



COVID-19 Literature Digest – 09/11/2020

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 The reports include both preprints, which should be treated with caution as they are NOT peer-reviewed and may be subject to change, and also research that has been subject to peer review and wider scrutiny.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Report for 09.11.2020 (please note that papers that have **NOT been peer-reviewed** are highlighted in red).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
03.11.2020	Seropositivity and risk factors for SARS-CoV-2 infection in staff working in care homes during the COVID-19 pandemic	J Infect / Letter	<ul style="list-style-type: none"> • In order to control the outbreak in four London care homes, weekly nasal swabbing was performed for all residents and staff for four weeks starting 3 May 2020 to rapidly identify and isolate infected individuals. • The authors explored risk factors for antibody positivity in staff including age, gender, co-morbidities, ethnicity, employment, household composition and travel to work. • Found SARS-CoV-2 seropositivity rates among staff working in care homes affected by COVID-19 outbreaks to be several times higher than community seroprevalence in London. • SARS-CoV-2 antibody positivity was significantly, independently and positively associated with Asian ethnicity and having a household member who also worked in care homes.
04.11.2020	Characterising heterogeneity and sero-reversion in antibody responses to mild SARS-CoV-2 infection: a cohort study using time series analysis and mechanistic modelling	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Study of 729 health care workers from the first SARS-CoV-2 epidemic peak in London, undergoing weekly symptom screen, viral PCR and blood sampling over 16-21 weeks. • A total of 157/729 (21.5%) participants developed positive SARS-CoV-2 serology by one or other assay, of whom 31% were asymptomatic and there were no deaths. • Mild SARS CoV 2 infection is associated with heterogenous serological responses in Euroimmun anti-S1 and Roche anti-NP assays. Anti-S1 responses showed faster rates of clearance, more rapid transition from high to low level production rate and greater reduction in production rate after this transition. • The application of individual assays for diagnostic and epidemiological serology requires validation in time series analysis.
05.11.2020	COVID-19 seropositivity and asymptomatic rates in healthcare workers are associated with job function and masking	Clin Infect Dis / Accepted manuscript	<ul style="list-style-type: none"> • Online assessment (demographic, clinical, exposure information) plus blood sample collected from 20,614 healthcare workers (HCWs) across Detroit, U.S. • 1,818 (8.8%) participants were seropositive between April 13 and May 28; 44% reported that asymptomatic during the month prior to blood collection. • Healthcare roles such as phlebotomy, respiratory therapy, and nursing/nursing support exhibited significantly higher seropositivity. • Direct exposure to COVID-19: N95/PAPR mask meant significantly lower

			seropositivity rate (10.2%) compared to surgical/other masks (13.1%) or no mask (17.5%).
06.11.2020	Persistence of SARS-CoV-2 specific B- and T-cell responses in convalescent COVID-19 patients 6-8 months after the infection	bioRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Cohort study of COVID-19 patients from the Lombardy region in Italy with mild to critical disease, and Swedish volunteers with mild symptoms. • Although serum levels of anti-SARS-CoV-2 IgG antibodies started to decline, virus-specific T and/or memory B cell responses increased with time and maintained during the study period (6-8 months after infection).

