

COVID-19 Literature Digest – 05/02/2021

Based on feedback received from our January survey, and our current staffing capacity, we have reduced the number of digests to one per week. This is the first of our new weekly digests.

The following changes to the Digest are being trialled until mid-March:

- the frequency of the Digest will be reduced from three days a week to once a week (Friday)
- the frequency of the Guest Editorials will be reduced from once a week to once every two weeks – so you will receive the next editorial on Friday 12th February

Feedback welcome.

Dear all,

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

PHE'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 The reports include both preprints, which should be treated with caution as they are NOT peer-reviewed and may be subject to change, and also research that has been subject to peer review and wider scrutiny.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 PHE. 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 PHE Behavioural Sciences Weekly Report.

Best wishes,

Emma Farrow, James Robinson

On behalf of the PHE COVID-19 Literature Digest Team

Report for 05.02.2021 (please note that papers that have **NOT been peer-reviewed** are highlighted in red).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
03.02.2021	Impact of the B.1.1.7 variant on neutralizing monoclonal antibodies recognizing diverse epitopes on SARS-CoV-2 Spike	bioRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none">• From >100 Spike-reactive monoclonal antibodies from SARS-CoV-2 infected individuals, ≈45% showed neutralising activity of which ≈20% were N-terminal domain (NTD)-specific.• NTD-specific mAbs formed two groups: group one was highly potent against infectious virus; group two was less potent and displayed glycan-dependant neutralisation activity.• Mutations present in B.1.1.7 Spike frequently conferred resistance to neutralisation by the NTD-specific neutralizing antibodies.
02.02.2021	Antibodies to SARS-CoV-2 protect against re-infection during outbreaks in care homes, September and October 2020	Eurosurveillance / Rapid communication	<ul style="list-style-type: none">• Provides an overview of investigations at two London care homes in London which experienced a second COVID-19 outbreak in Autumn 2020, and discusses the role of antibodies in protecting against SARS-CoV-2 re-infection.

27.01.2021	Resurgence of COVID-19 in Manaus, Brazil, despite high seroprevalence	Lancet / Comment	<ul style="list-style-type: none"> • In Manaus, Brazil, a study of blood donors indicated that 76% (95% CI 67–98) of population had been infected with SARS-CoV-2 by October, 2020. • Estimated attack rate above theoretical herd immunity threshold (67%), given a basic case reproduction number (R0) of 3; abrupt increase in COVID-19 hospital admissions - 3431 in Jan 1–19, 2021, vs 552 in Dec 1–19, 2020 - is unexpected and of concern.
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Vaccines

Publication Date	Title/URL	Journal / Article type	Digest
29.01.2021	Johnson & Johnson Announces Single-Shot Janssen COVID-19 Vaccine Candidate Met Primary Endpoints in Interim Analysis of its Phase 3 ENSEMBLE Trial	Johnson & Johnson / Press Release	<ul style="list-style-type: none"> • Vaccine candidate 72% effective in the US and 66% effective overall at preventing Moderate to Severe COVID-19, 28 Days after vaccination • 85% effective overall in preventing severe disease and demonstrated complete protection against COVID-19 related Hospitalization and Death as of Day 28 • Protection against severe disease across geographies, ages, and multiple virus variants, including the SARS-CoV-2 variant from the B.1.351 Lineage observed in South Africa.
01.02.2021	Post-Vaccination COVID-19 among Healthcare Workers, Israel	Emerg Infect Dis / Article	<ul style="list-style-type: none"> • 4,081 vaccinated Israeli healthcare workers: 22 (0.54%) developed COVID-19 from 1–10 days (median 3.5 days) after immunisation. • Efficacy of the BNT162b was 52% a week after first dose; positive COVID-19 cases were described among vaccinees even early after second dose. Clinicians should promptly test for COVID-19.
29.01.2021	The effectiveness of the first dose of BNT162 b 2 vaccine in reducing SARS-CoV-2 infection 13-24 days after immunization: real-world evidence	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Analysed data for 503,875 patients of a state-mandated health provider in Israel vaccinated with a first dose of BNT162b2. • BNT162b2 vaccine demonstrated an effectiveness of 51% of against SARS-CoV-2 infection 13-24 days after immunisation with the first dose.
01.02.2021	Single Dose Administration, And The Influence Of The Timing Of The Booster Dose On Immunogenicity and Efficacy Of ChAdOx1 nCoV-19 (AZD1222) Vaccine	Preprints with the Lancet (non-peer reviewed) / Article	<ul style="list-style-type: none"> • In phase III trials, a single dose of ChAdOx1 nCoV-19 was 76% effective from day 22 to day 90. • Modelling indicates antibody levels were similarly maintained in this 90 day period. • Efficacy was higher with a longer prime-boost interval: VE 82.4% at 12+ weeks, compared with VE 54.9% at <6 weeks.

