



COVID-19 Literature Digest – 04/01/2021

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 three times per week (Mon, Wed, 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 The reports include both preprints, which should be treated with caution as they are NOT peer-reviewed and may be subject to change, and also research that has been subject to peer review and wider scrutiny.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,

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On behalf of the PHE COVID-19 Literature Digest Team

Report for 04.01.2021 (please note that papers that have **NOT been peer-reviewed** are highlighted in red).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
23.12.2020	Antibody Status and Incidence of SARS-CoV-2 Infection in Health Care Workers	N Engl J Med / Article	<ul style="list-style-type: none"> • Study of the relationship between the presence of antibodies to SARS-CoV-2 and risk of subsequent reinfection. 12,541 UK health care workers [HCW] participated and had anti-spike IgG measured; 11,364 were followed up after negative antibody results and 1265 after positive results, including 88 in whom seroconversion occurred during follow-up. • 223 anti-spike–seronegative HCW had a positive PCR test (1.09 per 10,000 days at risk), 100 during screening while they were asymptomatic and 123 while symptomatic. • 2 anti-spike–seropositive HCW had a positive PCR test (0.13 per 10,000 days at risk); both workers were asymptomatic when tested (adjusted incidence rate ratio, 0.11; 95% confidence interval, 0.03 to 0.44; P=0.002). • The presence of anti-spike or anti-nucleocapsid IgG antibodies was associated with a substantially reduced risk of SARS-CoV-2 reinfection in the ensuing 6 months.
23.12.2020	Discordant neutralizing antibody and T cell responses in asymptomatic and mild SARS-CoV-2 infection	Sci Immunol / Article	<ul style="list-style-type: none"> • Authors analysed T cell and neutralizing antibody responses in 136 healthcare workers (HCW) 16-18 weeks after UK lockdown; 76 had mild/asymptomatic SARS-CoV-2 infection. • Neutralizing antibodies (nAb) present in 89% of previously infected HCW. T cell responses tended to be lower following asymptomatic infection. nAb titres maintained irrespective of symptoms. • T cell and antibody responses were sometimes discordant. 11% lacked nAb and had undetectable T cell responses to spike protein but had T cells reactive with other SARS-CoV-2 antigens. • Findings suggest majority of individuals with mild or asymptomatic SARS-CoV-2 infection carry nAb complemented by multispecific T cell responses at 16-18 weeks after infection.
29.12.2020	Antibody response to SARS-CoV-2 infection in humans: A systematic review	PLoS One / Letter	<ul style="list-style-type: none"> • This review comprehensively evaluated evidence describing the antibody response to SARS-CoV-2 published from 01/01/2020-26/06/2020. • 150 papers were included. Most studies (113 or 75%) were observational in design, were based wholly or primarily on data from hospitalised patients (108, 72%) and had important methodological limitations. • Initial findings of low neutralising antibody titres and possible waning of titres over time may have implications for sero-surveillance and disease control policy, although further evidence is needed.

			<ul style="list-style-type: none"> • The detection of potent neutralising antibodies in convalescent plasma is important in the context of development of therapeutics and vaccines.
23.12.2020	Adaptive immunity to SARS-CoV-2 in cancer patients: The CAPTURE study	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Study evaluated 529 blood samples and 1051 oronasopharyngeal swabs from 144 cancer patients and 73 healthcare workers (HCWs) in the CAPTURE cohort, and correlated with >200 clinical variables. • In patients with solid cancers and HCWs, S1-reactive and neutralising antibodies to SARS-CoV-2 were detectable five months post-infection. • SARS-CoV-2-specific T-cell responses were detected, and CD4+ T-cell responses correlated with S1 antibody levels. • Overall, cancer stage, disease status, and therapies did not correlate with immune responses. • Findings have implications for understanding individual risks and potential effectiveness of SARS-CoV-2 vaccination in the cancer population.

