



COVID-19 Literature Digest – 16/10/2020

Dear all,

This week's guest editor is Dr André Charlett who heads PHE's Statistics, Modelling and Economics Department and is currently working within the PHE Joint Modelling Cell.

If you only read three papers this week...

We are currently observing widespread, increasing incidence of SARS-CoV-2 across England. Understanding transmission is critical to enable effective control measures to be instigated, and the three papers I have picked hang together around this theme.

Concerns around SARS-CoV-2 transmission as students from across the country return to universities have been subject to a large amount of deliberation. A recent [paper](#) in MMWR describes the epidemiology of 18 to 22 year old adults in the USA. During the period August 2 to September 5, COVID-19 cases increased by 55% nationally in persons aged 18 to 22 years old, with heterogeneity observed between regions. Increases in reported incidence and test positivity were absent in other age groups. Some of this increase is likely to reflect ascertainment from increased testing. However, the picture presented shows increasing case numbers in the age group containing most university students. Mitigation and preventive measures targeted to young adults is recommended.

The question of whether super-spreading events (SSEs) "kick-started" this pandemic has been studied by [Wang et al.](#) Using phylogenetic analyses of 208 sequences from the initial phase of the outbreak in China, they estimate the offspring distribution. This is the distribution of the number of secondary cases caused by each case, the mean of which provides an estimate of R_0 . Assuming a negative binomial model for this distribution, they estimate the mean to be 1.23 (95% credible interval (CI) 1.09 to 1.39) and the variance 8.35 (95% CI 5.06 to 13.39). The dispersion estimate for this distribution was 0.23 (95% CI 0.13 to 0.39), providing a strong indication of SSEs during the initial phase. Results are in line with SARS and Ebola, for which SSEs are well recognised. This study highlights the importance of recognising such events in the initial stages, as they can greatly aggravate the spread of COVID-19.

Finally, a very interesting analysis of an outbreak in a German meat packing plant is provided by [Gunther et al.](#) This is also shown to be a SSE with an index case in May, who caused 27 secondary cases among fellow early shift workers. They describe a situation of limited ability to social distance due to production needs, low levels of air exchange, and physically demanding work leading to heavy breathing. Notable is distances in excess of 8 metres over which infections were transmitted in this environment, with their analysis pointing towards aerosol rather than droplet transmission. Eventually a total of 1,413 cases were detected in this outbreak.

André

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

Report for 16.10.2020 (please note that papers that have **NOT been peer-reviewed** are highlighted in red).

Sections:

[Serology and immunology](#)

[Diagnostics](#)

[Epidemiology and clinical – children / pregnancy](#)

[Epidemiology and clinical – risk factors](#)

[Epidemiology and clinical – long term complications / sequelae](#)

[Epidemiology and clinical – other](#)

[Infection control / non-pharmaceutical interventions](#)

[Treatment](#)

[Vaccine development](#)

[Modelling](#)

[Guidance and consensus statements \(no digest\)](#)

[Overviews, comments and editorials \(no digest\)](#)

Serology and immunology

Publication Date	Title / URL	Journal / Article type	Digest
------------------	-------------	------------------------	--------