02.02.2021	Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: an interim analysis of a randomised controlled phase 3 trial in Russia	The Lancet / Article	<ul style="list-style-type: none"> • Interim analysis of a phase 3 trial (19,866 participants) suggests Gam-COVID-Vac (Sputnik V) showed 91.6% efficacy against COVID-19 and was well tolerated.
03.02.2021	Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine (CoronaVac) in healthy adults aged 60 years and older: a randomised, double-blind, placebo-controlled, phase 1/2 clinical trial	The Lancet Infectious Diseases / Article	<ul style="list-style-type: none"> • Phase 1/2 trials (74 participants) suggest the COVID-19 vaccine candidate CoronaVac is safe and well tolerated in adults aged over 60 years. • Neutralising antibody titres induced by 3 µg dose were similar to those of 6 µg dose, supporting use of 3 µg dose in phase 3 trials.

Diagnosics and genomics

Publication Date	Title/URL	Journal / Article type	Digest
02.02.2021	Sixteen novel lineages of SARS-CoV-2 in South Africa	Nat Med / Letter	<ul style="list-style-type: none"> • Authors analysed 1,365 near whole genomes, identify 16 new lineages of SARS-CoV-2 isolated between 6 March and 26 August 2020. Most have unique mutations not identified elsewhere. • Three lineages (B.1.1.54, B.1.1.56 and C.1) spread widely in South Africa during the first wave, comprising ~42% of all infections in the country at the time. • C.1 has 16 nucleotide mutations compared with original Wuhan sequence; most geographically widespread lineage in South Africa by the end of August 2020.
02.02.2021	Genomic Signatures of SARS-CoV-2 Associated with Patient Mortality	Viruses / Article	<ul style="list-style-type: none"> • Authors tested for associations between SARS-CoV-2 genomic variants from an international cohort of 2508 patients and mortality rates • 4 well-resolved clades had significantly different mortality rates, even after adjusting for patient demographic and geographic characteristics. • 10 single-nucleotide polymorphisms (SNPs) in the SARS-CoV-2 genome that were associated with patient mortality.
03.02.2021	Investigation of novel SARS-CoV-2 variant: 202012/01. Technical briefing 5	Gov.uk / Guidance	<ul style="list-style-type: none"> • This briefing provides an update on the briefing of 14 January 2021. • VOC202012/01 continues to predominate across all UK regions. • S gene target failure remains a well correlated proxy measure of VOC 202012/01. • An assessment of severity of disease has been conducted by

			<p>NERVTAG.</p> <ul style="list-style-type: none"> • A limited number of B.1.1.7 VOC 202012/01 genomes with E484K mutation have been detected.
29.01.2021	The SARS-CoV-2 Y453F mink variant displays a striking increase in ACE-2 affinity but does not challenge antibody neutralization	bioRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Following emergence of a genetic variant (“cluster-five”) among farmed minks in Denmark, this study presents functional data on the Y453F cluster-five RBD. • It does not decrease established humoral immunity or affect the neutralising response in a vaccine model based on wild-type RBD or spike. • However, there is potential for enhanced transmission capacity due to its binding the human ACE-2 receptor with a four-fold higher affinity.
28.01.2021	Mutational signatures and heterogeneous host response revealed via large-scale characterization of SARS-CoV-2 genomic diversity	iScience / Article	<ul style="list-style-type: none"> • Host-related processes are revealed by intra-host genomic diversity of SARS-CoV-2 samples • Three non-overlapping mutational signatures are inferred from decomposition of minor variant profiles • With some exceptions, mutational processes are affected by purifying selection. • Several mutations appear to transit toward clonality. • Phylogenomic analysis shows presence of homoplasies and supports the hypothesis of transmission of minor variants. • Note: previously included in the Digest as a preprint.
28.01.2021	Characteristics and outcomes of clinically diagnosed RT-PCR swab negative COVID-19: a retrospective cohort study	Sci Rep / Article	<ul style="list-style-type: none"> • Retrospective cohort study in two large London hospitals to characterise demographic, clinical, and hospitalisation outcome characteristics of swab-negative clinical COVID-19 patients. • 1 in 5 (94/456) patients with a negative swab and clinical suspicion of COVID-19 received a clinical diagnosis of COVID-19 within clinical documentation, discharge summary or death certificate. • Compared to similar swab-positive cohort, swab-negative clinical COVID-19 patients had better outcomes, shorter hospital stay, reduced need for > 60% supplementary oxygen, reduced mortality.
03.02.2021	The Limit of Detection Matters: The Case for Benchmarking Severe Acute Respiratory Syndrome Coronavirus 2 Testing	Clin Infect Dis / Corrected proof	<ul style="list-style-type: none"> • Findings suggest the assay limit of detection (LoD) meaningfully impacts clinical performance of SARS-CoV-2 tests. • The highest LoDs on the market will miss a majority of infected patients, therefore assays should be benchmarked against a universal standard to allow cross-comparison of detection methods.

