



COVID-19 Literature Digest – 30/10/2020

OFFICIAL

Dear all,

This week's guest editor is Dr Sharon Bahia – Operational Lead for the European Collection of Authenticated Cell Cultures and Senior Programme Lead for the COVID-19 Public Health Advice, Guidance and Expertise Pillar.

If you only read three papers this week...

I've chosen to highlight three papers this week that cover symptoms, individual susceptibility and detection of SARS-CoV-2.

The full re-opening of schools in September triggered many discussions concerning co-presentation of COVID-19 and common cold symptoms in children and young people (CYP). A recent (yet to be peer-reviewed) paper by [Viner et al., \(2020\)](#) summarises data from 18 review articles that looked at symptoms present in CYP under 20 years of age who were hospitalised with COVID-19. The authors cite previous reports that indicate that CYP may have 8-10 upper respiratory infections (URI) annually, with many cases occurring in winter months. Fever and cough are symptoms that can both indicate presence of SARS-CoV-2 and other URI causing viruses. The authors concluded that the symptoms most frequently displayed in CYP patients admitted to hospital with COVID-19 were fever (in 46 – 64.2% of cases) and cough (in 32 – 55.9% of cases). The presence of other symptoms such as sore throat, rhinorrhoea, headache, fatigue, diarrhoea and nausea only occurred in 10 to 20% of cases. Limitations of the review are that more than 80% of the cases related to CYP hospital admissions before June 2020 and there was a geographical bias with most cases reported from China. Nonetheless, the study contributes to the argument that URI related symptoms should not be included in the COVID-19 diagnosis criteria for CYP.

The association between blood type and disease has intrigued researchers since blood groups were identified by Karl Landsteiner in the early 1900s. [Hoiland et al., \(2020\)](#) explore the correlation between ABO blood groups and the severity of SARS-CoV-2 infection. The authors acquired data from 95 RT-PCR confirmed COVID-19 patients in intensive care units (ICUs) in 6 Vancouver hospitals between February and April 2020. Patient data was divided into two groups, 57 patients with anti-A antibodies (blood groups O and B), and 38 patients without anti-A antibodies (blood groups A and AB). The findings showed that 84% of patients with blood group A or AB required mechanical ventilation compared with 61% of O and B blood group patients (adjusted for sex, age and comorbidity status). Continuous renal replacement therapy was required by 32% of A and AB patients and only by 9% of O and B patients. A and AB patients had significantly higher white blood cell counts, fibrin D-primer, AST, ALT and serum creatinine levels compared with O and B patients. However, there was no difference in serum inflammatory cytokine markers. Likewise, significant variances were not detected in the overall length of stay in hospital, but A and AB patients spent longer in ICU. The authors acknowledge the limitations of retrospectively analysing a small pool of patients and thus this data is described as indicative of a trend rather than conclusive evidence. The key variances highlighted in this paper are that COVID-19 patients with A and AB blood groups may be more likely to require mechanical ventilation and may exhibit increased disease severity compared to patients with O and B blood groups.

There are numerous companies now offering detection of COVID-19 infection using antibody testing. [Manthei et al., \(2020\)](#) review the specificity and sensitivity of four commercially available assays. The EUROIMMUN and DiaSorin assays were IgG-specific against spike proteins S1 and S1/S2, respectively. The Siemens assay was a total antibody assay against the RBD region of the S1 spike protein and the Roche assay was a total antibody assay against a nucleocapsid protein. All four assays were tested with common sets of serum from SARS-CoV-2 negative and positive individuals, with samples taken from positive patients between day 0 to 59 from symptom onset. The authors found an increasing prevalence of positive results in serum samples taken 14 days after symptom onset, across all four platforms, which aligns with findings reported by others. The sensitivity of the assays increased with time indicating the occurrence of an adaptive immune response in COVID-19 patients. The specificity/sensitivity results of each assay were Siemens (100% / 98.3%), Roche (100% / 96.6%), EUROIMMUN (86.3 – 96.4% / 93.1% to 96.6%) and DiaSorin (96.1 – 97.0% / 87.7%). The authors preferred the Roche and Siemens assays and found that they performed as detailed by the manufacturers and reported by others. However, each assay presented implementation challenges such as the bracketed daily cleaning procedure required with the Siemens assay, and the absence of QC material and a short 3-day reagent stability with the Roche assay.

Sharon

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, James Robinson
On behalf of the PHE COVID-19 Literature Digest Team

Report for 30.10.2020 (please note that papers that have **NOT been peer-reviewed** are highlighted in red).