13.10.2020	Orthogonal SARS-CoV-2 Serological Assays Enable Surveillance of Low Prevalence Communities and Reveal Durable Humoral Immunity	Immunity / Report	<ul style="list-style-type: none"> • Conducted a serological study to define correlates of immunity against SARS-CoV-2. Relative to mild COVID-19 cases, individuals with severe disease exhibited elevated virus-neutralizing titres and antibodies against nucleocapsid (N) and the receptor binding domain (RBD) of spike protein. Age and sex played lesser roles. • Inclusion of multiple independent assays improved the accuracy of antibody tests in low seroprevalence communities and revealed differences in antibody kinetics depending on the antigen. • Conclude that neutralizing antibodies are stably produced for at least 5-7 months after SARS-CoV-2 infection.
08.10.2020	Persistence of serum and saliva antibody responses to SARS-CoV-2 spike antigens in COVID-19 patients	Sci Immunol / Article	<ul style="list-style-type: none"> • Profiled IgG, IgA and IgM responses to the SARS-CoV-2 spike protein and its receptor-binding domain (RBD) in serum and saliva of acute and convalescent patients with laboratory-diagnosed COVID-19 ranging from 3–115 days post-symptom onset (PSO), compared to negative controls. • This study confirms that serum and saliva IgG antibodies to SARS-CoV-2 are maintained in the majority of COVID-19 patients for at least 3 months PSO. IgG responses in saliva may serve as a surrogate measure of systemic immunity to SARS-CoV-2 based on their correlation with serum IgG responses.
08.10.2020	Persistence and decay of human antibody responses to the receptor binding domain of SARS-CoV-2 spike protein in COVID-19 patients	Sci Immunol / Article	<ul style="list-style-type: none"> • Measured plasma and/or serum antibody responses to the receptor-binding domain (RBD) of the spike (S) protein of SARS-CoV-2 in 343 North American patients infected with SARS-CoV-2 (of which 93% required hospitalization) up to 122 days after symptom onset and compared them to responses in 1548 individuals whose blood samples were obtained prior to the pandemic. • Data suggest that RBD-targeted antibodies are excellent markers of previous and recent infection, that differential isotype measurements can help distinguish between recent and older infections, and that IgG responses persist over the first few months after infection and are highly correlated with neutralizing antibodies. • Observed no cross-reactivity of the SARS-CoV-2 RBD-targeted antibodies with other widely circulating coronaviruses (HKU1, 229 E, OC43, NL63).
13.10.2020	Healthcare workers with mild / asymptomatic SARS-CoV-2 infection show T cell responses and neutralising antibodies after the first wave	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Cross-sectional, case-control study of 136 healthcare workers (HCW) at 16-18 weeks after UK lockdown, with 76 having had laboratory-confirmed SARS-CoV-2 mild or asymptomatic infection. • Data suggests the majority of HCW with mild or asymptomatic SARS-CoV-2 infection carry neutralising antibodies complemented by multi-specific T cell responses for at least 4 months after mild or asymptomatic SARS-CoV-2 infection.
13.10.2020	IgM autoantibodies recognizing ACE2 are associated with severe COVID-19	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Demonstrates robust IgM autoantibodies that recognize angiotensin converting enzyme-2 (ACE2) in 18/66 (27%) patients with severe COVID-19, which are rare (2/52; 3.8%) in hospitalised patients who are not ventilated. • The antibodies do not undergo class-switching to IgG, suggesting a T-

			<p>independent antibody response.</p> <ul style="list-style-type: none"> • Pathological analysis of lung obtained at autopsy shows endothelial cell staining for IgM in blood vessels in some patients. • Authors propose that vascular endothelial ACE2 expression focuses the pathogenic effects of these autoantibodies on blood vessels, and contributes to the angiocentric pathology observed in some severe COVID-19 patients.
--	--	--	---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------

Diagnostics

Publication Date	Title / URL	Journal / Article type	Digest
09.10.2020	Development and evaluation of an artificial intelligence system for COVID-19 diagnosis	Nat Commun / Article	<ul style="list-style-type: none"> • Developed and evaluated an artificial intelligence (AI) system for rapid COVID-19 detection on a large dataset with more than 10,00 CT volumes from COVID-19, influenza-A/B, non-viral community acquired pneumonia (CAP) and non-pneumonia subjects.

Epidemiology and clinical – children / pregnancy

Publication Date	Title / URL	Journal / Article type	Digest
15.10.2020	Synthesis and systematic review of reported neonatal SARS-CoV-2 infections	Nature Communications / Article	<ul style="list-style-type: none"> • Present a meta-analysis of 176 published cases of neonatal SARS-CoV-2 infections that were defined by at least one positive nasopharyngeal swab and/or the presence of specific IgM. • 70% and 30% of infections are due to environmental and vertical transmission. • 55% of infected neonates developed COVID-19; the most common symptoms were fever (44%), gastrointestinal (36%), respiratory (52%) and neurological manifestations (18%), and lung imaging was abnormal in 64% of cases. • A lack of mother–neonate separation from birth is associated with late SARS-CoV-2 infection, while breastfeeding is not.
13.10.2020	Clinical characteristics, symptoms, management and health outcomes in 8,598 pregnant women diagnosed with COVID-19 compared to 27,510 with seasonal influenza in France, Spain and the US: a network cohort analysis	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Examined aspects of COVID-19 in pregnant women (8,598 women diagnosed with COVID-19, of which 2,031 hospitalised), and in comparison to pregnant women with influenza. • Comorbidities more prevalent with COVID-19 hospitalisation (compared to COVID-19 diagnosed) in pregnancy included renal impairment (2.2% diagnosed vs 5.1% hospitalised) and anaemia (15.5% diagnosed vs 21.3% hospitalised). • Multiple medications were used to treat pregnant women hospitalised with COVID-19, some with little evidence of benefit. • Anosmia and dyspnea were indicative symptoms of COVID-19 in pregnancy

