



UK Health
Security
Agency

COVID-19 Literature Digest – 12/11/2021

Dear all,

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

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 The reports include both preprints, which should be treated with caution as they are NOT peer-reviewed and may be subject to change, and also research that has been subject to peer review and wider scrutiny.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

To join our email distribution list 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Report for 12.11.2021 (please note that papers that have **NOT been peer-reviewed** are highlighted in red).

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Serology and immunology

Publication Date	Title/URL	Journal / Article type	Digest
05.11.2021	Waning of SARS-CoV-2 antibodies targeting the Spike protein in individuals post second dose of ChAdOx1 and BNT162b2 COVID-19 vaccines and risk of breakthrough infections: analysis of the Virus Watch community cohort	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none">• Authors compared anti-S levels after BNT162b2 [Pfizer] or ChAdOx1 [AstraZeneca] vaccination using time since second dose of vaccination, age, sex and clinical vulnerability to investigate antibody waning.• 24049 samples from 8858 individuals (5549 who received a second dose of ChAdOx1 and 3205 BNT162b2) who remained anti-N negative were included in the analysis of anti-S waning over time.• Anti-S levels substantially higher following 2nd dose BNT162b2 compared to ChAdOx1.• Anti-S levels are an important correlate of protection as demonstrated by those with anti-S levels < 500U/ml following vaccination being at significantly greater risk of subsequent infection.
04.11.2021	Correlation of SARS-CoV-2-breakthrough infections to time-from-vaccine	Nat Commun / Article	<ul style="list-style-type: none">• Analysis of data from a large health service in Israel (n= 1,352,444 participants) between 1 June and 27 July 2021 found a 1.51-fold increased risk for breakthrough COVID-19 infection for early vaccinees compared to those vaccinated later; this was similar across all ages groups.• The increased risk reached 2.26- fold when comparing those who were vaccinated in January 2021 to those vaccinated in April 2021.
10.11.2021	Pre-existing polymerase-specific T cells expand in abortive seronegative SARS-CoV-2	Nature / Article	<ul style="list-style-type: none">• Authors measured SARS-CoV-2-reactive T-cells in intensively monitored seronegative healthcare workers (SN-HCW).• SN-HCW had stronger, more multi-specific memory T-cells than an unexposed pre-pandemic cohort, and more frequently directed against the replication transcription complex (RTC) than the structural protein-dominated responses seen post-detectable infection.• SN-HCW with the strongest RTC-specific T-cells had an increase in IFI27, suggesting abortive infection.

			<ul style="list-style-type: none"> • RNA-polymerase within RTC was the largest region of high sequence conservation across human seasonal coronaviruses (HCoV) and SARS-CoV-2 clades. • RNA-polymerase was preferentially targeted (amongst regions tested) by T-cells from pre-pandemic cohorts and SN-HCW. • RTC epitope-specific T-cells cross-recognising HCoV variants were identified in SN-HCW. • Enriched pre-existing RNA-polymerase-specific T-cells expanded in vivo to preferentially accumulate in the memory response after putative abortive compared to overt SARS-CoV-2 infection.
02.11.2021	Anti-membrane and anti-spike antibodies are long-lasting and together discriminate between past COVID-19 infection and vaccination	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Authors demonstrate that anti-membrane IgG is a sensitive and specific marker of past COVID-19 infection and persists at least one year. • Anti-receptor binding domain (RBD) Ig is a long-lasting, sensitive, and specific marker of past infection and vaccination, while anti-nucleocapsid IgG lacks specificity and quickly declines after COVID-19. • A combination of anti-membrane and anti-RBD antibodies accurately differentiates between distant COVID-19 infection, vaccination, and naive states.
05.11.2021	Antibody Titers Before and After a Third Dose of the SARS-CoV-2 BNT162b2 Vaccine in Adults Aged ≥60 Years	Jama / Research letter	<ul style="list-style-type: none"> • Serological study of 97 adults aged ≥60 years found that a third BNT162b2 (Pfizer-BioNTech) dose was associated with significantly increased IgG titers after 10-19 days (from a median of 440 AU/mL to 25,468 AU/mL), with no major adverse events
08.11.2021	COVID-19 convalescents exhibit deficient humoral and T cell responses to variant of concern Spike antigens at 12 month post-infection	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Australian study assessing immune memory to primary infection and immunity to VoC at 12 months after mild-COVID-19 / in absence of viral re-exposure or vaccination. • Convalescents (n=43) and healthy SARS-CoV-2-seronegative controls (n=15-40). • >90% of convalescents remained seropositive for RBD-IgG; 88.9% had circulating RBD-specific memory B cells. • Despite this, only 51.2% had serum neutralising activity against homologous live-SARS-CoV-2 virus; decreasing to 44.2% against live B.1.1.7 [Alpha], 4.6% against B.1.351 [Beta], 11.6% against P.1 [Gamma] and 16.2%, against B.1.617.2 [Delta] variants of concern (VoC). • Immunity retained in significant proportion of mild COVID-19 convalescents, but changes in amino acid sequence of Spike antigen in current VoC result in virus evasion of neutralising antibodies / functional T cell responses.