Vaccines

Publication Date	Title / URL	Journal / Article type	Digest
30.12.2020	Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine	N Engl J Med / Article	<ul style="list-style-type: none"> • Trial enrolled 30,420 volunteers, randomly assigned in a 1:1 ratio to receive either vaccine or placebo (15,210 participants in each group). More than 96% of participants received both injections, and 2.2% had evidence (serologic, virologic, or both) of SARS-CoV-2 infection at baseline. • Symptomatic Covid-19 illness was confirmed in 185 participants in placebo group (56.5 per 1000 person-years; 95% confidence interval [CI], 48.7 to 65.3) and in 11 participants in the mRNA-1273 group (3.3 per 1000 person-years; 95% CI, 1.7 to 6.0); vaccine efficacy was 94.1% (95% CI, 89.3 to 96.8%; P<0.001). • The mRNA-1273 vaccine showed 94.1% efficacy at preventing Covid-19 illness, including severe disease. Aside from transient local and systemic reactions, no safety concerns were identified.
02.01.2021	Predictors of COVID-19 vaccine hesitancy in the UK Household Longitudinal Study	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Analysis of survey data from 12,035 UK participants collected from 24 Nov to 1 Dec 2020 to investigate COVID-19 vaccine hesitancy. • Overall intention to be vaccinated was high (82% likely/very likely). • Vaccine hesitancy was higher in women (21.0% vs 14.7%), younger age groups (26.5% in 16-24 year olds vs 4.5% in 75+) and less educated (18.6% no qualifications vs 13.2% degree qualified). • Vaccine hesitancy was particularly high in Black (71.8%), Pakistani/Bangladeshi (42.3%), Mixed (32.4%) and non-UK/Irish White (26.4%) ethnic groups. • Fully adjusted models showed gender, education and ethnicity were

			independently associated with vaccine hesitancy. <ul style="list-style-type: none"> The main reason for hesitancy was fears over unknown future effects.
29.12.2020	National Trends in the US Public's Likelihood of Getting a COVID-19 Vaccine-April 1 to December 8, 2020	Jama / Research letter	<ul style="list-style-type: none"> 8,167 Understanding America Study (UAS) panel respondents consented to participate in biweekly COVID-19 tracking surveys; nationally representative survey. Self-reported likelihood of getting a COVID-19 vaccine Nov 25-Dec 8: lower among women than men (51% vs 62%; aRR, 0.9 [95% CI, 0.8-0.9]) and Black vs White individuals (38% vs 59%; aRR, 0.7 [95% CI, 0.6-0.8]); higher among adults aged 65 years plus vs 18-49 years (69% vs 51%; aRR, 1.4 [95% CI, 1.3-1.5]) and those with at least a bachelor's degree vs a high school education or less (70% vs 48%; aRR, 1.5 [95% CI, 1.3-1.6]) Self-reported likelihood declined from 74% in early April to 56% in early Dec, despite Nov press releases of high vaccine efficacy for 2 vaccines in phase 3 trials.

Diagnostics and genomics

Publication Date	Title / URL	Journal / Article type	Digest
01.01.2021	Performance of an Antigen-Based Test for Asymptomatic and Symptomatic SARS-CoV-2 Testing at Two University Campuses - Wisconsin, September-October 2020	MMWR Morb Mortal Wkly Rep / Article	<ul style="list-style-type: none"> Comparison of Sofia SARS Antigen FIA and real-time RT-PCR for SARS-CoV-2 detection among asymptomatic and symptomatic persons at two U.S universities. 1,098 paired nasal swabs were tested, Sept 28 - Oct 9. Sofia antigen test had a sensitivity of 80.0% / specificity of 98.9% among symptomatic persons. Accuracy was lower (sensitivity 41.2% / specificity 98.4%) when screening asymptomatic persons. To account for reduced antigen test accuracy, confirmatory testing with a nucleic acid amplification test (e.g., RT-PCR) should be considered after negative antigen test results in symptomatic persons and positive antigen test results in asymptomatic persons.
24.12.2020	Validation testing to determine the effectiveness of lateral flow testing for asymptomatic SARS-CoV-2 detection in low prevalence settings	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> Presents data on the performance of Lateral Flow devices to test almost 8,000 students at the University of Birmingham from 2 to 9 Dec 2020. Performance was validated against almost 800 samples using PCR, and theoretically validated on thousands of Pillar 2 PCR testing results performed on low-prevalence care home testing samples. Data suggests Lateral Flow Devices do not detect infections presenting with PCR Ct values over 29-30, meaning only 3.2% (95% CI 0.6% to 15.6%) of total cases in the student population were detected, but that as many of 85% of cases tested in the Pillar 2 PCR lab would have been detected theoretically.

