV-2-neutralising antibody geometric mean ratio (GMR) comparing the response in young adults from the Phase 3 COVE study was 1.5, with a seroresponsiveness representing a difference of 0.6% to the Phase 3 benchmark.</li> </ul>
27.10.2021	<a href="#">Waning Immunity after the BNT162b2 Vaccine in Israel</a>	N Engl J Med / Article	<ul style="list-style-type: none"> <li>• Analyses data on all PCR positive SARS-CoV-2 test results between 11-31 July 2021 in individuals vaccinated with BNT162b2 (Pfizer) vaccine before June 2021 and not returning from abroad</li> <li>• The rates of both documented SARS-CoV-2 infections and severe COVID-19 exhibited a significant increase as time from second vaccine dose elapsed</li> <li>• Elderly individuals (60+) who received their second dose in March 2021 were 1.6 times more protected against infection and 1.7 times more protected against severe COVID-19 compared to those who received their second dose in January 2021. Similar results were found for different age groups.</li> <li>• Preprint previously included</li> </ul>
25.10.2021	<a href="#">Longitudinal Study after Sputnik V Vaccination Shows Durable SARS-CoV-2 Neutralizing Antibodies and Reduced Viral Variant Escape over Time</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• Longitudinal analysis of a collection of 472 serum samples obtained at 4 time points from September 2021 up to 120 days post-vaccination from 118 volunteers</li> <li>• Analysis indicates that while anti-spike IgG levels significantly wane over time, the neutralising capacity of the first-wave lineages of SARS-CoV-2 and VOC are maintained within four months of vaccination</li> <li>• Observations indicate that serum neutralizing antibodies are maintained for at least 4 months post-vaccination with improved antibody cross-neutralizing ability to circulating variants of concern (Beta and Gamma) observed over time of vaccination.</li> </ul>

25.10.2021	<a href="#">Immunogenicity of The BNT162b2 mRNA COVID-19 Vaccine in Patients With Primary Brain Tumors: A Prospective Cohort Study</a>	Research Square (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• Prospective study analysed 17 primary brain tumour (PBT) patients and 12 healthy controls. • Blood samples extracted at i) 37 days after second vaccine dose (01.03.2021 – 10.06.2021), and; ii) at least two months after second vaccine dose (18.05.2021 to 22.07.2021).</li> <li>• At median 44 days after second vaccine dose, 88.2% (15/17) of PBT patients achieved seroconversion compared with 100% (12/12) of HCs; median IgG titer was significantly lower in the PBT group (1,908 AU/mL vs 8,198 AU/mL, respectively).</li> <li>• At median 130 days after second dose, 80% (12/15) of PBT achieved seroconversion compared with 100% (10/10) of HCs; median IgG titer remained significantly lower in the PBT group (410 AU/mL vs 8,198 AU/mL, respectively). All PBT patients who failed to seroconvert had been treated with corticosteroids during vaccination.</li> </ul>
23.10.2021	<a href="#">Autoimmune conditions following mRNA (BNT162b2) and inactivated (CoronaVac) COVID-19 vaccination: a descriptive cohort study among 1.1 million vaccinated people in Hong Kong</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• 1,122,793 in a cohort of 3.9 million aged ≥16 years received at least one dose of mRNA (BNT162b2: 388,579,998; CoronaVac: 542,795), and 721,588 completed two doses (BNT162b2: 388,579,998; CoronaVac: 542,795).</li> <li>• Vaccination records between 23.02.2021 – 30.06.2021 were linked to Hospital Authority (HA) Hospital admission related to a spectrum 16 auto-immune diseases (AID) was assessed.</li> <li>• Within 28 days following BNT162b2 and CoronaVac vaccination, autoimmune conditions and hospitalization are rare and similar to disease occurrence among the non-vaccinated.</li> <li>• The association between first dose BNT162b2 vaccination and immune-related symptoms warrants further research.</li> </ul>
19.10.2021	<a href="#">Humoral and cellular response to SARS-CoV-2 BNT162b2 mRNA vaccine in hemodialysis patients</a>	BMC Immunol / Research Article	<ul style="list-style-type: none"> <li>• Immune response of 50 haemodialysis (HD) patients (mean age 69.4 years, 62% male) 4-12 weeks after 2-dose Pfizer vaccination</li> <li>• &gt;40% of the HD patients did not develop a cellular response to the spike protein</li> <li>• Most HD patients develop a B- and/or T-cell response after vaccination against COVID-19, but with a limited immunological response.</li> <li>• Only 2 patients without a serological response displayed a cellular response, suggesting that a serological response adds little to measurable protection against Covid-19.</li> </ul>
22.10.2021	<a href="#">Two-dose COVID-19 vaccination and possible arthritis flare among patients with rheumatoid arthritis in Hong Kong</a>	Ann Rheum Dis / Article	<ul style="list-style-type: none"> <li>• Among 5493 patients with rheumatoid arthritis (RA) (BNT162b2, n=653; CoronaVac, n=4169), propensity-scored weighted Poisson regression showed no significant association between flare and COVID-19 vaccination (BNT162b2: adjusted incidence rate ratio 0.86; CoronaVac: 0.86).</li> <li>• The distribution of weekly rheumatic drug prescriptions showed no significant difference between groups since the launch of the mass vaccination programme.</li> </ul>
25.10.2021	<a href="#">Neurological complications after first dose of COVID-19 vaccines and SARS-CoV-2 infection</a>	Nat Med / Article	<ul style="list-style-type: none"> <li>• Self-controlled case series study investigated hospital admissions from neurological complications 28 days after first dose of ChAdOx1nCoV-19 (AstraZeneca, n = 20,417,752) or BNT162b2 (n = 12,134,782), and after a SARS-CoV-2-positive test (n = 2,005,280).</li> <li>• Findings: i) increased risk of Guillain–Barré syndrome (incidence rate ratio (IRR), 1.29 at 15–21 days) with ChAdOx1nCoV-19; ii) increased risk of haemiparesis (IRR, 1.29 at 15–21 days) with BNT162b2; and iii) substantially higher risk of all neurological complications after a positive SARS-CoV-2 test, including Guillain–Barré syndrome (IRR, 5.25).</li> </ul>