05.11.2021	Humoral immune response to Covid-19 vaccination in diabetes: age-dependent but independent of type of diabetes and glycaemic control-the prospective COVAC-DM cohort study	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Prospective, multicentre cohort study analysed people with type 1 (n=75) and type 2 (n=75) diabetes, well or insufficiently controlled, and healthy controls (n=86). • After first vaccination, only 52.7% in type 1/ 48.0% in type 2 diabetes groups showed antibody levels above cut-off for positivity. • Antibody levels after second vaccination were similar in people with type1, type 2 diabetes and healthy controls if adjusted for age, sex and multiple testing (p>0.05). • Age and renal function were significantly associated with antibody response.
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Vaccines

Publication Date	Title/URL	Journal / Article type	Digest
06.11.2021	Safety Assessment of BNT162b2 Vaccine in Adolescents Aged 12-15 Years	medRxiv (non-peer reviewed) / Rapid Review	<ul style="list-style-type: none"> • A rapid systematic review to determine safety profile of BNT162b2 (Pfizer) vaccine 12-15 year olds (search up to 15/08/2021) included 4 studies (64,969 subjects who received at least one dose of vaccine) • Major events in clinical phase and post-authorisation observational studies were pain at injection site, fatigue, headache, chills, diarrhoea and joint pain • High adherence rate (>97% participants received second dose) in clinical phase 3, and significantly lower incident of major local and systemic events in post-authorisation observational study indicates that Pfizer vaccine has highly favourable safety profile in adolescents aged 12-15 years • Limitations: limited studies and only short-term safety data available
09.11.2021	Evaluation of the BNT162b2 Covid-19 Vaccine in Children 5 to 11 Years of Age	N Engl J Med / Article	<ul style="list-style-type: none"> • Ongoing phase 2/3 trial: children were randomly assigned to receive 10 µg of BNT162b2 (Pfizer-BioNTech) vaccine (n=1517) or placebo (n=751) • One month after second dose, geometric mean ratio of SARS-CoV-2 neutralising titers in 5-to-11-year-olds to those in 16-to-25-year-olds was 1.04, a ratio meeting the prespecified immunogenicity success criterion • Covid-19 with onset 7+ days after second dose was reported in three BNT162b2 recipients and 16 placebo recipients (vaccine efficacy, 90.7%). • Associated comment: https://www.bmj.com/content/375/bmj.n2746