01.02.2021	Accuracy of four lateral flow immunoassays for anti SARS-CoV-2 antibodies: a head-to-head comparative study	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • In a comparison of four lateral flow immunoassays the IgG band of the SureScreen device and the Rapid Test Consortium AbC-19TM device had higher specificities, but OrientGene and Biomerica devices had higher sensitivities. • SureScreen IgG band had the highest specificity (98.9%) based on pre-pandemic samples. • All four devices showed higher but varied sensitivity at higher antibody concentrations.
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Epidemiology and clinical - children and pregnancy

Publication Date	Title/URL	Journal / Article type	Digest
29.01.2021	Assessment of Maternal and Neonatal Cord Blood SARS-CoV-2 Antibodies and Placental Transfer Ratios	JAMA Pediatr / Original Investigation	<ul style="list-style-type: none"> • U.S cohort study, 1714 pregnant women: 83 (6%) had detectable IgG and/or IgM antibodies at delivery, majority of infants born to seropositive mothers (72 of 83 [87%]) had detectable IgG antibody at birth. • Transplacental transfer efficient regardless of presence of symptoms in the mother or the severity of disease • Associated editorial: https://jamanetwork.com/journals/jamapediatrics/fullarticle/2775944

Epidemiology and clinical - long-term complications / sequelae

Publication Date	Title/URL	Journal / Article type	Digest
03.02.2021	Short-term Neuropsychiatric Outcomes and Quality of Life in COVID-19 Survivors	J Intern Med / Article	<ul style="list-style-type: none"> • Study of hospitalised COVID-19 survivors (n=179) found a considerable prevalence of neurocognitive impairment, psychiatric morbidity, and poor quality of life in the short-term. Long term impact is not yet known.
29.01.2021	Multinational Prevalence of Neurological Phenotypes in Patients Hospitalized with COVID-19	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Study of 35,177 hospitalised COVID-19 patients in 6 countries found increased prevalence of disorders of consciousness (5.8%) and unspecified disorders of the brain (8.1%), compared to pre-admission prevalence. • Patients with severe COVID-19 had increased relative risk of

		disorders of consciousness (22%), other cerebrovascular diseases (24%), non-traumatic intracranial haemorrhage (34%), encephalitis and/or myelitis (37%), and myopathy (72%).
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Epidemiology and clinical – risk factors

Publication Date	Title/URL	Journal / Article type	Digest
03.02.2021	Short report: Ethnicity and COVID-19 death in the early part of the COVID-19 second wave in England: an analysis of OpenSAFELY data from 1st September to 9th November 2020	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> Findings suggest ethnic inequalities in the risk of COVID-19-related death changed between the first and second wave of the epidemic in England, with people of South Asian ethnicity at higher risk than white ethnicity, and little evidence of raised risk for black or other ethnic groups compared to white ethnicity.
03.02.2021	Extremely high SARS-CoV-2 seroprevalence in a strictly-Orthodox Jewish community in the UK	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> Study of a tightly-knit minority religious population in the UK (1,759 participants; 343 households) found a very high overall level of SARS-CoV-2 seroprevalence (64.3%). Seroprevalence was lowest in children <5 years (27.6%), but much higher in secondary school children and adults (73.8% and 74%, respectively).

