COVID-19 Literature Digest – 09/10/2020

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, contains new data / insights or emerging trends. The Digest team generate a report three times per week (Mon, Wed, Fri), which includes both preliminary reports of work (preprints) that have NOT been peer-reviewed and research that has been subject to peer review and wider scrutiny.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,

Bláthnaid Mahon, Emma Farrow, James Robinson
On behalf of the PHE COVID-19 Literature Digest Team
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Report for 09.10.2020 (please note that papers that have **NOT been peer-reviewed** are highlighted in red).

Sections:

Serology and immunology

Publication Date	Title / URL	Journal / Article type	Digest
06.10.2020	Risk for SARS-CoV-2 Infection in Healthcare Workers, Turin, Italy	Emerg Infect Dis / Research Letter	• The authors measured SARS-CoV-2 spike protein subunits S1/S2 antibodies by using capillary electrophoresis and a chemiluminescence immunoassay for 5,444 active healthcare workers in Italy. • Seroprevalence was 6.9% and higher among participants having contact with patients. • Seroconversion was not observed in 37/213 previously infected participants.
08.10.2020	Prevalence of SARS-CoV-2 Antibodies among Swiss Hospital Workers - Results of a Prospective Cohort Study	Infect Control Hosp Epidemiol / Communication	• In this prospective cohort of 1,012 Swiss hospital employees, three different assays were used to screen serum for SARS-CoV-2 antibodies. • Seropositivity was 1%; the positive predictive value of the lateral-flow immunoassay was 64% (IgG) and 13% (IgM). • History of fever and myalgia most effectively differentiated seropositive and seronegative participants.
07.10.2020	Extrafollicular B cell responses correlate with neutralizing antibodies and morbidity in COVID-19	Nat Immunol / Article	• The authors performed detailed characterization of B cell responses through high-dimensional flow cytometry to reveal substantial heterogeneity in both effector and immature populations. • Overall, findings suggest a pathogenic role for immune activation in subsets of patients with COVID-19.

Diagnostics

Publication Date	Title / URL	Journal / Article type	Digest
08.10.2020	Clinical impact of molecular point-of-care testing for suspected COVID-19 in hospital (COV-19POC): a prospective, interventional, non-randomised, controlled study	Lancet Respiratory Medicine / Article	• A prospective, interventional, non-randomised, controlled study of molecular point-of-care testing in patients aged 18 years or older presenting with suspected COVID-19 to the emergency department or other acute areas of Southampton General Hospital. • Between Mar 20 and April 29, 2020, 499 were recruited to the point-of-care testing group and tested by the QIAstat-Dx Respiratory SARS-CoV-2 Panel. 555 were included in the control group and tested by laboratory PCR. The two groups were similar with regard to the distribution of sex, age, and ethnicity.

			• 197 (39%) patients in the point-of-care testing group and 155 (28%) in the control group tested positive for COVID-19. Median time to results was 1·7 h (IQR 1·6–1·9) in the point-of-care testing group and 21·3 h (16·0–27·9) in the control group.
02.10.2020	[Antigen-based testing but not real-time PCR correlates with SARS-CoV-2 virus culture](#)	medRxiv (non-peer reviewed) / Article	• Using the BD Veritor System for Rapid Detection of SARS-CoV-2 later flow antigen detection test, the authors demonstrate a higher concordance of antigen-positive test results with the presence of cultured, infectious virus when compared to RT-PCR. • When compared to infectious virus isolation, the sensitivity of antigen-based testing is similar to RT-PCR. • The correlation between SARS-CoV-2 antigen and SARS-CoV-2 culture represents a significant advancement in determining the risk for potential transmissibility beyond that which can be achieved by detection of SARS-CoV-2 genomic RNA. • Suggests antigen-based testing could facilitate effective implementation of testing and public health interventions to better contain COVID-19.