08.11.2021	Immunogenicity of COVID-19 vaccines in patients with haematological malignancy: A systematic review and meta-analysis	medRxiv (non-peer reviewed) / Systematic Review	<ul style="list-style-type: none"> • Systematic review and meta-analysis of over 7000 patients with haematological malignancy (search up to 31.08.2021). • 44 studies (16 mixed group, 28 disease specific) included. 23 (52%) evaluated as good or fair quality with low risk of bias, 21 rated poor quality. • Rate of seropositivity was 61-67% following 2 doses and 37-51% following 1 dose of COVID-19 vaccination. • Lowest seropositivity rate was 51% in chronic lymphocytic leukaemia patients; highest in patients with acute leukaemia (93%). • Following 1 dose, nAb and cellular response rates were 18-63% and 33-86% respectively. • Active treatment, ongoing or recent treatment with targeted and CD-20 monoclonal antibody therapies within 12 months associated with poor vaccine immune responses.
05.11.2021	SARS-CoV-2 vaccine uptake in a multi-ethnic UK healthcare workforce: A cross-sectional study	PLoS Med / Article	<ul style="list-style-type: none"> • Cross-sectional study of healthcare workers (HCWs; n=19,044) at University Hospitals of Leicester NHS Trust. • Factors negatively associated with vaccine uptake: younger age, female sex, increased deprivation, pregnancy, and non-White ethnicity (Black: adjusted odds ratio [aOR] 0.30; South Asian: aOR 0.67). • Limitations include single centre, and lack of data on staff vaccinated outside the hospital system or after data collection.
08.11.2021	Describing the population experiencing COVID-19 vaccine breakthrough following second vaccination in England: A cohort study from OpenSAFELY	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Retrospective cohort study using routine clinical data of fully vaccinated individuals in England (10,782,870 individuals as of 30.06.2021). • 16,815 (0.1%) reported a positive test. For every 1000 years of patient follow-up time, corresponding incidence rate was 12.33. • 955 COVID-19 hospital admissions / 145 COVID-19-related deaths. Corresponding incidence rates 0.70 / 0.12 respectively. • Higher rates of hospitalisation and death seen in those in care homes. • Comorbidities with highest breakthrough rates included renal replacement therapy, organ transplant, haematological malignancy, and immunocompromised.
02.11.2021	A RCT of a third dose CoronaVac or BNT162b2 vaccine in adults with two doses of CoronaVac	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • 376 healthy adults (19-77 years old) who had received 2 doses of CoronaVac (Sinovac) with low antibody response were randomly assigned to receive booster of BNT162b2 (Pfizer) or CoronaVac. • One month after third dose, BNT162b2 elicited significantly higher surrogate virus neutralizing test (sVNT), spike receptor binding, spike N terminal domain binding, spike S2 domain binding levels. • Mean results of sVNT against wild type, beta, gamma and delta variants with BNT162b2 booster: 96.83%, 92.29%, 92.51% and 95.33% respectively.

			For CoronaVac boosted group: Wild type: 57.75%; Beta: 38.79 %; Gamma: 32.22%; Delta: 48.87%.
29.10.2021	Effectiveness of a third dose of the BNT162b2 mRNA COVID-19 vaccine for preventing severe outcomes in Israel: an observational study	Lancet / Article	<ul style="list-style-type: none"> • Study of 728,321 individuals receiving a third dose of BNT162b2 (Pfizer-BioNTech) vaccine between 30.07.2020 and 23.09.2021, matched 1:1 to a control group. • Compared with receiving only two doses at least 5 months ago, vaccine effectiveness at least 7 days after receipt of third dose was estimated to be 93% for admission to hospital, 92% for severe disease, and 81% for COVID-19-related death.
10.11.2021	Association between vaccination with the BNT162b2 mRNA COVID-19 vaccine and Bell's palsy: a population-based study	Lancet Reg Health Eur / Article	<ul style="list-style-type: none"> • A total of 132 cases of Bell's palsy were reported among 2,594,990 vaccinees within 21 days of first dose of BNT162b2 (Pfizer-BioNTech), and 152 cases within 30 days the second dose (2,434,674 vaccinees). • Age and sex weighted standardized incidence ratios (SIRs) were 1.36 and 1.16 after first and second vaccine dose, respectively. • SIRs tended to be higher in older age groups after either dose; estimates were more pronounced in older females after the first vaccine dose (SIR=1.71 at age 45-64, and 2.51 at age ≥65 years). • The highest attributable risk (AR) was 4.46 per 100,000 vaccinees detected in females aged ≥65 years. • In patients with previous history of Bell's palsy, only 4 cases of Bell's palsy were reported in 7,567 vaccinees and 10 cases in 7,045 vaccinees after first and second dose, respectively (age and sex weighted SIRs 1.15 and 2.15), respectively.
10.11.2021	Differences in COVID-19 vaccination coverage by occupation in England: a national linked data study	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Nationwide population-level data used to calculate proportion of double vaccinated (assessed on 31.08.2021) adults aged 40-64 by detailed occupational categories. • Study population: 14,298,147 adults with vaccination rates differing markedly by occupation • Higher in administrative / secretarial occupations (90.8%); professional occupations (90.7%); managers, directors, senior officials (90.6%). • Lowest (83.1%) in people working in elementary occupations. • Vaccination rates lower (i) in occupations which cannot be done from home (ii) in many occupations involving contact with the public or with vulnerable people.
11.11.2021	The SARS-CoV-2 Lambda variant and its neutralisation efficiency following vaccination with Comirnaty, Israel, April to June 2021	Euro Surveill / Rapid Communication	<ul style="list-style-type: none"> • Describes appearance of the Lambda variant (Pango lineage designation C.37) in Israel in April–June 2021 and the neutralising response of sera from 36 naive individuals following two doses of Comirnaty (BNT162b2, BioNTech-Pfizer) vaccine.