			<ul style="list-style-type: none"> <li>• An independent Scottish cohort provided further support for association between Guillain–Barré (IRR, 2.32 at 1–28 days).</li> <li>• Overall, estimates 38 excess cases of Guillain–Barré per 10 million people receiving a positive SARS-CoV-2 test.</li> </ul>
25.10.2021	<a href="#">Immune response to COVID-19 vaccination is attenuated by poor disease control and antimyeloma therapy with vaccine driven divergent T cell response</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• Prospective study of 214 myeloma patients in UK Rudy Study cohort assessing humoral gamma release assay (IGRA) cellular immune responses ≥3 weeks following a second vaccine</li> <li>• Positive Anti-Spike antibody levels (&gt; 50 IU/ml) were detected in 92.7%. Positive cellular immune responses were detected in 61.4% myeloma patients and 60.1% were positive for both anti-Spike protein serology</li> <li>• 6.3% patients had both negative IGRA and negative Anti-Spike protein antibody response</li> <li>• Predictors of a poor immune response included male gender, myeloma therapy received prior to vaccination, and receipt of Pfizer-BioNTech vaccination.</li> <li>• NOTE: Partly funded by Janssen UK.</li> </ul>
22.10.2021	<a href="#">Immunogenicity and reactogenicity of booster vaccinations after Ad26.COVS.S priming</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• 434 healthcare workers (HCWs) who received a single Ad26.COVS.S [Janssen] vaccine, no booster, or a booster with AstraZeneca, mRNA-1273 [Moderna], or BNT162b2 [Pfizer-BioNTech] (participant)-blinded, multi-centre, randomised controlled trial (RCT)</li> <li>• SARS-CoV-2 specific T-cells were detectable in only 65.8% of participants 3 months after priming with Ad26.COVS.S. This increased rapidly following booster, especially with mRNA-based vaccines</li> <li>• Severity and duration of adverse effects were greater following heterologous booster vaccination, however all were mild to moderate, did not require hospitalisation and generally resolved within 48 hours</li> <li>• Boosting of Ad26.COVS.S-primed HCWs was well-tolerated and immunogenic, with no adverse effects observed following mRNA-based boosters</li> </ul>
22.10.2021	<a href="#">COVID-19 vaccine response in people with multiple sclerosis</a>	Ann Neurol / Research	<ul style="list-style-type: none"> <li>• Study of 473 people with multiple sclerosis: compared to no disease modifying therapy, treatment with monoclonal antibodies (OR 0.03) and fingolimod (OR 0.04) were associated with lower seroconversion following SARS-CoV2 vaccine.</li> <li>• Time since last anti-CD20 treatment and total time on treatment were both significantly associated with response to vaccination.</li> <li>• Vaccine type significantly predicted seroconversion, but not in those on anti-CD20</li> <li>• Preliminary data on cellular T-cell immunity showed 40% of seronegative subjects had detectable CoV2 T cell responses.</li> </ul>

[Back to menu](#)

#### Diagnostics and genomics

Publication Date	Title/URL	Journal / Article type	Digest
------------------	-----------	------------------------	--------