Diagnostics

Publication Date	Title / URL	Journal / Article type	Digest
04.11.2020	Evidence summary for the incubation period of COVID-19, or time to first positive test, in individuals exposed to SARS-CoV-2	HIQA / Evidence summary	<ul style="list-style-type: none"> • This evidence summary looked at 98 studies; with 96 containing data relevant to the incubation period, and three with data on time to first positive test in asymptomatic individuals based on serial testing. • The results of this analysis indicate that the median incubation period of COVID-19 is between five and six days. • On average, approximately 95% of individuals who experience symptoms will do so by day 14, indicating that approximately 1 in 20 develop symptoms after this time. Approximately 82% to 87% of individuals will develop symptoms by day 10, indicating that approximately one in six develop symptoms at a later date. Some individuals may take 21 days or more to exhibit symptoms; however, there is considerable uncertainty associated with the tail of the distribution.
04.11.2020	At what times during infection is SARS-CoV-2 detectable and no longer detectable using RT-PCR-based tests? A systematic review of individual participant data	BMC Med / Article	<ul style="list-style-type: none"> • Individual participant data (IPD) systematic review of longitudinal studies of RT-PCR test results in symptomatic SARS-CoV-2. • 32 studies included, with 1023 infected participants and 1619 test results, from – 6 to 66 days post-symptom onset and hospitalisation. • Highest percentage virus detection = nasopharyngeal sampling 0 - 4 days post-symptom onset at 89% (95% confidence interval (CI) 83 to 93) dropping to 54% (95% CI 47 to 61) after 10 to 14 days. • Average duration of detectable virus longer with lower respiratory tract (LRT) sampling than upper respiratory tract (URT). • Duration of faecal and respiratory tract virus detection varied greatly within individual participants. For some, virus still detectable at 46 days post-symptom onset. • RT-PCR misses detection of people with SARS-CoV-2 infection; early sampling minimises false negative diagnoses. Beyond 10 days post-symptom onset, lower RT or faecal testing may be preferred sampling sites.

- Included studies are open to substantial risk of bias, so the positivity rates are probably overestimated.

Epidemiology and clinical – risk factors

Publication Date	Title / URL	Journal / Article type	Digest
06.11.2020	ECDC to assess risk associated with spread of SARS-CoV-2 in mink farms	European Centre for Disease Prevention and Control / News story	<ul style="list-style-type: none"> • ECDC will assess the human implications of an extensive spread of SARS-CoV-2 in mink farms in Denmark, where by 3 Nov 197 farms had been affected in the country. • Denmark is currently implementing strong control measures, including culling, restrictions of movement of people living in nearby areas and enhanced testing among the general population. • The Danish public health agency, Statens Serum Institut (SSI), has identified seven unique mutations in the spike protein of the SARS-CoV-2 variants in mink. This variant has also been identified in human cases. • The possibility of an antigenic mutation in SARS-CoV-2 may have implications for immunity, reinfections and the effectiveness of COVID-19 vaccines, but there is currently a high level of uncertainty over this. • Further analyses and scientific studies are needed to better understand the identified mutations and their potential implications.
05.11.2020	Characteristics and outcomes of COVID-19-associated stroke: a UK multicentre case-control study	J Neurol Neurosurg Psychiatry / Article	<ul style="list-style-type: none"> • Case-control study of stroke patients admitted to 13 hospitals in England and Scotland, between 9 Mar - 5 July: 86 with evidence of COVID-19 at stroke onset (Cases) compared with 1384 strokes admitted during same time period with no evidence of COVID-19 (Controls). • Cases with ischaemic stroke more likely: in Asians (18.8% vs 6.7%, $p<0.0002$); to involve multiple large vessel occlusions (17.9% vs 8.1%, $p<0.03$); more severe (median NIHSS 8 vs 5, $p<0.002$); associated with higher D-dimer levels ($p<0.01$), more severe disability on discharge (median mRS 4 vs 3, $p<0.0001$), inpatient death (19.8% vs 9.6%, $p<0.0001$). • Data suggest that COVID-19 may be an important modifier of the onset, characteristics and outcome of acute ischaemic stroke.
06.11.2020	Validation of home oxygen saturations as a marker of clinical deterioration in patients with suspected COVID-19	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Analysis of vital signs in 1,080 adults with a COVID-19 diagnosis who were conveyed by ambulance to two hospitals (Basingstoke & North Hampshire Hospital, or the Royal Hampshire County Hospital) between 01 Mar and 31 July. • Oxygen saturations were the most predictive of mortality or ICU admission (AUROC 0.772 (95 % CI: 0.712-0.833)), followed by the NEWS2 score (AUROC 0.715 (95 % CI: 0.670-0.760)), patient age (AUROC 0.690 (95 % CI: 0.642-0.737)), and