- Micro-neutralisation assays following vaccination demonstrated significant (1.6-fold) reduction in neutralising titres compared with wild type virus, suggesting increased susceptibility of vaccinated individuals to infection.

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Diagnostics and genomics

Publication Date	Title/URL	Journal / Article type	Digest
09.11.2021	Structure-based evidence for the enhanced transmissibility of the dominant SARS-CoV-2 B.1.1.7 variant (Alpha)	Cell Discov / Correspondence	<ul style="list-style-type: none"> • Cryo-electron microscopy single-particle analysis found that mutations in the B.1.1.7 (Alpha) S protein can significantly enhance its viral fusion activity and its infectivity. • The structure of the B.1.1.7 S-trimer/hACE2 complex revealed multiple structural effects of mutations on the S protein, such as enhancing ACE2 affinity, enhancing prefusion state stability, increasing propensity for the RBD “up” conformation, and promoting furin cleavage activity.
05.11.2021	Surveillance of COVID-19 in a Vaccinated Population: A Rapid Literature Review	medRxiv (non-peer reviewed) / Rapid Review	<ul style="list-style-type: none"> • A rapid literature review to identify evidence and guidance on surveillance approaches to monitor SARS-Cov-2 in a vaccinated population (search up to 13/06/2021) included 33 studies and 26 international guidance documents • Population PCR screening, supplemented by rapid antigen tests, was the most frequently used surveillance method and the most commonly recommended across jurisdictions • Other overarching surveillance methods included genomic screening, serosurveillance, wastewater surveillance, health record screening and syndromic surveillance; most recent guidance on COVID-19 surveillance was not specific to vaccinated individuals • Limitations: unable to carry-out exhaustive search or to address quality of evidence reported in guidance
10.11.2021	Prospective Study of the Performance of Parent-Collected Nasal and Saliva Swab Samples, Compared with Nurse-Collected Swab Samples, for the Molecular Detection of Respiratory Microorganisms	Microbiol Spectr / Article	<ul style="list-style-type: none"> • Prospective observational study: parent-collected (PC) and nurse-collected (NC) paired nasal and saliva swab samples were collected from 91 and 92 children, respectively. • Performance and interrater agreement (Cohen’s κ) of PC versus NC nasal swab samples for viruses combined showed sensitivity of 91.6% and κ of 0.84, respectively; the respective values for bacteria combined were 91.4% and κ of 0.85.

			<ul style="list-style-type: none"> • In saliva samples, viral and bacterial sensitivities were lower (69.0% and 78.1%), as were κ values (0.64 and 0.70). • At-home PC nasal swab samples performed comparably to NC swab samples, whereas PC saliva swab samples lacked sensitivity for detection of respiratory microbes.
08.11.2021	Symptoms and SARS-CoV-2 positivity in the general population in the UK	Clin Infect Dis / Accepted manuscript	<ul style="list-style-type: none"> • Analysed COVID-19 Infection Survey from April 2020 to August 2021, comprising 27,869 SARS-CoV-2 PCR-positive episodes (n=27,692 participants) and 3,806,692 test-negative visits (n=457,215 participants) • Sensitivity of symptom-based detection increased from 74% using 'classic' symptoms (cough, fever, loss of taste/smell), to 81% adding fatigue/weakness, and 90% including all eight additional symptoms. However, this increased 'tests per case' from 4.6 to 5.3 to 8.7.
08.11.2021	Regional and temporal variations affect the accuracy of variant-specific SARS-CoV-2 PCR assays	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Authors show how to design variant-specific PCR assays with high sensitivity and specificity across different geographical regions by incorporating sequences deposited in the GISAID database. • Several previously developed PCR assays have decreased accuracy outside their study areas. • PRIMES algorithm enables the design of reliable PCR assays, as demonstrated in experiments tracking dominant SARS-CoV-2 variants in local sewage samples.
05.11.2021	Simultaneous identification of viruses and SARS-CoV-2 variants with programmable DNA nanobait	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Authors demonstrate simultaneous identification of nucleic acids from multiple viruses by combining DNA nanotechnology and nanopore sensing. • An easily programmable nanobait discriminated SARS-CoV-2 WT RNA from variant RNA, including three variants of concern. • Oropharyngeal swab samples from negative and positive SARS-CoV-2 patients were discriminated using programmable target cleavage without pre-amplification. • A new scalable approach for diagnostics of multiple respiratory viruses in a single assay.