23.10.2021	<a href="#">Factors that Influence the Reported Sensitivity of Rapid Antigen Testing for SARS-CoV-2</a>	Front Microbiol / Systematic review	<ul style="list-style-type: none"> <li>• Systematic review, including 83 studies published between 01.01.2020 - 01.02.2021, comparing the diagnostic accuracy of SARS-CoV-2 antigen detection in COVID-19 symptomatic and asymptomatic individuals compared to quantitative reverse transcription polymerase chain reaction (qRT-PCR).</li> <li>• Meta-analysis confirms that viral load is clearly the most important factor that influences the sensitivity of SARS-CoV-2 antigen testing. Antigen test sensitivity is highest in individuals with a high viral load and who are being infectious at the time of testing.</li> <li>• Other factors include symptom presence, days from symptom onset (DSO), anatomical site of specimen collection, and the storage conditions for specimen collection could all affect the measured performance of antigen tests.</li> </ul>
08.10.2021	<a href="#">Development of a Multiplex Tandem PCR (MT-PCR) Assay for the Detection of Emerging SARS-CoV-2 Variants</a>	Viruses / Article	<ul style="list-style-type: none"> <li>• Authors have developed a SARS-CoV-2 typing assay focused on five positions in the N-glycan (N501, K417, E484 and P681); it can identify a range of variants, including all current variants of concern.</li> <li>• Evaluation at four UK hospitals demonstrated excellent concordance with the known variants derived from full sequence analysis.</li> <li>• The assay has a turnaround time of about three hours for a set of up to 24 samples.</li> </ul>
25.10.2021	<a href="#">Retrospective diagnosis of SARS-CoV-2 infection in patients with Long COVID by measuring specific T cell mediated IL-2 release</a>	Research Square (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• Authors design a SARS-CoV-2 specific T cell assay and use it to follow up a cohort of mostly non-hospitalised patients with Long COVID for up to 13 months.</li> <li>• Findings demonstrate that IL-2 release from SARS-CoV-2-specific memory T cells is significantly elevated and &gt;88% specificity in identifying individuals with confirmed SARS-CoV-2 infection on a positive PCR test.</li> </ul>
26.10.2021	<a href="#">Nucleocapsid antibody positivity as a marker of past SARS-CoV-2 infection in population serosurveillance studies: impact of variant, vaccination, and choice of assay cut-off</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• UKHSA Study of seroconversion rates and antibody titres following Alpha and Delta variant vaccine breakthrough infections.</li> <li>• N-antibody rates were lower following vaccination and differ by variant, which was more pronounced for Alpha-variant infection than Delta.</li> <li>• Findings suggest that population estimates of N antibody seropositivity are likely to underestimate the proportion of the population who have experienced Covid-19 in the highly vaccinated population, particularly following Alpha variant wave or mild infection.</li> </ul>
22.10.2021	<a href="#"><math>\delta</math>1 variant of SARS-COV-2 acquires spike V1176F and yields a highly mutated subvariant in Europe</a>	bioRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• Study to investigate whether <math>\delta</math>1, the dominant subvariant of Delta in India, Europe and the US, is likely to evolve and acquires additional mutations.</li> <li>• Findings suggest that V1176F is a recurrent spike substitution that is frequently acquired by other variants to improve viral fitness.</li> </ul>

[Back to menu](#)

#### Epidemiology and clinical - children and pregnancy

Publication Date	Title/URL	Journal / Article type	Digest
------------------	-----------	------------------------	--------

21.10.2021	<a href="#">Fertility rates and birth outcomes after ChAdOx1 nCoV-19 (AZD1222) vaccination</a>	Lancet / Correspondence	<ul style="list-style-type: none"> <li>• Authors analysed pregnancies (1%, 121/9755 participants) reported during four (AstraZeneca) phase 1 to 3 clinical trials in UK, Brazil, South Africa.</li> <li>• Rate of miscarriage no higher in vaccine group than in control group.</li> <li>• No evidence of an association between reduced fertility and vaccination with ChAdOx1 nCoV-19.</li> </ul>
------------	--	-------------------------	---

[Back to menu](#)

### Epidemiology and clinical - long-term complications / sequelae

Publication Date	Title/URL	Journal / Article type	Digest
25.10.2021	<a href="#">Long-term health-related quality of life in non-hospitalised COVID-19 cases with confirmed SARS-CoV-2 infection in England: Longitudinal analysis and cross-sectional comparison with controls</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• Prospective cohort study of 548 non-hospitalised COVID-19 cases aged 12-85 years, followed up for 6 months from 01.12.2020, with cross-sectional comparison to controls</li> <li>• 16.8% report ongoing symptoms at 6 months, most frequently extreme tiredness, loss of taste and/or smell, and shortness of breath.</li> <li>• 10% report prolonged loss of function compared to pre-COVID-19 baselines. A marked increase in loss of function was observed among older COVID-19 cases and those with persistent physical symptoms.</li> </ul>
27.10.2021	<a href="#">COVCOG 1: Factors predicting Cognitive Symptoms in Long COVID. A First Publication from the COVID and Cognition Study</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• Findings from UK study including 181 individuals who had suffered COVID-19 infection and were experiencing ongoing cognitive symptoms at the time of testing.</li> <li>• Investigation of factors predictive of ongoing symptoms and their severity, an analysis of the relationship between cognitive symptoms and physical symptoms, and an exploration of the presence and severity of cognitive symptoms, both through the acute illness and at the time of testing.</li> <li>• Experience of neurological symptoms during the acute illness may be significant predictors of ongoing cognitive impairment and are suggestive of different types of neurological sequelae, reflecting neuroinflammation and encephalitis</li> <li>• Of those experiencing Long COVID, &gt;50% (and 75% of those with severe symptoms) were unable to work. 35% (~50% of those with severe ongoing symptoms) had lost their job due to illness.</li> </ul>
22.10.2021	<a href="#">Post COVID-19 in children, adolescents, and adults: results of a matched cohort study including more than 150,000 individuals with COVID-19</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• Study included 157,134 individuals with confirmed COVID-19 up to 30.06.2020.</li> <li>• COVID-19 and control cohorts (1:5) were followed for incident morbidity outcomes up to 12 months after diagnosis,</li> <li>• 96 pre-defined outcomes were aggregated into 13 diagnosis/symptom complexes (physical health, mental health, physical/mental overlap domain).</li> <li>• Findings indicate substantial new-onset post COVID-19 morbidity in paediatric and adult populations based on routine health care documentation.</li> </ul>
22.10.2021	<a href="#">Symptoms compatible with long-COVID in healthcare workers with and without SARS-CoV-2 infection - results of a prospective multicenter cohort</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• Data from Aug 2020 – Mar 2021, using baseline and weekly questionnaires, serology, and physical health assessments, including psychometric tests.</li> </ul>