Epidemiology and clinical – other

Publication Date	Title/URL	Journal / Article type	Digest
03.02.2021	SARS-CoV-2 infects and replicates in cells of the human endocrine and exocrine pancreas	Nat Metab / Article	<ul style="list-style-type: none"> Authors' data identify the human pancreas as a target of SARS-CoV-2 infection and suggest that β-cell infection could contribute to the metabolic dysregulation observed in patients with COVID-19.
03.02.2021	UK Biobank study shows that COVID-19 antibodies remain for at least 6 months post-infection for the vast majority of people who have had the virus	ukbiobank.ac.uk / Article	<ul style="list-style-type: none"> Analysis of UK Biobank participants, their adult children and grandchildren (18,893 participants in total) found 99% of participants who had previously tested positive for SARS-CoV-2 retained antibodies 3 months after being infected, and 88% did for 6 months of the study. Presence of detectable antibodies was higher in younger people (13.5% among those <30) and lowest in the elderly (6.7% among those >70) Seroprevalence was highest among participants of black ethnicity

			<p>(16.3%) and lowest among those of white (8.5%) and Chinese ethnicities (7.5%)</p> <ul style="list-style-type: none"> • Loss of sense of taste and smell was the most common symptom of sero-positive participants (43%), while 24% were asymptomatic.
28.01.2021	The effect of SARS-CoV-2 variant B.1.1.7 on symptomatology, re-infection and transmissibility	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Longitudinal reports from 36,920 Covid Symptom Study app users who tested positive for COVID-19 found no evidence for changes in reported symptoms, disease severity or disease duration associated with variant B.1.1.7. • Reinfection rate estimated at 0.7%, but no evidence this was higher compared to older strains. • R(t) increased by a factor of 1.35, but lockdowns reduced R(t) below 1 in regions with very high proportions of B.1.1.7.
03.02.2021	Increased hazard of death in community-tested cases of SARS-CoV-2 Variant of Concern 202012/01	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Analysis of a large database of SARS-CoV-2 community test results and COVID-19 deaths for England suggests hazard of death among S gene target failure (SGTF) COVID-19 cases is 30% higher than among non-SGTF cases. • Estimated risk of death for males aged 55-69 increases from 0.56% to 0.73% over the 28 days following a positive SARS-CoV-2 test. • Estimated 35% higher hazard of death associated with VOC 202012/01.
29.01.2021	Interpretation of COVID-19 case fatality risk measures in England	J Epidemiol Community Health / Letter	<ul style="list-style-type: none"> • Case fatality risk (CFR) is an informative indicator of crude mortality risk for individuals diagnosed with COVID-19. The differences in observed CFR are multifactorial and reflective of differences in testing strategy and population demographics.
28.01.2021	REACT-1 round 8 final report: high average prevalence with regional heterogeneity of trends in SARS-CoV-2 infection in the community in England during January 2021	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Data from round 8 of the REACT-1 study estimates the R number in England at 0.98 between 6 and 26 January 2021. • Prevalence was high throughout the study period, but with some evidence of a decline at the end. • Prevalence was highest in the low-risk 18 to 24 year old group (2.44%), but also in those over 65 years who are more at risk (0.93%). • Neighbourhood deprivation, large household size, and Black or Asian ethnicity were all associated with higher levels of infections. • Healthcare and care home workers, and some other key workers, were more likely to test positive than other workers.
05.02.2021	Healthcare Workers Bioresource: Study outline and baseline characteristics of a prospective healthcare	Wellcome Open Res / Research article	<ul style="list-style-type: none"> • UK COVID-19 bioresource, to provide longitudinal assessments of incident infection and immune responses in health care workers

	worker cohort to study immune protection and pathogenesis in COVID-19		(HCWs) through natural time course of disease and convalescence. <ul style="list-style-type: none"> • Preliminary baseline results for first 731 HCWs (400 single-centre, 331 multicentre extension) are presented.
28.01.2021	Severe Acute Respiratory Syndrome Coronavirus-2 Infections in Critical Care Staff: Beware the Risks Beyond the Bedside	Crit Care Med / Article	<ul style="list-style-type: none"> • In this London hospital, source of COVID-19 infection in staff was less likely from patients in critical care; more likely sources are other staff, other areas of the hospital, and wider community. PPE was effective.
02.02.2021	Age groups that sustain resurging COVID-19 epidemics in the United States	Science / Research Article	<ul style="list-style-type: none"> • Authors analyse aggregated, age-specific mobility trends from more than 10 million individuals in the US and link these mechanistically to age-specific COVID-19 mortality data. • As of Oct 2020, 20-49 year olds are only age groups sustaining resurgent SARS-CoV-2 transmission with reproduction numbers well above one; at least 65 of 100 COVID-19 infections originate from individuals aged 20-49 in the US.