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Epidemiology and clinical - children and pregnancy

Publication Date	Title/URL	Journal / Article type	Digest
11.11.2021	Deaths in children and young people in England after SARS-CoV-2 infection during the first pandemic year	Nat Med / Article	<ul style="list-style-type: none"> • Analysis of health data in England found that during the first pandemic year 25 children and young people (CYP; <18 years) died of SARS-CoV-2 infection (22 from acute infection, 3 from PIMS-TS), equating to a mortality rate of 2 per million for the 12,023,568 CYP in England. • Another 36 children were SARS-Cov-2 positive at time of death but probably died from other causes. • While overall risks were still low, CYP who died were more likely to be >10 years, of Asian and Black ethnic backgrounds, and with co-morbidities. • Data suggests SARS-CoV-2 is very rarely fatal in CYP: 99-995% of CYP with a positive test survived. • These data are specific to the time period studied and before advent of the Delta variant. • Preprint previously included.

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Epidemiology and clinical - long-term complications / sequelae

Publication Date	Title/URL	Journal / Article type	Digest
09.11.2021	Olfactory recovery following infection with COVID-19: A systematic review	PLoS One / Ssystematic Review	<ul style="list-style-type: none"> • Systematic review up to March 2021 included 44 studies (assorted observational designs with sample sizes ranging between 7 and 1363 participants). Most were adult patients with mild to moderate COVID-19. • Olfactory recovery was found to occur as early as 7 days, with most patients recovering olfaction within 30 days; few studies included follow-up of 6 months or longer. • Poor olfaction at initial presentation was associated with poor recovery rates; few studies assessed olfactory retraining and steroid therapy. • Limitations include high level of heterogeneity across studies, and the possibility of recall bias in studies using retrospective assessment.
02.11.2021	Visualizing in deceased COVID-19 patients how SARS-CoV-2 attacks the respiratory and olfactory mucosae but spares the olfactory bulb	Cell / Article	<ul style="list-style-type: none"> • Postmortem procedure to sample respiratory and olfactory mucosae and whole olfactory bulbs from 85 COVID-19 and control cases.

			<ul style="list-style-type: none"> • Ciliated cells main target cell type for SARS-CoV-2 in respiratory mucosa; sustentacular cells (non-neuronal) are the main target cell type in olfactory mucosa. • No evidence for infection of olfactory sensory neurons or olfactory bulb parenchyma
04.11.2021	Longitudinal Changes of Cardiac and Aortic Imaging Phenotypes Following COVID-19 in the UK Biobank Cohort	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Second imaging assessment of 1285 UK Biobank volunteers who had an assessment including cardiac magnetic resonance (CMR) pre-pandemic. • 640 cases with evidence of previous SARS-CoV-2 infection matched to controls, with similar cardiac and aortic imaging phenotypes at first imaging assessment. • Changes between CMR imaging measures before and after infection not significantly different from matched control group. • Additional adjustment for comorbidities made no material difference to the results. • Preliminary results do not suggest clinically significant persistent cardiac pathology after generally milder (non-hospitalised) SARS-CoV-2 infection.

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Epidemiology and clinical – risk factors

Publication Date	Title/URL	Journal / Article type	Digest
08.11.2021	COVID-19 and CAR-T cells: current challenges and future directions-a report from the EPICOVIDEHA survey by EHA-IDWP	Blood Adv / Article	<ul style="list-style-type: none"> • Among 459 patients treated with chimeric antigen receptor T cells (CAR-T cells) in 18 European centres: the prevalence of COVID-19 cases was 4.8%; severe infection occurred in 66.7% of patients; 43.3% required admission to ICU; and the COVID-19 mortality was 33%.
08.11.2021	Poor outcome of patients with COVID-19 after CAR T-cell therapy for B-cell malignancies: results of a multicenter study on behalf of the European Society for Blood and Marrow Transplantation (EBMT) Infectious Diseases Working Party and the European Hematology Association (EHA) Lymphoma Group	Leukemia / Letter	<ul style="list-style-type: none"> • Multi-centre survey study of patients with COVID-19 after Chimeric Antigen Receptor T-cell (CAR-T-cell) therapy for hematologic malignancies (n=56) • Results suggest COVID-19 mortality rate of 41%. • In multivariate analysis, older age (10-year-effect, HR 1.39), not being in complete remission at time of COVID-19 diagnosis (HR 2.40) and having metabolic comorbidities (HR 2.75) were associated with higher mortality risk, and better performance status (10 point effect, HR 0.71) with lower mortality risk.