			<ul style="list-style-type: none"> <li>• Results compared between healthcare workers (HCW) with positive nasopharyngeal seropositive HCW without positive NPS (presumable a-/pauci-symptomatic infectious controls</li> <li>• Of 3,334 HCW, 556 (17%) had a positive NPS and 228 (7%) were only seropositive nasopharyngeal swabs (NPS) more frequently reported <math>\geq 1</math> symptom compared to controls</li> <li>• Seropositive HCW without positive NPS are only mildly affected by long-COVID. E common, even in non-infected HCW.</li> <li>• Physical activity might be protective against neurocognitive impairment/fatigue s 19.</li> </ul>
28.10.2021	<a href="#">Six-month sequelae of post-vaccination SARS-CoV-2 infection: a retrospective cohort study of 10,024 breakthrough infections</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• Retrospective cohort study and time-to-event analysis, comparing COVID-19 outcomes in individuals who received a COVID-19 vaccine <math>\geq 2</math> weeks before SARS-CoV-2 infection to unvaccinated controls, unvaccinated for COVID-19 but who had received an influenza vaccine.</li> <li>• Receiving at least one COVID-19 vaccine dose was associated with a significantly lower risk of COVID-19 failure, ICU admission, intubation/ventilation, hypoxaemia, oxygen requirement, hospitalization, thromboembolism, seizures, psychotic disorder, and hair loss</li> <li>• COVID-19 vaccination is associated with lower risk of several, but not all, COVID-19 breakthrough SARS-CoV-2 infection. Benefits of vaccination were clear in younger and older over-60s.</li> </ul>

[Back to menu](#)

### Epidemiology and clinical – risk factors

Publication Date	Title/URL	Journal / Article type	Digest
29.10.2021	<a href="#">Immunogenicity Rates After SARS-CoV-2 Vaccination in People With End-stage Kidney Disease: A Systematic Review and Meta-analysis</a>	JAMA Netw Open / Systematic review	<ul style="list-style-type: none"> <li>• Systematic review of immunogenicity rates in people with end-stage kidney disease receiving COVID-19 vaccines. Search until 30.07.2021; 32 studies included.</li> <li>• Overall immunogenicity rate of dialysis group was 86%. Prevalence of diabetes had a significant association with immunogenicity rate.</li> <li>• Findings suggest the immunogenicity rate among patients receiving dialysis was 89% after the second dose.</li> <li>• Diabetes may be risk factor for nonresponse in dialysis population. Patients received lower antibody response rate, particularly after first dose.</li> </ul>
11.10.2021	<a href="#">Does prior exposure to immune checkpoint inhibitors treatment affect incidence and mortality of COVID-19 among the cancer patients: The systematic review and meta-analysis</a>	Int Immunopharmacol / Systematic Review	<ul style="list-style-type: none"> <li>• Systematic Review of immune checkpoint inhibitors (ICIs) treatment among cancer patients from 2010 to 2021. 23 studies involving 117,735 cancer patients (19 retrospective / 4 prospective)</li> <li>• No significant difference on incidence and mortality of COVID-19 between prior exposure to ICI and other anti-tumor treatments.</li> <li>• ICIs may reduce infection susceptibility of COVID-19 in metastatic cancer patients.</li> </ul>