27.12.2020	S-variant SARS-CoV-2 is associated with significantly higher viral loads in samples tested by ThermoFisher TaqPath RT-QPCR	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Since more recent information became available regarding the presence of SARS-CoV-2 variants of concern (S-VoC), which can show a suboptimal profile in RT-QPCR tests such as the ThermoFisher TaqPath used at the majority of Lighthouse laboratories, the authors analysed recently published data for trends and significance of the S-gene 'dropout' variant. • Analysis suggests that patients whose samples exhibit the S-dropout profile in the TaqPath test are more likely to have high viral loads at the time of sampling. • The relevance of this to epidemiological reports of fast spread of the SARS-CoV-2 in regions of the UK is discussed.
22.12.2020	Emergence and rapid spread of a new severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) lineage with multiple spike mutations in South Africa	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Describes a new SARS-CoV-2 lineage (501Y.V2) characterised by eight lineage-defining mutations in the spike protein, including three at important residues in the receptor-binding domain (K417N, E484K and N501Y) that may have functional significance. • This lineage emerged in South Africa after the first epidemic wave in a severely affected metropolitan area, Nelson Mandela Bay, and within weeks became the dominant lineage in the Eastern Cape and Western Cape Provinces. • Genomic data, showing rapid displacement of other lineages, suggests this lineage may be associated with increased transmissibility.
28.12.2020	SARS-CoV-2 escape in vitro from a highly neutralizing COVID-19 convalescent plasma	bioRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Authors co-incubated SARS-CoV-2 virus with a highly neutralising plasma from a COVID-19 convalescent patient to investigate evolution of SARS-CoV-2 in the immune population. • The plasma fully neutralised the virus for 7 passages, but after 45 days, the deletion of F140 in the spike N-terminal domain (NTD) N3 loop led to partial breakthrough. • At day 73, an E484K substitution in the receptor-binding domain (RBD) occurred, followed at day 80 by an insertion in the NTD N5 loop containing a new glycan sequon, which generated a variant completely resistant to plasma neutralisation. • Modelling suggests the deletion and insertion in loops N3 and N5 prevent binding of neutralising antibodies. • Three mutations allowed SARS-CoV-2 to evade the polyclonal antibody response of a highly neutralizing COVID-19 convalescent plasma.

Epidemiology and clinical – risk factors

Publication Date	Title / URL	Journal / Article type	Digest
29.12.2020	Risk Assessment: Risk related to spread of new SARS-CoV-2 variants of concern in the EU/EEA	European Centre for Disease Prevention and Control / Risk assessment	<ul style="list-style-type: none"> • This risk assessment presents the latest available information on the recent emergence of two variants of potential concern, VOC 202012/01 discovered in the UK and another variant, 501.V2 identified in South Africa. • It also assesses the risk of these variants of concern being introduced and spread in the EU/EEA, as well as the increased impact this would have on health systems in the coming weeks.
23.12.2020	Risks of and risk factors for COVID-19 disease in people with diabetes: a cohort study of the total population of Scotland	Lancet Diabetes Endocrinol / Article	<ul style="list-style-type: none"> • Of Scottish population on Mar 1 (n=5 463 300), diabetes population 319,349 (5.8%): 1082 (0.3%) developed fatal or critical care unit-treated COVID-19 by July 31; 972 (89.8%) aged 60 years or older. • Overall odds ratio (OR) for diabetes, adjusted for age and sex, was 1.395 (95% CI 1.304–1.494; p<0.0001, compared with the risk in those without diabetes. The OR was 2.396 (1.815–3.163; p<0.0001) in type 1 diabetes and 1.369 (1.276–1.468; p<0.0001) in type 2 diabetes. • Overall risks of fatal or critical care unit-treated COVID-19 substantially elevated in those with type 1 and type 2 diabetes. The risk varies widely among those with diabetes but can be predicted reasonably well using previous clinical history.