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Epidemiology and clinical – other

Publication Date	Title/URL	Journal / Article type	Digest
07.11.2021	Ethnicity and outcomes in COVID-19 in the United Kingdom: a systematic review and meta-analysis	medRxiv (non-peer reviewed) / Systematic Review	<ul style="list-style-type: none"> • This systematic review and meta-analysis looking at the clinical outcomes of COVID-19 in UK ethnic minorities in comparison with White ethnic group (search up to April 2021) included 14 studies (12 cohort and 2 case-control studies) • Mortality outcome was higher for the Black, Asian, and Mixed and Other (MO) groups, compared to the White group • Odds ratios (OR) of intensive care admission were more than double for all ethnicities; in the adjusted analysis of mechanical ventilation need the ORs were similarly significantly raised • Limitations: a broad ethnic classification was used; mainly UK based studies so results less generalisable
30.10.2021	An exploration of factors characterising unusual spatial clusters of COVID-19 cases in the East Midlands region, UK: a geospatial analysis of ambulance 999 data	Landsc Urban Plan / Article	<ul style="list-style-type: none"> • Authors analysed spatial distribution of >10,000 suspected severe COVID-19 cases using provisional diagnoses by paramedics attending medical emergencies. • In-depth analysis of 13 clusters of severe illness in East Midlands, UK including urban and rural dynamics, physical characteristics of landscapes, socio-economic conditions. • Dynamics of relative vulnerability to severe illness and/or death (VSID) vary depending on wider geographic location. • Vulnerable communities and regions occur in more deprived urban centres as well as more affluent peri-urban and rural areas.

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Infection control / non-pharmaceutical interventions

Publication Date	Title/URL	Journal / Article type	Digest
09.11.2021	The effectiveness of face coverings to reduce transmission of COVID-19 in community settings. A rapid review [Update 2]	UKHSA / Rapid Review	<ul style="list-style-type: none"> • An updated rapid review looking at effectiveness of face coverings when used in the community (search up to 14/09/2021) included 25 studies (2 randomised controlled trials (RCTs) and 23 observational).

			<ul style="list-style-type: none"> • The evidence predominantly suggests that face coverings reduce the spread of COVID-19 in the community, through source control, wearer protection and universal masking. • Results are broadly in line with results of original review, but the addition of RCTs and more individual-level observational studies increases certainty and strengthens evidence for effectiveness of face coverings in reducing transmission in community settings.
04.11.2021	The effect of eye protection on SARS-CoV-2 transmission: a systematic review	Antimicrob Resist Infect Control / Systematic Review	<ul style="list-style-type: none"> • A systematic review looking at the impact of eye protection on transmission of SARS-CoV-2 (search up to 01/06/2021) included 5 observational studies from 4 countries • Four studies showed substantial and statistically significant reductions in COVID-19 infections of health care workers after mandatory eye protection (mainly face shields) was introduced; one case-control study showed an increase which was partly explained by an increase in community transmission • Limitations: studies were non-randomised so the overall risk of bias was high; high heterogeneity precluded any meaningful meta-analysis • Preprint previously included
05.11.2021	The Impact of Returning University Students on COVID-19 Infections in England, 2020.	SSRN (non-peer reviewed) / Article	<ul style="list-style-type: none"> • 53,430 student cases in England between 01.09.2020 - 31.12.2020; 2.7% of all cases (n=1,999,180) in this period. • 39,032 reported attendance at a university during contact tracing; 19,901 resided in student accommodation. • Cases increased rapidly following start of term, driven initially by cases in student accommodation. Over two thirds (72.2% n=14,375) of cases in student accommodation were part of a residential outbreak. • Towns/cities with universities saw a threefold increase in rates amongst 18–23 year olds, compared to non-university towns.
07.11.2021	Ranking the Effectiveness of Non-Pharmaceutical Interventions to Counter COVID-19 in UK Universities with Vaccinated Population	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • UK modelling study: best non-pharmaceutical prevention strategy to maximize on-campus activities while keeping spread under control within universities. • Models staff-to-staff / student-to-student / environment-to-individual infections, student-to-staff cross infections. • Shows significance of mask wearing and social distancing in universities with vaccinated population (with proportions according to UK data). • Quarantining infected students has a higher importance than quarantining staff. • Other measures such as environmental disinfection seems to be less important.