Genomics

Publication Date	Title / URL	Journal / Article type	Digest
07.10.2020	[Analysis of Genomic Characteristics and Transmission Routes of Patients With Confirmed SARS-CoV-2 in Southern California During the Early Stage of the US COVID-19 Pandemic](#)	JAMA Netw Open / Original investigation	• 192 consecutive COVID-19 patients genomes sequenced. • Los Angeles isolates pinpointed i) community transmission of 13 patients within a 3.81 km2 radius; ii) cluster of 10 patients that contained 5 residents at a skilled nursing facility, 1 resident of a nearby skilled nursing facility, 3 health care workers, and a family member of a resident of one of the skilled nursing facilities; iii) Person-to-person transmission in a cluster of 5 patients who shared the same single-nucleotide variation. • High viral genomic diversity identified: 20 Los Angeles isolates (15.0%) resembled genomes from Asia; 109 Los Angeles isolates (82.0%) similar to isolates originating from Europe. • Findings highlight precision of detecting person-to-person transmission and accurate contact tracing directly through genome isolation and sequencing.
06.10.2020	[Inference of person-to-person transmission of COVID-19 reveals hidden super-spreading events during the early outbreak phase](#)	Nat Commun / Article	• Analysed 208 publicly available SARS-CoV-2 genome sequences collected during the early outbreak phase. • Combined phylogenetic analysis with Bayesian inference under an epidemiological model to trace person-to-person transmission. The dispersion parameter of the offspring distribution in the inferred transmission chain was

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			estimated to be 0.23 (95% CI: 0.13–0.38), indicating there are individuals who directly infected a disproportionately large number of people. • Results showed that super-spreading events played an important role in the early stage of the COVID-19 outbreak.
06.10.2020	MAJORA: Continuous integration supporting decentralised sequencing for SARS-CoV-2 genomic surveillance	bioRxiv (non-peer reviewed) / Article	• Describes the development and deployment of MAJORA, a digital infrastructure to address the challenge of collecting and integrating both genomic sequencing data and sample-associated metadata produced across the COVID-19 Genomics UK (COG-UK) network. • The system was designed and implemented pragmatically to stand up capacity rapidly in a pandemic caused by a novel virus.

Epidemiology and clinical – risk factors

Publication Date	Title / URL	Journal / Article type	Digest
06.10.2020	Low-density lipoprotein cholesterol levels are associated with poor clinical outcomes in COVID-19	medRxiv (non-peer reviewed) / Article	• A retrospective study of consecutively admitted COVID-19 patients (n=654) at a Spanish hospital evaluated the association of lipid markers with 30-day all-cause mortality. Estimated 30-day mortality was 22.8% (n=149). • Non-survivors had lower total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-c) levels during the entire course of the disease with complete resolution among survivors. • Both showed a significant inverse correlation with inflammatory markers and a positive correlation with lymphocyte count. • In a multivariate analysis, LDL-c < 69 mg/dl, C-reactive protein > 88 mg/dl, and lymphopenia < 1000 cells/ml at admission were independently associated with 30-day mortality. This association was maintained 7 days after admission.
07.10.2020	Increased risk of COVID-19 infection and mortality in people with mental disorders: analysis from electronic health records in the United States	World Psychiatry / Research report	• Analysed a nation-wide database of electronic health records of 61 million adult patients from 360 hospitals and 317,000 providers, across 50 states in the US, up to July 29, 2020. • Findings identify individuals with a recent diagnosis of a mental disorder as being at increased risk for COVID-19 infection, which is further exacerbated among African Americans and women, and as having a higher frequency of some adverse outcomes of the infection. • This evidence highlights the need to identify and address modifiable vulnerability factors for COVID-19 infection and to prevent delays in health care provision in this population.

06.10.2020	[Machine learning based early warning system enables accurate mortality risk prediction for COVID-19](#)	Nat Commun / Article	• Present a mortality risk prediction model for COVID-19 (MRPMC) that uses patients' clinical data on admission to stratify patients by mortality risk, which enables prediction of physiological deterioration and death up to 20 days in advance.
07.10.2020	[A novel severity score to predict inpatient mortality in COVID-19 patients](#)	Sci Rep / Article	• Authors propose a novel severity score specifically for COVID-19 to help predict disease severity and mortality; 4711 COVID-19 patients included. • A COVID-19 severity score ranging from 0 to 10, consisting of age, oxygen saturation, mean arterial pressure, blood urea nitrogen, C-Reactive protein, and the international normalized ratio was developed.