23.10.2021	<a href="#">Clinical outcomes in COVID-19 and cirrhosis: a systematic review and meta-analysis of observational studies</a>	BMJ Open Gastroenterol / Systematic review	<ul style="list-style-type: none"> <li>• Systematic Review: effect of cirrhosis on COVID-19 outcomes.</li> <li>• Search until 03.02.2021; 63 studies included (17 case reports, 9 case series, 10 systematic reviews, 22 multicentre cohort studies and 5 registry studies). 16 in meta-analysis.</li> <li>• No evidence of bias.</li> <li>• Pooled crude OR for mortality of 2.48 is comparable to other established significant risk factors such as diabetes, hypertension and cardiovascular disease.</li> <li>• Cirrhosis associated with increased risk of all-cause mortality in COVID-19 infection in cirrhotic patients.</li> </ul>
22.10.2021	<a href="#">Vitamin D insufficiency in COVID-19 and influenza A, and critical illness survivors: a cross-sectional study</a>	BMJ Open / Article	<ul style="list-style-type: none"> <li>• Cross-sectional study: plasma obtained from people hospitalised with COVID-19 (n=93), and survivors of non-selected critical illness prior to the COVID-19 pandemic (n=93).</li> <li>• Vitamin D insufficiency (total 25(OH)D 25-50 nmol/L) and deficiency (&lt;25 nmol/L) were present in COVID-19 (29.3% and 44.4%, respectively), influenza A (47.3% and 37.6%) and critical illness survivors (30.2% and 56.8%).</li> <li>• In COVID-19 and influenza A, total 25(OH)D measured early in illness was lower in those who received invasive mechanical ventilation (IMV) (19.6 vs 31.9 nmol/L and 22.9 vs 31.1 nmol/L).</li> <li>• In COVID-19, biologically active free 25(OH)D correlated with total 25(OH)D and was lower in those who received IMV, but was not associated with selected circulating inflammatory mediators.</li> </ul>
26.10.2021	<a href="#">COVID-19 Infection, Admission and Death Amongst People with Rare Autoimmune Rheumatic Disease in England. Results from the RECORDER Project</a>	Rheumatology / Article	<ul style="list-style-type: none"> <li>• Analysis of health records identified a cohort of 168,680 people with rare autoimmune rheumatic disease (RAIRD) in England, of whom 1874 (1.11%) tested COVID-19 positive. Mortalities were higher in the death certificate occurred in 713 (0.42%) people with RAIRD.</li> <li>• Compared to the general population, the age standardised infection rate was 1.5 times higher. The age/sex standardised mortality rate for COVID-19 related death was 2.41 times higher in RAIRD. These increases were seen despite shielding policies.</li> <li>• No evidence of an increase in deaths from other causes in the RAIRD population.</li> <li>• Preprint previously included.</li> </ul>

[Back to menu](#)

#### Epidemiology and clinical – other

Publication Date	Title/URL	Journal / Article type	Digest
23.09.2021	<a href="#">Bloodstream Infections in Hospitalized Patients with COVID-19: A Systematic Review and Meta-Analysis</a>	Microorganisms / Systematic review	<ul style="list-style-type: none"> <li>• Systematic review until April 2021 and meta-analysis: estimating pooled occurrence of bloodstream infections (BSIs) among hospitalised COVID-19 patients / mortality of this patient population.</li> <li>• Forty-six studies included; 42,694 patients evaluated.</li> <li>• Main finding: 7% of hospitalised COVID-19 patients may experience a BSI.</li> <li>• Four-times higher occurrence estimated among patients admitted to ICU.</li> </ul>

06.10.2021	<a href="#">A Systematic Review and Meta-Analysis of Inpatient Mortality Associated With Nosocomial and Community COVID-19 Exposes the Vulnerability of Immunosuppressed Adults</a>	Front Immunol / Systematic review	<ul style="list-style-type: none"> <li>• Systematic review, 1/1/2020 to 9/2/2021: 21 studies describing 8,251 COVID-19 countries during first wave (1513 probable or definite nosocomial; 6738 community)</li> <li>• Observational case series, cohort studies included; single case studies excluded.</li> <li>• Main finding: risk of mortality x1.3 higher in nosocomial patients across all studies acquired (driven by individuals with malignancy / who have undergone transplants)</li> <li>• Similar rates of critical care admission between groups.</li> <li>• Immunosuppressed patients: death in hospital twice as likely with nosocomial vs community infection.</li> <li>• Preprint previously included.</li> </ul>
27.10.2021	<a href="#">COVID-19 Schools Infection Survey technical article estimating pupils testing positive for antibodies, England: November 2020 to July 2021</a>	Office for National Statistics / COVID-19 Schools Infection Survey	<ul style="list-style-type: none"> <li>• Calculating the proportion of pupils that “ever tested” positive for antibodies relative to the proportion previously infected with COVID-19 in the local authorities sampled, Round 6 tests in the Schools Infection Survey (SIS).</li> <li>• An estimated 15.30% of primary pupils and 17.29% of secondary pupils in the local authorities had at least one test that recorded antibody levels above the limit of detection.</li> </ul>
14.09.2021	<a href="#">Multinational Observational Cohort Study of COVID-19–Associated Pulmonary Aspergillosis</a>	Emerg Infect Dis / Article	<ul style="list-style-type: none"> <li>• Observational study of 823 ICU-hospitalised COVID-19 patients in two cohorts (North America and Europe) found 10%–15% incidence of coronavirus disease–associated pulmonary aspergillosis. Mortality rates were 43%–52%</li> <li>• CAPA seems to develop later after ICU admission than influenza-associated pulmonary aspergillosis</li> <li>• Chronic obstructive pulmonary disease, HIV/AIDS, and use of immunosuppressants and corticosteroids before ICU admission were associated with CAPA.</li> </ul>
13.10.2021	<a href="#">Serum Neurofilament Light is elevated in COVID-19 Positive Adults in the ICU and is associated with Co-Morbid Cardiovascular Disease, Neurological Complications, and Acuity of Illness</a>	Cardiol Cardiovasc Med / Article	<ul style="list-style-type: none"> <li>• Observational study of 100 ICU patients in Arizona, USA (April to August 2020): 88 COVID-positive (COVID-pos), 11 negative (COVID-neg). A healthy control group (n=8) was included</li> <li>• COVID-pos patients had significantly higher mean levels of serum neurofilament light (a measure of neuronal injury) (<math>229.6 \pm 163</math> pg/ml) compared to COVID-neg patients and healthy controls (<math>12.3 \pm 3.1</math> pg/ml).</li> <li>• Levels of Nfl in COVID-pos patients were significantly higher in patients with congestive heart failure, chronic kidney disease and diabetes (<math>n=35</math>, log Nfl <math>1.6 \pm .09</math>), and correlated with higher SOFA scores</li> <li>• Suggests that in severe COVID-19, central neuronal and axonal damage may be due to effects of systemic cardiovascular disease and peripheral inflammation.</li> </ul>