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Transmission

Publication Date	Title/URL	Journal / Article type	Digest
04.11.2021	Aerosol emission from the respiratory tract: an analysis of aerosol generation from oxygen delivery systems	Thorax / Article	<ul style="list-style-type: none">• In healthy volunteers (n = 25), continuous positive airways pressure was associated with less aerosol emission than breathing, speaking or coughing.• High-flow nasal oxygen did not appear to increase aerosol emission from the respiratory tract.• Preprint previously included.

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Treatment

Publication Date	Title/URL	Journal / Article type	Digest
09.11.2021	Effect of Prone Positioning on Clinical Outcomes of Non-Intubated Subjects with COVID-19: A Comparative Systematic Review and Meta-Analysis	Respir Care / Systematic review	<ul style="list-style-type: none">• Systematic review of awake prone positioning (APP) during treatment for COVID-19 includes fourteen studies up to 30 August 2021 (five randomised controlled trials [RCTs] and nine observational studies) involving 3324 subjects (n=1495 receiving APP, n=1829 controls).• There was a significant reduction in the mortality rate in APP group compared to control (RR 0.68) with no significant effect on intubation (RR 0.85) or length of hospital stay (MD -3.09 days).• Subgroup analysis of RCTs found significant reduction in intubation rate (RR 0.83).
06.11.2021	Clinical efficacy and safety of interferon-β-containing regimens in the treatment of patients with COVID-19: a systematic review and meta-analysis of randomized controlled trials	Expert Rev Anti Infect Ther / Systematic Review	<ul style="list-style-type: none">• A meta-analysis comparing the efficacy and safety of interferon-β (IFN-β) for treatment of hospitalised patients with COVID-19 (search up to 17/07/2021) included 8 randomised controlled trials (RCTs)• Findings showed no significant difference in 28-day all-cause mortality rate between the IFN-β and control groups, but IFN-β groups had a lower rate of intensive care unit admissions• INF-β was not associated with an increased risk of any adverse events• Limitations: high heterogeneity between studies; small number of included studies and patients in many RCTs; outcome of study group could be due to both INF-β and other combined anti-viral agents

08.11.2021	New phase 3 analyses show that a single dose of REGEN-COV® (Casirivimab and Imdevimab) provides long-term protection against COVID-19	Regeneron (non-peer reviewed) / Press Release	<ul style="list-style-type: none"> • In a phase 3 trial uninfected participants received a single dose of REGEN-COV (Casirivimab and Imdevimab; n=841) or placebo (n=842). • Compared to placebo, REGEN-COV group experienced an 81.6% reduced risk of developing COVID-19 between months 2-8 (7 REGEN-COV, 38 placebo), maintaining the 81.4% risk reduction previously reported during month one. • During the 8-month assessment: zero participants in REGEN-COV group were hospitalised due to COVID-19, compared to 6 in the placebo group; no deaths due to COVID-19 were reported in either group; no new safety signals were identified for REGEN-COV.
05.11.2021	Pfizer's Novel COVID-19 Oral Antiviral Treatment Candidate Reduced Risk of Hospitalization or Death by 89% in Interim Analysis of Phase 2/3 EPIC-HR Study	Pfizer (non-peer reviewed) / News	<ul style="list-style-type: none"> • Pfizer announced interim analysis of Phase 2/3 EPIC-HR (Evaluation of Protease Inhibition for COVID-19 in High-Risk Patients) randomized, double-blind study of non-hospitalised adult COVID-19 patients, at high risk of progressing to severe illness. • PAXLOVID™ (PF-07321332; ritonavir) was found to reduce the risk of hospitalization or death by 89% compared to placebo in non-hospitalized high-risk adults with COVID-19.
11.12.2021	Intravenous immunoglobulins in patients with COVID-19-associated moderate-to-severe acute respiratory distress syndrome (ICAR): multicentre, double-blind, placebo-controlled, phase 3 trial	Lancet Respir Med / Article	<ul style="list-style-type: none"> • French multicentre, double-blind, placebo-controlled trial (03.04.2020-Oct.2020). • 146 patients who received invasive mechanical ventilation for moderate-to-severe COVID-19-associated acute respiratory distress syndrome (ARDS) were randomly assigned intravenous immunoglobulin (IVIg, 2 g/kg over 4 days; 69 patients) or placebo (77 patients). • No statistical difference in median number of ventilation-free days at day 28 between the IVIG and placebo groups. • IVIG did not improve clinical outcomes at day 28; was associated with increased frequency of serious adverse events, although not significant. • Associated comment: https://doi.org/10.1016/S2213-2600(21)00450-1
08.11.2021	Favipiravir In Adults with Moderate to Severe COVID-19: A Phase 3 Multicentre, Randomized, Double-Blind, Placebo-Controlled Trial	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Double-blind, multicentre, phase 3 trial: 353 moderate to severe COVID-19 patients requiring hospitalisation. • Randomised 1:1 to oral favipiravir (day 1: 1800 mg BID and days 2-10: 800 mg BID) (FPV) plus standard supportive care (SoC) versus placebo plus SoC (placebo). • Primary endpoint was time to resolution of hypoxia: 76% (240/315, 78% in FPV vs. 75% in placebo group) reached resolution of hypoxia on or before day 28. • 'Lower risk' FPV subgroup more likely to achieve shorter time to resolution of hypoxia / hospital discharge / improvement.