Epidemiology and clinical – long term complications / sequelae

Publication Date	Title / URL	Journal / Article type	Digest
05.10.2020	[Follow-up of adults with non-critical COVID-19 two months after symptoms' onset](#)	Clin Microbiol Infect / Article	• A descriptive clinical follow-up (days 7, 30 and 60) of 150 patients with non-critical COVID-19 at Tours University Hospital, France, from 17 March to 3 June 2020. • Up to 2 months after symptom onset, two thirds of adults with non-critical COVID-19 had complaints, mainly anosmia/ageusia, dyspnea or asthenia.

Epidemiology and clinical – other

Publication Date	Title / URL	Journal / Article type	Digest
08.10.2020	[Deaths due to COVID-19 compared with deaths from influenza and pneumonia](#)	Gov.uk / Official statistics	• Of all death occurrences between Jan and Aug 2020 in England and Wales, there were 48,168 deaths due to COVID-19 compared with 13,619 deaths due to pneumonia and 394 due to influenza.
06.10.2020	[Deep phenotyping of 34,128 adult patients hospitalised with COVID-19 in an international network study](#)	Nat Commun / Article	• Authors summarise characteristics of hospitalised COVID-19 adults compared with influenza patients. • 34,128 (US: 8362, South Korea: 7341, Spain: 18,425) COVID-19 patients, summarising between 4811 and 11,643 unique aggregate characteristics. • Compared to 84,585 individuals hospitalised with influenza in 2014-19, COVID-19 patients typically male, younger, fewer comorbidities, lower medication use.
07.10.2020	[Stringent containment measures without complete city lockdown to achieve low incidence and mortality across two waves of COVID-19 in Hong Kong](#)	BMJ Glob Health / Original research	• Analysed first 1038 Hong Kong cases (Jan 23 - April 25): epidemiological characteristics including age/gender-specific incidence, clustering, R number (R(t)) and containment delay; in relation to the containment measures implemented. • Aggressive escalation of border control correlated with reductions in Rt from 1.35 to 0.57 and 0.92 to 0.18, and aversions of 450 and 1650 local infections

			during the first and second waves, respectively. • Implementing COVID-19 tests for overseas returners correlated with upsurge of asymptomatic case detection / shortened containment delay in second wave. • Medium-sized cluster events: family gatherings in first wave; leisure activities among youngsters in second wave. • A higher incidence rate was observed for males, raising possibility of gender predilection in susceptibility of developing symptoms.
08.10.2020	Epidemiological parameters of COVID-19 and its implication for infectivity among patients in China, 1 January to 11 February 2020	Eurosurveillance / Research	• Estimated the distributions of four epidemiological parameters of SARS-CoV-2 transmission using a large database of COVID-19 cases and potential transmission pairs of cases, and assessed their heterogeneity by demographics, epidemic phase and geographical region. • The median incubation period was 7.2 days. Paediatric cases < 18 years had a longer incubation period than adult age groups (p = 0.007). • The median incubation period increased from 4.4 days before 25 Jan to 11.5 days after 31 Jan (p < 0.001), whereas the median serial (generation) interval contracted from 5.9 (4.8) days before 25 January to 3.4 (3.7) days after. • The median time from symptom onset to discharge was also shortened from 18.3 before 22 January to 14.1 days after. • Peak infectivity occurred 1 day before symptom onset on average, and the incubation period accounted for 70% of transmission.
06.10.2020	Plasma ACE2 activity is persistently elevated following SARS-CoV-2 infection: implications for COVID-19 pathogenesis and consequences	medRxiv (non-peer reviewed) / Article	• Plasma ACE2 catalytic activity was measured in a cohort of Australian adults who had recovered from mild, moderate or severe SARS-CoV-2 infection (n=66) and matched uninfected controls (n=70). • Plasma ACE2 activity at a median of 35 days post-infection was 97-fold higher in recovered SARS-CoV-2 patients compared to controls (p<0.0001). • There was a significant difference in plasma ACE2 activity according to disease severity (p=0.033), with severe COVID-19 associated with higher ACE2 activity compared to mild disease (p=0.027). • The authors state this is the first description that plasma ACE2 activity is elevated after COVID-19 infection, and the first with longitudinal data indicating plasma ACE2 activity remains elevated out to a median of 114 days post-infection.