Epidemiology and clinical – other

Publication Date	Title / URL	Journal / Article type	Digest
30.12.2020	Microvascular Injury in the Brains of Patients with Covid-19	N Engl J Med / Correspondence	<ul style="list-style-type: none"> • In a convenience sample of patients who had died from Covid-19, multifocal microvascular injury was observed in the brain and olfactory bulbs by means of magnetic resonance microscopy, histopathological evaluation, and immunohistochemical analysis of corresponding sections, without evidence of viral infection. • These findings may inform the interpretation of changes observed on magnetic resonance imaging of punctate hyperintensities and linear hypointensities in patients with Covid-19.
01.01.2021	SARS-CoV-2 positivity in asymptomatic-screened dental patients	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • In the first report of a COVID-19 testing survey in asymptomatic-screened patients presenting in a dental setting, 4,032 patients (>5 years old) across Scotland completed demographic and symptom history questionnaires and provided a combined oropharyngeal and nasal swab sample. • A total of 22 (0.5%) tested positive for SARS-CoV-2, reflecting the underlying prevalence in community at the time.

- The positivity rate increased over the period, commensurate with uptick in community prevalence identified across all national testing monitoring data streams.
- Authors suggest dental settings are a valuable location for public health surveillance.

Infection control / non-pharmaceutical interventions

Publication Date	Title / URL	Journal / Article type	Digest
23.12.2020	Association of tiered restrictions and a second lockdown with COVID-19 deaths and hospital admissions in England: a modelling study	Lancet Infect Dis / Article	<ul style="list-style-type: none"> • Authors examined impact of UK's tiered restrictions - and alternatives for lockdown stringency, timing, duration - on SARS-CoV-2 transmission, hospital admissions / deaths from COVID-19. • Estimated reduction in effective reproduction number (R(t)) of 2% (95% credible interval [CrI] 0-4) for tier 2, 10% (6-14) for tier 3, 35% (30-41) for a Northern Ireland-stringency lockdown with schools closed, and 44% (37-49) for a Wales-stringency lockdown with schools closed. • Tiered restrictions, in particular the most stringent tier 3, probably helped to slow transmission, although these restrictions have a much lesser effect on reducing hospital admissions and deaths than do lockdown scenarios. • A 4-week lockdown intervention would probably have a strong but temporary effect, reducing Rt to well below one during the lockdown period, with sustained reductions in cases, deaths, and hospital admissions for several months afterwards.
01.01.2021	Implications of Shortened Quarantine Among Household Contacts of Index Patients with Confirmed SARS-CoV-2 Infection - Tennessee and Wisconsin, April-September 2020	MMWR Morb Mortal Wkly Rep / Article	<ul style="list-style-type: none"> • Interim data for ongoing household transmission study. Among persons exposed to COVID-19 in the household who were asymptomatic and had negative laboratory test results through 7 days after symptom onset in index patient, 19% experienced symptoms or received positive test results in the following week. • A shorter quarantine after household exposure may be easier to adhere to, but risks onward transmission. Persons released from quarantine before 14 days should continue to avoid close contact and wear masks when around others until 14 days after their last exposure.
29.12.2020	Masks and Face Coverings for the Lay Public : A Narrative Update	Ann Intern Med / Reviews	<ul style="list-style-type: none"> • Evidence that the virus can be airborne (and therefore be inhaled) and that masking policies, when effectively delivered, save lives is now strong. • There is no evidence of serious harms from masks and face coverings, although discomfort, communication difficulties, and environmental effects are not insignificant. • Randomized trials are sparse and have not addressed the question of source control.