			<p>compared to influenza.</p> <ul style="list-style-type: none"> • Despite low fatality (N<5 in each of 6 databases), pregnancy and maternal outcomes were worse in COVID-19 than influenza.
11.10.2020	What is the evidence for transmission of COVID-19 by children in schools? A living systematic review	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Investigates the extent of SARS-CoV-2 transmission in schools (2,178 articles retrieved, 11 studies included). • Five cohort studies reported a combined 22 student and 21 staff index cases that exposed 3,345 contacts with 18 transmissions [overall infection attack rate (IAR): 0.08% (95% CI: 0.00%-0.86%)]. IARs for students and school staff were 0.15% (95% CI: 0.00%-0.93%) and 0.70% (95% CI: 0.00%-3.56%) respectively. • Six cross-sectional studies reported 639 SARS-CoV-2 positive cases in 6,682 study participants tested [overall positivity rate: 8.00% (95% CI: 2.17%-16.95%)]. • Positivity rate was estimated to be 8.74% (95% CI: 2.34%-18.53%) among students, compared to 13.68% (95% CI: 1.68%-33.89%) among school staff. • Overall, study quality was judged to be poor with risk of performance and attrition bias.

Epidemiology and clinical – risk factors

Publication Date	Title / URL	Journal / Article type	Digest
01.01.2021	Superspreading Event of SARS-CoV-2 Infection at a Bar, Ho Chi Minh City, Vietnam	Emerg Infect Dis / Letter (early release)	<ul style="list-style-type: none"> • Report a superspreading event of SARS-CoV-2 infection initiated at a bar in Vietnam with evidence of symptomatic and asymptomatic transmission, based on ministry of health reports, patient interviews, and whole-genome sequence analysis. • Crowds in enclosed indoor settings with poor ventilation may be considered at high risk for transmission.
13.10.2020	Nightlife clusters of coronavirus disease in Tokyo between March and April 2020	Epidemiol Infect / Article	<ul style="list-style-type: none"> • Collected clinical and epidemiological information of the patients who underwent SARS-CoV-2 PCR testing at the National Centre for Global Health and Medicine, Tokyo, from 9 Mar to 26 Apr 2020. A nightlife group was defined as those who had worked at or visited the businesses. • Included 1517 individuals; 196 (12.9%) were categorized as the nightlife group. The proportion of positive test results in the nightlife group was significantly higher than that in the non-nightlife group after matching (nightlife, 63.8%; non-nightlife, 23.0%). • Exposure to nightlife businesses was significantly associated with positive SARS-CoV-2 PCR test results.

13.10.2020	Epidemiological Analysis of Patients Presenting to a West London District General Hospital Requiring Admission with Covid-19	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • A retrospective, observational case series of adults admitted with COVID-19 in a West London District General Hospital. • Local clusters of infection were identified within the target population, and appeared to correlate with higher indices of deprivation, poorer overall health and high household occupancy. • The authors suggest a role for targeted public health measures in more deprived areas.
07.10.2020	Low zinc levels at clinical admission associates with poor outcomes in COVID-19	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Study of 249 COVID-19 patients admitted to a Spanish hospital investigated whether serum zinc content influences COVID-19 disease progression and thus might represent a useful biomarker. • Serum zinc levels lower than 50 mcgg/dl at admission correlated with worse clinical presentation, longer time to reach stability, and higher mortality. • In vitro results indicate that low zinc levels favour viral expansion in SARS-CoV2 infected cells.
13.10.2020	Impact of COVID-19 on Obesity Management Services in the United Kingdom (The COMS-UK study)	Obes Surg / Brief communication	<ul style="list-style-type: none"> • This study found that the COVID-19 pandemic has had a severe impact on the services involved in the management of patients suffering from severe, complex obesity in the UK.

Epidemiology and clinical – long term complications / sequelae

Publication Date	Title / URL	Journal / Article type	Digest
15.10.2020	Living with Covid-19	NIHR / Themed review	<ul style="list-style-type: none"> • This rapid and dynamic review draws on the lived experience of patients and expert consensus as well as published evidence to better understand the impact of ongoing effects of Covid-19, how health and social care services should respond, and what future research questions might be. • There is a widespread perception that people either die, get admitted to hospital or recover after two weeks. • A major obstacle is the lack of consensus on diagnostic criteria for ongoing Covid-19. • The fluctuating and multisystem symptoms need to be acknowledged.
13.10.2020	Persistent symptoms after Covid-19: qualitative study of 114 long Covid patients and draft quality criteria for services	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Qualitative study (n = 59; female = 70%) investigating patient experiences of long Covid, accounts of accessing and receiving healthcare, and ideas for improving services. • Themes raised include: a sense of loss and stigma; difficulty accessing and navigating services; difficulty achieving a diagnosis; disjointed and siloed care; variation in standards; variable quality of the therapeutic relationship; and possible

			critical events (e.g. deterioration after being unable to access services). • Authors put forward several quality principles for a long Covid service.
--	--	--	-----------------------------------------------------------------------------------------------------------------------------------------------------------