Infection control / non-pharmaceutical interventions

Publication Date	Title/URL	Journal / Article type	Digest
07.01.2021	Local measures enable COVID-19 containment with fewer restrictions due to cooperative effects	EClinicalMedicine / Research Paper	<ul style="list-style-type: none"> • Modelling study to determine efficacy of regional containment strategies, where contact restrictions are triggered locally in individual regions upon crossing critical infection number thresholds. • Substantially reduced restriction time for regional containment, if R0 is only slightly larger than 1 and the proportion of cross-regional contacts (the so-called leakiness) is low. • Leakiness and the regional structure itself were crucial parameters for the performance of the regional strategy.
29.01.2021	Application of physical distancing and fabric face coverings in mitigating the B117 variant SARS-CoV-2 virus in public, workplace and community settings	Gov.uk / Research and analysis	<ul style="list-style-type: none"> • Paper on physical distancing and fabric face coverings in non-healthcare settings, prepared by the Environmental Modelling Group for the Scientific Advisory Group on Emergencies. • Physical distancing and fabric face coverings are likely to be needed to be applied more consistently and effectively to be able to mitigate transmission of the B117 variant.

Transmission

Publication Date	Title/URL	Journal / Article type	Digest
03.02.2021	Mechanistic transmission modeling of COVID-19 on the Diamond Princess cruise ship demonstrates the importance of aerosol transmission	Proc Natl Acad Sci U S A / Research article	<ul style="list-style-type: none"> • Modelling of the COVID-19 outbreak on the Diamond Princess cruise ship estimates the mean contributions of short-range, long-range, and fomite transmission modes to infected cases were 35%, 35%, and 30%, respectively. Mean contributions of larger and smaller respiratory aerosols were 41% and 59%, respectively. • Aerosol inhalation was likely the dominant contributor to COVID-19 transmission among passengers, even if high ventilation rates and no air recirculation are assumed.
01.02.2021	Aerosol emission from the respiratory tract: an analysis of relative risks from oxygen delivery systems	medRxiv (non-peer reviewed) / 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.

Treatment

Publication Date	Title/URL	Journal / Article type	Digest
02.02.2021	Azithromycin in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial	The Lancet / Article	<ul style="list-style-type: none"> • In a trial with 7763 patients admitted to UK hospitals with COVID-19, azithromycin did not improve survival or other pre-specified clinical outcomes. • Azithromycin use in hospitalised COVID-19 patients should be limited to those in whom there is a clear antimicrobial indication.
01.02.2021	Association of Intravenous Immunoglobulins Plus Methylprednisolone vs Immunoglobulins Alone With Course of Fever in Multisystem Inflammatory Syndrome in Children	JAMA / Original Investigation	<ul style="list-style-type: none"> • French retrospective cohort study of 111 children with MIS-C. • Rate of treatment failure for those who received IVIG plus methylprednisolone vs IVIGs alone was 9% vs 51%.

Modelling

Publication Date	Title/URL	Journal / Article type	Digest
01.02.2021	Understanding soaring coronavirus cases and the effect of contagion policies in the UK	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none">• Modelling suggests: the new SARS-CoV-2 variant is as transmissible as previous strains; relaxation of preventive measures is closely related with the ongoing surge in UK cases; and lockdown policies are not fully effective to flatten the curve.

Guidance and consensus statements

Publication Date	Title/URL	Journal / Article type
01.02.2021	COVID-19: rapid point of care or near-person testing for service providers	Gov.uk / Guidance

Overviews, comments and editorials

Publication Date	Title/URL	Journal / Article type
04.02.2021	World-first COVID-19 alternating dose vaccine study launches in UK	Gov.uk / Press release
03.02.2021	Put to the test: use of rapid testing technologies for covid-19	BMJ / Analysis
29.01.2021	NERVTAG: Brief note on SARS-CoV-2 variants, 13 January 2021	Gov.uk / Research and analysis
03.02.2021	Recurrent deletions in the SARS-CoV-2 spike glycoprotein drive antibody escape	Science / Report
04.02.2021	Preliminary report of an outbreak of SARS-CoV-2 in mink and mink farmers associated with community spread, Denmark, June to November 2020	Eurosurveillance / Rapid communication
27.01.2021	Coronavirus (COVID-19) Infection Survey: characteristics of people testing positive for COVID-19 in England, 27 January 2021	ONS / Report
03.02.2021	Coronavirus (COVID-19) Infection Survey: antibody data for the UK: 3 February 2021	ONS / Report
29.01.2021	SPI-M-O: Medium-term projections - 13 January 2021	Gov.uk / Research and analysis
29.01.2021	SAGE return for COVID-19 strategy: sequencing of social distancing behavioural and social interventions, 6 May 2020	Gov.uk / Research and analysis
02.02.2021	Understanding the drivers of transmission of SARS-CoV-2	The Lancet Infectious Diseases / Comment

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