			<p>respiration rate (AUROC 0.662 (95 % CI: 0.599-0.729)).</p> <ul style="list-style-type: none"> Combining age with the NEWS2 score (AUROC 0.771 (95 % CI: 0.718-0.824)) or the measured oxygen saturation (AUROC 0.820 (95 % CI: 0.785-0.854)) increased the predictive ability but did not reach significance.
05.11.2020	Severity of Respiratory Infections due to SARS-CoV-2 in Working Population: Age and Body Mass Index Outweigh ABO Blood Group	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> Study of adult volunteers (N=157,544) recruited via a stem cell donation centre to identify risk factors for COVID-19 courses. A total of 7,948 reported SARS-CoV-2 detection, of which 947 (11.9%) reported asymptomatic course, 5,014 (63.1%) mild/moderate respiratory infections, and 1,987 (25%) severe respiratory tract infections. Risk of hospitalisation in comparison to a 20-year old of normal weight was 2.1-fold higher (p=0.01) for a 20-year old with BMI between 35-40 kg/m², and it was 5.33-fold higher (p<0.001) for a 55-year old with normal weight and 11.2-fold higher (p<0.001) for a 55-year old with a BMI between 35-40 kg/m². Blood group A associated with a 1.15-fold higher risk for contracting SARS-CoV-2 (p<0.001) than blood group O but did not impact COVID-19 severity.
14.10.2020	Outcomes of Nursing Home COVID-19 Patients by Initial Symptoms and Comorbidity: Results of Universal Testing of 1970 Residents	J Am Med Dir Assoc / Article	<ul style="list-style-type: none"> Assessed the association of symptom status and medical comorbidities on mortality and hospitalization risk associated with COVID-19 in residents across 15 nursing homes in Maryland. 1970 residents (mean age 73.8, 57% female, 68% black): 752 (38.2%) positive on first test. Positive plus multiple symptoms when tested: highest risk of mortality [hazard ratio (HR) 4.44, 95% confidence interval (CI) 2.97, 6.65] and hospitalization (sub hazard ratio 2.38, 95% CI 1.70, 3.33), even after accounting for comorbidity burden. Asymptomatic infection in nursing home setting was associated with increased risk of death; closer monitoring needed, particularly residents with underlying cardiovascular and respiratory comorbidities.

Epidemiology and clinical – other

Publication Date	Title / URL	Journal / Article type	Digest
03.11.2020	Persistence of viral RNA, pneumocyte syncytia and thrombosis are hallmarks of advanced COVID-19 pathology	EBioMedicine / Article	<ul style="list-style-type: none"> Report the systematic analysis of 41 consecutive post-mortem samples from individuals who died of COVID-19. Concluded that COVID-19 is a unique disease characterized by extensive lung thrombosis, long-term persistence of viral RNA in pneumocytes and endothelial cells, along with the presence of infected cell syncytia. Several of COVID-19 features might be consequent to the persistence of virus-infected cells for the duration of the disease.

Transmission

Publication Date	Title / URL	Journal / Article type	Digest
06.11.2020	Seasonality and its impact on COVID-19, 22 October 2020	Gov.uk / Research and analysis	<ul style="list-style-type: none"> • Paper prepared by NERVTAG and EMG on seasonality and its impact on COVID-19. • The direct effect of winter environmental conditions on transmission is likely to be small. Winter conditions will increase viral persistence on outdoor surfaces due to reduced temperatures and UV levels, in unheated indoor environments due to lower temperatures and in day-time outdoor aerosols due to reduced UV levels (high confidence). However, the outdoor environment is not dominant in SARS-CoV-2 transmission, and indoor environmental conditions (where the vast majority of transmission is likely to occur) are more constant. • It seems likely that co-infection with influenza viruses worsens the clinical course (medium confidence). • There is no evidence, at present, to suggest that other physiological changes that may occur over winter will affect the severity of disease.
06.11.2020	SARS-COV-2: Transmission Routes and Environments, 22 October 2020	Gov.uk / Research and analysis	<ul style="list-style-type: none"> • Paper prepared by EMG and NERVTAG on SARS-COV-2 transmission routes and environments. • Evidence continues to indicate the SARS-CoV-2 can be transmitted by three main routes: close-range respiratory droplets and aerosols, longer range respiratory aerosols, and direct contact with surfaces contaminated with virus. Close-range transmission is likely to be the most significant, but there is not yet sufficient evidence to confidently separate out the relative importance of these routes or how they vary between settings. • A wide range of social, residential and workplace settings have been associated with transmission. • Evidence continues to suggest that super-spreading events may play a very important role in the epidemic. Estimates suggest that fewer than 20% of infections lead to approximately 80% of secondary cases.