[Back to menu](#)

#### Infection control / non-pharmaceutical interventions

Publication Date	Title/URL	Journal / Article type	Digest
------------------	-----------	------------------------	--------

25.10.2021	<a href="#">Factors affecting adherence to non-pharmaceutical interventions for COVID-19 infections in the first year of the pandemic in the UK</a>	BMJ Open / Article	<ul style="list-style-type: none"> <li>• The COVID-19 Infection Study (CIS) was used from 10.05.2020 to 02.02.2021: a total of 100,138 adults [aged 18–64].</li> <li>• Inability to comply with non-pharmaceutical interventions (NPIs) predicted higher risk of infection in individuals reported not wearing a face covering outside [main effect for inability to wear face covering/masks, OR 0.29; interaction term OR 1.25].</li> <li>• Youngest age groups had significantly higher risk of infection (OR 1.52) as did those aged 65+ (OR 1.04).</li> <li>• Wearing a face covering outside was a significant predictor of lower chance of infection in December 2020, when a stricter second lockdown was implemented (OR 0.44).</li> </ul>
26.10.2021	<a href="#">Network analysis of England single parent household COVID-19 control policy impact; a proof-of-concept study</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• Network modelling study investigated two policy approaches whereby children from single parent households (SPHs) could (i) move between parental homes and (ii) SPH support bubble households were also permitted, enabling larger within-household networks</li> <li>• Support bubbles between SPHs were found to have little impact on COVID-19 outbreak size. If one or more are discordant-parentage single parent households (DSPHs), the cumulative risk of forming bubbles with SPHs or DSPHs likely speeds up the formation of giant components and large scale transmission would occur</li> </ul>

[Back to menu](#)

### Transmission

Publication Date	Title/URL	Journal / Article type	Digest
20.10.2021	<a href="#">Airborne transmission of SARS-CoV-2 over distances greater than two metres: a rapid systematic review</a>	medRxiv (non-peer reviewed) / Systematic review	<ul style="list-style-type: none"> <li>• Systematic review and narrative synthesis including 15 publications; observational studies between 27.07.2020-21.04.2021 and existing relevant systematic reviews of studies published between 01.01.2020-27.07.2020</li> <li>• Study found evidence of long-distance airborne transmission of SARS-CoV-2 in indoor settings and identified factors such as inadequate ventilation and the use of recirculating air conditioning contributed to this transmission in all included studies.</li> </ul>
28.10.2021	<a href="#">Community transmission and viral load kinetics of the SARS-CoV-2 delta (B.1.617.2) variant in vaccinated and unvaccinated individuals in the UK: a prospective, longitudinal, cohort study</a>	Lancet / Article	<ul style="list-style-type: none"> <li>• Cohort study of 602 community contacts (household and non-household) and 47 index cases</li> <li>• Secondary attack rate (SAR) in contacts exposed to delta variant was 25% for fully vaccinated and 38% in unvaccinated individuals.</li> <li>• SAR among household contacts exposed to fully vaccinated index cases was similar to those exposed to unvaccinated index cases (25% for vaccinated vs 23% for unvaccinated)</li> <li>• 12 (39%) of 31 infections in fully vaccinated household contacts arose from fully vaccinated epidemiologically linked index cases.</li> <li>• Peak viral load did not differ by vaccination status or variant type, but increased with age (difference of 0.39 in peak log<sub>10</sub> viral load per mL between those aged 10 years and those aged 60 years)</li> </ul>

		<ul style="list-style-type: none"> <li>• Fully vaccinated individuals with delta infection had faster mean rate of viral load decline (copies per mL per day) than unvaccinated individuals with pre-alpha (0.69), alpha (0.44) or delta variant infections.</li> <li>• Within individuals, faster viral load growth correlated with higher peak viral load and a slower decline (-0.44).</li> <li>• Associated comment: <a href="https://www.thelancet.com/pb-assets/Lancet/pdfs/s1473">https://www.thelancet.com/pb-assets/Lancet/pdfs/s1473</a></li> </ul>
--	--	---

[Back to menu](#)