			<ul style="list-style-type: none"> • Psychological effects of masks are culturally framed and shape acceptance and adherence.
23.12.2020	Assessment of Air Contamination by SARS-CoV-2 in Hospital Settings	JAMA Netw Open / Original investigation	<ul style="list-style-type: none"> • Systematic review of 24 studies to consider level of air contamination from SARS-CoV-2 in different hospital areas, and the factors associated with contamination. • 17% of air sampled from close patient environments was positive for SARS-CoV-2 RNA, with viability of the virus found in 9% of cultures. • Air both close to and distant from patients with COVID-19 was frequently contaminated with SARS-CoV-2 RNA; however, few of these samples contained viable viruses. • High viral loads found in toilets and bathrooms, staff areas, and public hallways suggest that these areas should be carefully considered.

Transmission

Publication Date	Title / URL	Journal / Article type	Digest
31.12.2020	Report 42 - Transmission of SARS-CoV-2 Lineage B.1.1.7 in England: insights from linking epidemiological and genetic data	Imperial College / Report	<ul style="list-style-type: none"> • The SARS-CoV-2 lineage B.1.1.7, now designated Variant of Concern 202012/01 (VOC) by Public Health England, originated in the UK in late Summer to early Autumn 2020. • Authors examined epidemiological evidence for this VOC having a transmission advantage from several perspectives. • WGS data collected from community-based diagnostic testing provides an indication of changing prevalence of different genetic variants through time. Phylodynamic modelling additionally indicates that genetic diversity of this lineage has changed in a manner consistent with exponential growth. • Show that the VOC has higher transmissibility than non-VOC lineages, even if the VOC has a different latent period or generation time.
24.12.2020	Estimated transmissibility and severity of novel SARS-CoV-2 Variant of Concern 202012/01 in England	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Authors fitted a two-strain mathematical model of SARS-CoV-2 transmission to observed COVID-19 hospital admissions, hospital and ICU bed occupancy, and deaths; SARS-CoV-2 PCR prevalence and seroprevalence; and the relative frequency of VOC 202012/01 in the three most heavily affected NHS England regions. • VOC 202012/01 is estimated to be 56% more transmissible than pre-existing variants. • There was no clear evidence that VOC 202012/01 results in greater or lesser severity of disease than pre-existing variants, however increased transmissibility is likely to lead to increased incidence, hospitalisations and deaths even if regional tiered restrictions are maintained. • Findings suggest that measures similar to the Nov 2020 lockdown in England are

			unlikely to reduce the effective Rt to less than 1, unless primary schools, secondary schools, and universities are also closed.
31.12.2020	EMG/SPI-B/TWEG: Mitigations to reduce transmission of the new variant SARS-CoV-2 virus, 22 December 2020	Gov.uk / Research and analysis	<ul style="list-style-type: none"> • Paper prepared by EMG, SPI-B and TWEG on mitigations to reduce transmission of the new variant of COVID-19.
31.12.2020	TFC: Children and transmission - update paper, 17 December 2020	Gov.uk / Research and analysis	<ul style="list-style-type: none"> • This paper provides an updated view on evidence relating to children and schools from the Children’s Task and Finish group. • Overall, accumulating evidence is consistent with increased transmission occurring amongst school children when schools are open, particularly in children of secondary school age (high confidence): multiple data sources show a reduction in transmission in children following schools closing for half term, and transmission rates increasing again following the post-half term return to school (medium confidence). • No two schools are the same, with differences for example in class sizes, structures and ventilation, among other things. Differences in the school environment and the level of mitigations in place will influence the potential for transmission in schools.

Overviews, comments and editorials

Publication Date	Title / URL	Journal / Article type
29.12.2020	Mandating COVID-19 Vaccines	JAMA / Viewpoint
30.12.2020	Maintaining Safety with SARS-CoV-2 Vaccines	N Engl J Med / Review article

Produced by the PHE COVID-19 Literature Digest Team

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