Infection control / non-pharmaceutical interventions

Publication Date	Title / URL	Journal / Article type	Digest
04.11.2020	Rapid review of recommendations from international guidance on the duration of restriction of movements	HIQA / Rapid review	<ul style="list-style-type: none"> • Updated rapid review of recommendations from international guidance on the duration of restriction of movements. • Included International public health recommendations, from a predefined list of 22 countries and four agencies.
04.11.2020	What is the current evidence for the effectiveness of using a visor rather than a surgical face mask in preventing the transmission of COVID-19 in a healthcare setting?	HSE / Evidence summary	<ul style="list-style-type: none"> • Summary of the current evidence for the effectiveness of using a visor rather than a surgical face mask in preventing the transmission of COVID-19 in a healthcare setting.
06.11.2020	Declines in SARS-CoV-2 Transmission, Hospitalizations, and Mortality After Implementation of Mitigation Measures— Delaware, March–June 2020	MMWR Morb Mortal Wkly Rep / Report (early release)	<ul style="list-style-type: none"> • State-mandated stay-at-home orders and public mask mandates coupled with case investigations with contact tracing contributed to an 82% reduction in COVID-19 incidence, 88% reduction in hospitalizations, and 100% reduction in mortality in Delaware during late April–June. • The combination of state-mandated community mitigation efforts and routine public health interventions can reduce the occurrence of new COVID-19 cases, hospitalizations, and deaths.
07.11.2020	Implication of backward contact tracing in the presence of overdispersed transmission in COVID-19 outbreaks	Wellcome Open Res / Article	<ul style="list-style-type: none"> • Backward contact tracing identifies source of newly detected cases; authors estimated typical size of clusters reachable / simulated incremental effectiveness of combining backward tracing with conventional forward tracing. • Expected to identify a primary case generating 3-10 times more infections than average, typically increasing proportion of subsequent cases averted by a factor of 2-3. • Backward contact tracing can be an effective tool for outbreak control, especially in presence of overdispersion as observed with SARS-CoV-2.

Treatment

Publication Date	Title / URL	Journal / Article type	Digest
04.11.2020	Selection, biophysical and structural analysis of synthetic nanobodies that effectively neutralize SARS-CoV-2	Nat Commun / Article	<ul style="list-style-type: none"> • Authors report the rapid isolation and characterization of nanobodies from a synthetic library, known as sybodies (Sb), that target the receptor-binding domain (RBD) of the SARS-CoV-2 spike protein. • Sb23 displayed high affinity and neutralized pseudovirus with an IC50 of 0.6 µg/ml. A cryo-EM structure of the spike bound to Sb23 showed that Sb23 binds competitively in the ACE2 binding site.

- The cryo-EM reconstruction revealed an unusual conformation of the spike where two RBDs are in the 'up' ACE2-binding conformation.
- The combined approach represents an alternative, fast workflow to select binders with neutralizing activity against newly emerging viruses.

Overviews, comments and editorials

Publication Date	Title / URL	Journal / Article type
07.11.2020	Mink-strain of COVID-19 virus in Denmark	WHO / News
04.11.2020	Challenges in creating herd immunity to SARS-CoV-2 infection by mass vaccination	Lancet / Comment
05.11.2020	Do point-of-care tests (POCTs) offer a new paradigm for the management of patients with influenza?	Eurosurveillance / Perspective

Produced by the PHE COVID-19 Literature Digest Team

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