### Treatment

Publication Date	Title/URL	Journal / Article type	Digest
22.10.2021	<a href="#">Antibiotics for the treatment of COVID-19</a>	Cochrane Database Syst Rev / Systematic Review	<ul style="list-style-type: none"> <li>• Systematic review of randomised controlled trials (RCTs) until 14.06.2021: 11 studies with 11,100 participants investigating antibiotics compared to placebo, standard of care alone or no treatment.</li> <li>• Hospitalised COVID-19 patients: risk of death not reduced by treatment with azithromycin.</li> <li>• Inpatients with moderate and severe disease: probably no benefit from azithromycin.</li> <li>• Outpatients: azithromycin may have no beneficial effect.</li> <li>• No evidence from RCTs available for other antibiotics.</li> <li>• Antibiotics should not be used for antiviral / anti-inflammatory treatment of COVID-19 in the absence of designed RCTs.</li> </ul>
27.10.2021	<a href="#">Early Treatment for Covid-19 with SARS-CoV-2 Neutralizing Antibody Sotrovimab</a>	N Engl J Med / Article	<ul style="list-style-type: none"> <li>• Ongoing, multicentre, phase 3 trial: 583 non-hospitalised symptomatic Covid-19 patients (median symptom onset) with <math>\geq 1</math> risk factor were randomised 1:1: single infusion of sotrovimab vs placebo.</li> <li>• 3 sotrovimab patients (1%) vs. 21 placebo (7%) had disease progression leading to hospitalisation or death.</li> <li>• Among high-risk patients with mild-to-moderate Covid-19, sotrovimab (a pan-sarbecovirus antibody) reduced the risk of disease progression.</li> </ul>
26.10.2021	<a href="#">Mesenchymal stem cell treatment improves outcome of COVID-19 patients via multiple immunomodulatory mechanisms</a>	Cell Res / Article	<ul style="list-style-type: none"> <li>• Phase 2 trial included 58 COVID-19 patients randomised to treatment with mesenchymal stem cells (MSCs) or placebo (n=29 patients per group) .</li> <li>• MSC group exhibited shorter hospital stay, less time required for symptoms remission and fewer adverse events than placebo.</li> <li>• Based on chest images, severe and critical patients treated with MSCs showed improvement in lung aeration by day 21.</li> <li>• MSC infusion reduced levels of C-reactive protein, proinflammatory cytokines, and neutrophil extracellular traps (NETs) and promoted maintenance of SARS-CoV-2-specific antibodies.</li> <li>• RNA sequencing identified a novel subpopulation of VNN2+ HSPC-like cells expressed in the lungs that were mobilised following MSC infusion.</li> <li>• Genes encoding chemotaxis factors - CX3CR1 and L-selectin - were upregulated in MSC-treated patients.</li> </ul>

27.10.2021	<a href="#">Effect of early treatment with fluvoxamine on risk of emergency care and hospitalisation among patients with COVID-19: the TOGETHER randomised, platform clinical trial</a>	Lancet Global Health / Article	<ul style="list-style-type: none"> <li>• Brazilian randomised controlled trial of high-risk, symptomatic adult outpatients with COVID-19.</li> <li>• Assigned 1:1: fluvoxamine, 100 mg twice daily for 10 days (741 patients) or placebo.</li> <li>• Treatment with fluvoxamine reduced the need for hospitalisation defined as reattendance of emergency setting or transfer to a tertiary hospital.</li> <li>• Associated comment: <a href="https://doi.org/10.1016/S2214-109X(21)00501-5">https://doi.org/10.1016/S2214-109X(21)00501-5</a></li> </ul>
------------	---	--------------------------------	---

[Back to menu](#)

## Modelling

Publication Date	Title/URL	Journal / Article type	Digest
23.10.2021	<a href="#">Methods for modelling excess mortality across England during the COVID-19 pandemic</a>	Stat Methods Med Res / Research article	<ul style="list-style-type: none"> <li>• Authors describe and differentiate the methods to help clarify the different measures of mortality published during the COVID-19 pandemic in England.</li> <li>• Model estimates are strikingly similar during first wave; larger differences are observed in subsequent waves.</li> <li>• Data and methodologies applied to five key measures are detailed. Results are discussed in the context of policy used.</li> </ul>
27.10.2021	<a href="#">Non-pharmaceutical interventions, vaccination, and the SARS-CoV-2 delta variant in England: a mathematical modelling study</a>	Lancet / Article	<ul style="list-style-type: none"> <li>• UK modelling study to assess UK Government's four-step process to easing lockdown in England.</li> <li>• With B.1.617.2 [Delta], fully lifting NPIs on 21.06.2021 might have led to 3900 per day hospital admissions. Delaying until 19.07.2021 reduced this threefold.</li> <li>• Phased lifting of NPIs, coordinated with vaccine roll-out, largely successfully kept hospital deaths at low levels since March, 2021.</li> <li>• High transmissibility of delta, imperfect vaccine effectiveness, future increases in cases likely lead to a substantial wave of transmission in the autumn.</li> <li>• Vaccination alone in absence of NPIs may be insufficient to control delta, even with high coverage.</li> </ul>
23.10.2021	<a href="#">Generation time of the Alpha and Delta SARS-CoV-2 variants</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• Analysis of transmission data from a UKHSA household study. The generation times of the Alpha and Delta variants were estimated by fitting a mathematical transmission model to the data.</li> <li>• The mean intrinsic generation time was 4.6 days for the Delta variant and 5.5 days for the Alpha variant within uncertainty ranges.</li> <li>• The realised mean household generation time for Delta and Alpha was 3.2 days and 4.1 days respectively. The higher transmissibility of the Delta variant led to faster susceptible depletion in households due to the reduced intrinsic generation time.</li> </ul>