Epidemiology and clinical – other

Publication Date	Title / URL	Journal / Article type	Digest
12.10.2020	High and increasing prevalence of SARS-CoV-2 swab positivity in England during end September beginning October 2020: REACT-1 round 5 updated report	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Presents results from the fifth round of REACT-1, with 175,000 volunteers tested across England between 18 Sept and 5 Oct. • Findings show a national prevalence of 0.60% (95% confidence interval 0.55%, 0.71%) and doubling of the virus every 29 (17, 84) days in England corresponding to an estimated national R of 1.16 (1.05, 1.27). • These results correspond to 1 in 170 people currently swab-positive for the virus and approximately 45,000 new infections each day. • At regional level, the highest prevalence is in the North West, Yorkshire and The Humber and the North East with strongest regional growth in North West, Yorkshire and The Humber and West Midlands. • Prevalence has increased in all age groups, including those at highest risk.
09.10.2020	Drivers of the higher COVID-19 incidence, morbidity and mortality among minority ethnic groups, 23 September 2020	Gov.uk / Research and analysis	<ul style="list-style-type: none"> • This paper summarises the available evidence on the epidemiology of ethnic inequalities in COVID-19 and potential explanations for differences observed.
13.10.2020	Validation of a Derived International Patient Severity Phenotype to Support COVID-19 Analytics from Electronic Health Record Data	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Developed an Electronic Health Record-based algorithm for COVID-19 severity and validated it at 12 international sites.
12.10.2020	The role of environmental factors on transmission rates of the COVID-19 outbreak: an initial assessment in two spatial scales	Sci Rep / Article	<ul style="list-style-type: none"> • Examined the spatial variability of the basic reproductive numbers of COVID-19 across provinces and cities in China and show that environmental variables alone cannot explain this variability. • Findings suggest that changes in weather (i.e., increase of temperature and humidity as spring and summer months arrive in the Northern Hemisphere) will not necessarily lead to declines in case counts without the implementation of drastic public health interventions.

Infection control / non-pharmaceutical interventions

Publication Date	Title / URL	Journal / Article type	Digest
------------------	-------------	------------------------	--------

16.10.2020	Epidemiological changes on the Isle of Wight after the launch of the NHS Test and Trace programme: a preliminary analysis	Lancet Digital Health / Article	<ul style="list-style-type: none"> • <i>This paper was previously included in the Digest as a preprint.</i> • The aim of the study was to make a preliminary assessment of the epidemiological impact of the Test and Trace programme using publicly available data. • Results show that the epidemic on the Isle of Wight was controlled quickly and effectively after the launch of Test and Trace. • Findings highlight the need for further research to determine the causes of the reduction in the spread of the disease, as these could be translated into local and national non-pharmaceutical intervention strategies in the period before a treatment or vaccination for COVID-19 becomes available.
13.10.2020	School closures and SARS-CoV-2. Evidence from Sweden's partial school closure	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Compares parents and teachers differently exposed to either open and closed schools during the COVID-19 pandemic in Sweden, but otherwise facing similar conditions. • Among parents, exposure to open rather than closed schools resulted in a small increase in PCR-confirmed infections [OR 1.15; CI95 1.03-1.27]. • Among lower secondary teachers the infection rate doubled relative to upper secondary teachers [OR 2.01; CI95 1.52-2.67], spilling over to the partners of lower secondary teachers who had a higher infection rate than their upper secondary counterparts [OR 1.30; CI95 1.00-1.68]. • When analysing COVID-19 diagnoses from healthcare visits and the incidence of severe health outcomes, results are similar for teachers but somewhat weaker for parents and teachers' partners.