- FPV not found to be effective in moderate to severe, hospitalized COVID-19 patients; favourable clinical trends observed in patients with lower NEWS-2 risk when early administration of FPV could be achieved.

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Modelling

Publication Date	Title/URL	Journal / Article type	Digest
08.11.2021	The effect of notification window length on the epidemiological impact of COVID-19 contact tracing mobile applications	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • UK authors use an epidemiological transmission model to consider trade-off between notification window on mobile contact tracing applications (apps) and active app-usage. • Review 5-day and 2-day windows used by England/Wales NHS COVID-19 app before and after 02.08.2021. • Short notification windows more effective at reducing transmission if associated with higher levels of active app usage and adherence to isolation upon notification.
06.11.2021	Increased close proximity airborne transmission of the SARS-CoV-2 Delta variant	Sci Total Environ / Article	<ul style="list-style-type: none"> • Modelling suggests 64% of Delta variant cases will reproduce infection in close proximity contacts versus 29% for wild-type SARS-CoV-2. • Maintaining at least 1.5m separation during conversation drives R(cp) below 1 even in a fully susceptible population. • Room-scale airborne transmission contributes significantly to R(0) for wild-type SARS-CoV-2, highlighting importance of mitigation measures e.g. ventilation.
05.11.2021	Burden of Disease Methods: A Guide to Calculate COVID-19 Disability-Adjusted Life Years	Int J Public Health / Hints and kinks	<ul style="list-style-type: none"> • Paper provides a step-by-step guide to define COVID-19 as a cause of disease burden, which can be used to calculate disability-adjusted life years (DALYs). • Authors recommend not including indirect effects in the COVID-19 disease model, and to make an explicit distinction between COVID-19 as a disease, and the COVID-19 crisis as a risk factor for ill-health.
04.11.2021	The United States COVID-19 Forecast Hub dataset	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • US dataset to establish a standardized and comparable set of short-term forecasts from modelling teams. • Able to develop ensemble models, communicate forecasts to public, create visualizations, compare models, and inform policies regarding COVID-19 mitigation. • Open-source data available from GitHub: https://github.com/reichlab/covid19-forecast-hub

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Overviews, comments and editorials

Publication Date	Title/URL	Journal / Article type
14.09.2021	SARS-CoV-2, COVID-19 and the Ageing Immune System	Nat Aging / Review Article
09.11.2021	Polymutant Spike Points Way Toward More Durable COVID-19 Vaccine	Jama / Comment
29.10.2021	What is the vaccine effect on reducing transmission in the context of the SARS-CoV-2 delta variant?	Lancet Infect Dis / Comment
05.11.2021	Covid-19 and ethnicity: we must seek to understand the drivers of higher transmission	Bmj / Opinion
08.11.2021	Monitoring key epidemiological parameters of SARS-CoV-2 transmission	Nat Med / Correspondence
10.11.2021	Covid-19: Pandemic reduced life expectancy in most developed countries, study finds	BMJ / News
08.11.2021	Should we look beyond the interferon signature in chilblain-like lesions associated with COVID-19?	Br J Dermatol / Commentary
29.10.2021	The course of action for effective anti-cytokine treatment in COVID-19	Lancet Respir Med

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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

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