			<ul style="list-style-type: none"> <li>• Delta variant transmits more quickly than previously circulating variants, with implications for interventions such as contact tracing, testing and isolation. Epidemiological models should be updated accordingly.</li> </ul>
29.10.2021	<a href="#">Synergistic interventions to control COVID-19: Mass testing and isolation mitigates reliance on distancing</a>	PLoS Comput Biol / Article	<ul style="list-style-type: none"> <li>• Multi-compartmental SARS-CoV-2 transmission model incorporates preventative interventions (NPIs) and testing/isolation to evaluate their combined effect.</li> <li>• Strategic changes in testing system, including test administration, test delays, and testing frequency, can reduce reliance on preventative NPIs without compromising public health outcomes.</li> <li>• Reducing reliance on NPIs is highly dependent on the ability of a testing program to identify unreported, asymptomatic infections.</li> </ul>
26.10.2021	<a href="#">Coronavirus seasonality, respiratory infections and weather</a>	BMC Infect Dis / Research article	<ul style="list-style-type: none"> <li>• Analysis of seasonal distribution of 985,524 viral infections in England and Wales showed that coronavirus infections had similar seasonal distribution to influenza A and bocavirus between weeks 2 to 8.</li> <li>• 90% of infections occurred where either: i) daily mean ambient temperatures were below 10 °C; ii) average global radiation exceeded 500 kJ/m<sup>2</sup>/h; iii) sunshine was less than 5 h per day; or iv) relative humidity was above 80%.</li> <li>• Coronavirus infections significantly more common where either: i) daily average global radiation under 300 kJ/m<sup>2</sup>/h (OR 4.3); ii) average relative humidity was over 84% (OR 1.9); iii) daily temperature was below 10 °C (OR 6.7); or iv) where sunshine was below 4 h (OR 2.1).</li> <li>• Seasonal coronavirus infections in children &lt;3 years old were more frequent at the start of the epidemic than at the end; suggests the susceptible child population may be imported.</li> </ul>

[Back to menu](#)

#### Guidance and consensus statements

Publication Date	Title/URL	Journal / Article type
28.10.2021	<a href="#">COVID-19 vaccination in patients with multiple myeloma: a consensus of the European Myeloma Network</a>	Lancet Haematol / Review

[Back to menu](#)

#### Overviews, comments and editorials

Publication Date	Title/URL	Journal / Article type
22.10.2021	<a href="#">T cells step up after SARS-CoV-2 vaccination with B cell depletion</a>	Nat Rev Neurol / News & Views

19.10.2021	<a href="#">The immunology of asymptomatic SARS-CoV-2 infection: what are the key questions?</a>	Nat Rev Immunol / Comment
28.10.2021	<a href="#">The intersection of COVID-19 and autoimmunity</a>	J Clin Invest / Review
21.10.2021	<a href="#">Does infection with or vaccination against SARS-CoV-2 lead to lasting immunity?</a>	Lancet Respir Med / Personal View
27.10.2021	<a href="#">Covid-19: Just a third of blood cancer patients had antibodies against delta variant after two vaccine doses, study finds</a>	BMJ / News
21.10.2021	<a href="#">COVID-19 interventions in children: a balancing act</a>	Arch Dis Child / Viewpoint
01.10.2021	<a href="#">Uncertainty around the Long-Term Implications of COVID-19</a>	Pathogens / Perspective
22.10.2021	<a href="#">Cardiac involvement in the long-term implications of COVID-19</a>	Nat Rev Cardiol / Perspectives
27.10.2021	<a href="#">Is COVID-19 less severe in CML patients than in those with other haematological cancers?</a>	Br J Haematol / Commentary
29.10.2021	<a href="#">How to capture the individual and societal impacts of syndemics: the lived experience of COVID-19</a>	BMJ Glob Health / Commentary
29.09.2021	<a href="#">Complexities in Case Definition of SARS-CoV-2 Reinfection: Clinical Evidence and Implications in COVID-19 Surveillance and Diagnosis</a>	Pathogens / Review

[Back to menu](#)



**UK Health  
Security  
Agency**

**COVID-19 Literature Digest Team**

Public Health Advice, Guidance and Expertise (PHAGE)

UK Health Security Agency

[COVID.LitDigest@phe.gov.uk](mailto:COVID.LitDigest@phe.gov.uk)

A selection of previous digests [can be found here](#)

<https://www.gov.uk/UKHSA> Follow us on Twitter [@UKHSA](#)



For our published rapid COVID-19 evidence reviews visit our page:

<https://ukhsalibrary.koha-ptfs.co.uk/covid19rapidreviews/>