Treatment

Publication Date	Title / URL	Journal / Article type	Digest
15.10.2020	Repurposed antiviral drugs for COVID-19; interim WHO SOLIDARITY trial results	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Mortality trials in hospitalised COVID-19 of four re-purposed antiviral drugs. • Across 30 countries, 11,266 adults were randomised to Remdesivir (n=2750), Hydroxychloroquine (n=954), Lopinavir (n=1411), Interferon (n=1412), Interferon plus Lopinavir (n=651), or no study drug (n=4088). • Remdesivir, Hydroxychloroquine, Lopinavir and Interferon regimens appeared to have little or no effect on hospitalized COVID-19, as indicated by overall mortality, initiation of ventilation and duration of hospital stay. • The mortality findings contain most of the randomised evidence on Remdesivir and Interferon, and are consistent with meta-analyses of mortality in all major trials.

Vaccine development

Publication Date	Title / URL	Journal / Article type	Digest
15.10.2020	Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBIBP-CorV: a randomised, double-blind, placebo-controlled, phase 1/2 trial	Lancet Infectious Diseases / Article	<ul style="list-style-type: none"> Assessed the safety and immunogenicity of an inactivated SARS-CoV-2 vaccine candidate, BBIBP-CorV, in humans. Concluded that the inactivated SARS-CoV-2 vaccine, BBIBP-CorV, is safe and well tolerated at all tested doses in two age groups (18–59 years and ≥60 years). Humoral responses against SARS-CoV-2 were induced in all vaccine recipients on day 42. Two-dose immunisation with 4 µg vaccine on days 0 and 21 or days 0 and 28 achieved higher neutralising antibody titres than the single 8 µg dose or 4 µg dose on days 0 and 14.
14.10.2020	Safety and Immunogenicity of Two RNA-Based Covid-19 Vaccine Candidates	N Engl J Med / Article	<ul style="list-style-type: none"> The safety and immunogenicity data from this U.S. phase 1 trial of two vaccine candidates in younger and older adults, added to earlier interim safety and immunogenicity data regarding BNT162b1 in younger adults from trials in Germany and the United States, support the selection of BNT162b2 for advancement to a pivotal phase 2–3 safety and efficacy evaluation.
14.10.2020	Immunogenicity of novel mRNA COVID-19 vaccine MRT5500 in mice and non-human primates	bioRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> 2P/GSAS vaccine formulation, now designated MRT5500, elicited potent nAbs as measured in two types of neutralization assays. In addition, MRT5500 elicited TH1-biased responses in both mouse and non-human primate species, a result that helps to address a hypothetical concern regarding potential vaccine-associated enhanced respiratory diseases associated with TH2-biased responses. These data position MRT5500 as a viable vaccine candidate for clinical development against COVID-19.

Modelling

Publication Date	Title / URL	Journal / Article type	Digest
13.10.2020	Precautionary breaks: planned, limited duration circuit breaks to control the prevalence of COVID-19	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> Age-structured models matched to the UK epidemic are used to investigate the potential impact of 'precautionary breaks' (a limited period of strict non-pharmaceutical interventions) on the prevalence of infection, and the total number of predicted hospitalisations or deaths. Suggests precautionary breaks provide the biggest gains when the growth rate is low, but may offer a much needed break on increasing infection when the growth rate is higher.

Guidance and consensus statements

Publication Date	Title / URL	Journal / Article type
16.10.2020	Guidance for discharge and ending of isolation of people with COVID-19	European Centre for Disease Prevention and Control / Technical report
09.10.2020	Strategic considerations in preparing for deployment of COVID-19 vaccine and vaccination in the WHO European Region	WHO Europe / Strategic considerations

Overviews, comments and editorials

Publication Date	Title / URL	Journal / Article type
15.10.2020	A promising inactivated whole-virion SARS-CoV-2 vaccine	Lancet Infectious Diseases / Comment
09.10.2020	COVID-19 and care homes - update paper, 23 September 2020	Gov.uk / Research and analysis
14.10.2020	Towards better contact-tracing in the UK	Lancet Digital Health / Comment
15.10.2020	Scientific consensus on the COVID-19 pandemic: we need to act now	Lancet / Correspondence
08.10.2020	The necessity for intra-action reviews during the COVID-19 pandemic	Lancet Glob Health / Comment
15.10.2020	The Lombardy region of Italy launches the first investigative COVID-19 commission	Lancet / Correspondence
01.11.2020	Developing health policies in patients presenting with SARS-CoV-2: consider tuberculosis	Lancet Global Health / Comment
14.10.2020	Supporting Clinicians during Covid-19 and Beyond — Learning from Past Failures and Envisioning New Strategies	N Engl J Med / Perspective

Produced by the PHE COVID-19 Literature Digest Team

To sign-up, email COVID.LitDigest@phe.gov.uk

A selection of previous digests [can be found here](#)

www.gov.uk/phe Follow us on Twitter @PHE_uk

Protecting and improving the nation's health