Infection control

Publication Date	Title / URL	Journal / Article type	Digest
09.10.2020	[Characteristics Associated with Adults Remembering to Wash Hands in Multiple Situations Before and During the COVID-19 Pandemic - United States, October 2019 and June 2020](#)	MMWR Morb Mortal Wkly Rep / Article	• U.S. adult Internet survey respondents in June 2020 were more likely to remember to wash their hands after experiencing respiratory symptoms, before eating in a restaurant, and before eating at home than were Oct 2019 survey respondents. • Importance of promoting frequent handwashing during pandemic, especially after coughing, sneezing, and blowing one's nose. • Men, young adults, and White adults continue to be less likely to remember to wash their hands, despite improvements made from 2019 to 2020.
05.10.2020	[Efficacy of face masks, neck gaiters and face shields for reducing the expulsion of simulated cough-generated aerosols](#)	medRxiv (non-peer reviewed) / Article	• A cough aerosol simulator with a headform was used to propel small aerosol particles (0 to 7 µm) into different face coverings. • The amount of cough aerosol blocked was as follows: N95 respirator (99%); procedure mask (59%); 3-ply cloth face mask (51%); polyester neck gaiter as a single layer (47%) and folded into a double layer (60%); face shield (2%).

Treatment

Publication Date	Title / URL	Journal / Article type	Digest
08.10.2020	[Remdesivir for the Treatment of Covid-19 — Final Report](#)	N Engl J Med / Article	• Conducted a double-blind, randomized, placebo-controlled trial of intravenous remdesivir in adults who were hospitalized with Covid-19 and had evidence of lower respiratory tract infection. • Patients were randomly assigned to receive either remdesivir (200 mg loading dose on day 1, followed by 100 mg daily for up to 9 additional days) or placebo for up to 10 days. The primary outcome was the time to recovery, defined by either discharge from the hospital or hospitalization for infection-control purposes only. • A total of 1062 patients underwent randomization (with 541 assigned to remdesivir and 521 to placebo). • Data show that remdesivir was superior to placebo in shortening the time to recovery in adults who were hospitalized with Covid-19 and had evidence of lower respiratory tract infection.
08.10.2020	[Compassionate Use of Remdesivir in Pregnant Women with Severe Covid-19](#)	Clin Infect Dis / Article	• Among 86 pregnant and postpartum women with severe COVID-19 who received compassionate use remdesivir, recovery rates were high, with a low rate of serious adverse events.

08.10.2020	[Effect of Hydroxychloroquine in Hospitalized Patients with Covid-19](#)	N Engl J Med / Article	• In this randomized, controlled, open-label platform trial comparing a range of possible treatments with usual care in patients hospitalized with Covid-19, they randomly assigned 1561 patients to receive hydroxychloroquine and 3155 to receive usual care. The primary outcome was 28-day mortality. • Among patients hospitalized with Covid-19, those who received hydroxychloroquine did not have a lower incidence of death at 28 days than those who received usual care.
06.10.2020	[Characteristics and outcomes of acute respiratory distress syndrome related to COVID-19 in Belgian and French intensive care units according to antiviral strategies: the COVADIS multicentre observational study](#)	Ann Intensive Care / Research	• In a multicentre observational study of moderate-to-severe Covid-19 related acute respiratory distress syndrome patients (n=415), treatment with hydroxychloroquine (n=220) or lopinavir/ritonavir (n=57) was not associated with higher ventilator-free days at day 28 compared with standard care (n=85). • The use of lopinavir/ritonavir treatment was associated with an increased need for renal replacement therapy.
06.10.2020	[Real-World Effectiveness of hydroxychloroquine, azithromycin, and ivermectin among hospitalized COVID-19 patients: Results of a target trial emulation using observational data from a nationwide Healthcare System in Peru](#)	medRxiv (non-peer reviewed) / Article	• A retrospective cohort study of 5683 hospitalised adult COVID-19 patients in Peru examined outcomes for those receiving standard care (n=2630) and five treatment groups: hydroxychloroquine/chloroquine alone (HCQ; n=200), ivermectin alone (IVM; n=203), azithromycin alone (AZIT; n=1600), HCQ + AZIT (n=692), and IVM + AZIT (n=358) within 48 hours of admission. • The AZIT + HCQ group was associated with 84% higher all-cause mortality hazard rate compared to standard care (wHR=1.84, 95%CI 1.12-3.02). • Consistently, AZIT + HCQ treatment was associated with deaths or ICU transfer ICU (wHR=1.49, 95%CI 1.01-2.19), and deaths or oxygen prescription (wHR=1.70, 95%CI 1.07-2.69). • HCQ treatment was only associated with death or oxygen prescription (wHR=1.77, 95% CI 1.01-3.11), and IVM was only associated with death or ICU transfer (wHR=1.58, 95%CI 1.11-2.25). • No effect was found for AZIT or AZIT + IVM.
06.10.2020	[Sofosbuvir terminated RNA is more resistant to SARS-CoV-2 proofreader than RNA terminated by Remdesivir](#)	Sci Rep / Article	• Report here that sofosbuvir terminated RNA resists removal by the exonuclease to a substantially higher extent than RNA terminated by remdesivir, another drug being used as a COVID-19 therapeutic. These results offer a molecular basis supporting the current use of sofosbuvir in combination with other drugs in COVID-19 clinical trials.

Modelling

Publication Date	Title / URL	Journal / Article type	Digest
07.10.2020	Effect of school closures on mortality from coronavirus disease 2019: old and new predictions	BMJ / Research	• Presents independent calculations using the CovidSim code, which implements Imperial College London's individual based model, to consider the spread of Covid-19 in Great Britain and Northern Ireland. • The CovidSim model would have produced a good forecast of subsequent data if initialised with a reproduction number of about 3.5. • Predicts school closures and isolation of younger people would increase the total number of deaths, albeit postponed to a second and subsequent waves. • Suggests prompt interventions were shown to be highly effective at reducing peak demand for intensive care unit beds but also prolong the epidemic, in some cases resulting in more deaths long term because Covid-19 mortality is highly skewed towards older age groups. • In the absence of an effective vaccination programme, none of the proposed mitigation strategies in the UK would reduce the predicted total number of deaths below 200,000.
28.09.2020	Modelling the potential impact of mask use in schools and society on COVID-19 control in the UK	medRxiv (non-peer reviewed) / Article	• Assessed the potential importance of mandatory masks in parts of community and in secondary schools. • Demonstrates that, assuming current test-trace-isolate (TTI) levels, adoption of masks in secondary schools in addition to community settings can reduce the size of a second wave, but will not prevent it. • To avoid a second wave in these circumstances, 68% or 46% of those with symptomatic infection would need to be tested if masks' effective coverage were 15% or 30% respectively, compared to 76% and 57% if masks are mandated in community settings but not secondary schools.

Overviews, comments and editorials

Publication Date	Title / URL	Journal / Article type
05.10.2020	Long-term Health Consequences of COVID-19	Jama / Viewpoint
06.10.2020	Cross-reactive memory T cells and herd immunity to SARS-CoV-2	Nat Rev Immunol / Perspective
06.10.2020	Do cross-reactive antibodies cause neuropathology in COVID-19?	Nat Rev Immunol / Comment
01.10.2020	Cerebrospinal fluid findings in COVID-19 indicate autoimmunity	Lancet Microbe / Correspondence
05.10.2020	Covid-19: how to prioritize worse-off populations in allocating safe and effective vaccines	Bmj / Feature

08.10.2020	Living with the COVID-19 pandemic: act now with the tools we have	Lancet / Comment
07.10.2020	Covid-19, Ebola, and HIV - Leveraging Lessons to Maximize Impact	N Engl J Med / Perspective
08.10.2020	Near-patient SARS-CoV-2 molecular platforms: new-old tools for new-old problems	Lancet Respiratory Medicine / Comment
07.10.2020	Many small steps towards a COVID-19 drug	Nat Commun /Comment
08.10.2020	China's successful control of COVID-19	Lancet Infectious Diseases / Newsdesk

Produced by the PHE COVID-19 Literature Digest Team

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