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

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Serology and immunology

Publication Date	Title / URL	Journal / Article type	Digest
28.10.2020	Robust neutralizing antibodies to SARS-CoV-2 infection persist for months	Science / Report	<ul style="list-style-type: none">• In a dataset of 30,082 individuals screened at a New York City hospital network, the vast majority of infected individuals with mild-to-moderate COVID-19 experience robust IgG antibody responses against the viral spike protein.• Titres are relatively stable for at least a period approximating 5 months and anti-spike binding titres significantly correlate with neutralization of authentic SARS-CoV-2.• Data suggests more than 90% of seroconverters make detectable neutralizing antibody responses.

Diagnostics

Publication Date	Title / URL	Journal / Article type	Digest
08.10.2020	Three Quarters of People with SARS-CoV-2 Infection are Asymptomatic: Analysis of English Household Survey Data	Clin Epidemiol / Original research	<ul style="list-style-type: none">• Assesses the value of COVID-19 symptoms as a marker for SARS-CoV-2 infection from a representative English survey (36,061 individuals with a SARS-CoV-2 test between 26 April and 27 June 2020).• Of the 115 (0.32%) with a positive SARS-CoV-2 test result, there were 27 (23.5%) who were symptomatic and 88 (76.5%) who were asymptomatic on the day of the test.• Among those testing positive, 16 (13.9%) reported symptoms, while 99 (86.1%) did not report specific symptoms on the day of the test.• Suggests COVID-19 symptoms are poor markers of SARS-CoV-2, and more widespread testing is necessary to capture "silent" transmission.
29.10.2020	Association of SARS-CoV-2 Genomic Load with COVID-19 Patient Outcomes	Ann Am Thorac Soc / Article	<ul style="list-style-type: none">• Retrospective cohort study at a New York City medical centre examined association of SARS-CoV-2 genomic load in nasopharyngeal samples with clinical outcomes.

			<ul style="list-style-type: none"> • Data suggests patients with a short duration of symptoms and high comorbidity index, as well as transplant recipients, were more likely to have a high SARS-CoV-2 genomic load at the time of hospital admission. • Patients with high genomic load had a more severe clinical presentation and 2 times higher odds of dying or being intubated, independently of age, comorbidities, and severity of illness on presentation.
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Genomics

Publication Date	Title / URL	Journal / Article type	Digest
25.10.2020	Emergence and spread of a SARS-CoV-2 variant through Europe in the summer of 2020	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Demonstrates that a variant of SARS-CoV-2 was exported from Spain to other European countries multiple times and that much of the diversity of this cluster in Spain (20A.EU1) is observed across Europe. • The variant was first observed in Spain in June 2020 and has been at >40% frequency since July 2020. • It increased from very low values prior to 15th July to 40-70% in Switzerland, Ireland, and the UK in Sept. It is also prevalent in Norway, Latvia, the Netherlands, and France. • Unclear whether a transmission advantage or tourist dissemination from Spain is sufficient to explain the multinational rise.
27.10.2020	SARS-CoV-2 spike D614G variant confers enhanced replication and transmissibility	bioRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • The authors generate isogenic SARS-CoV-2 variants and demonstrate that the S-614G variant has: (i) enhanced binding to human ACE2; (ii) increased replication in primary human bronchial and nasal airway epithelial cultures as well as in a novel human ACE2 knock-in mouse model, and; (iii) markedly increased replication and transmissibility in hamster and ferret models. • Data suggests that while the S-614G substitution results in subtle increases in binding and replication in vitro, it provides a real competitive advantage in vivo, particularly during the transmission bottle neck, providing an explanation for the global predominance of S-614G variant among the SARS-CoV-2 viruses currently circulating.

Epidemiology and clinical – risk factors

Publication Date	Title / URL	Journal / Article type	Digest
16.10.2020	An Outbreak of COVID-19 Associated with a Recreational Hockey Game — Florida, June 2020	MMWR Morb Mortal Wkly Rep / Repot	<ul style="list-style-type: none"> • On June 16, 2020, a recreational ice hockey game was played, Florida, US. Teams A and B, each consisting of 11 players, included men aged 19–53

			<p>years.</p> <ul style="list-style-type: none"> • During the 5 days after the game, 15 persons (14 of the 22 players and a rink staff member) experienced signs and symptoms compatible with COVID-19; 13 of the 15 ill persons had positive laboratory test results indicating infection with SARS-CoV-2. • The high proportion of infections that occurred in this outbreak provides evidence for SARS-CoV-2 transmission during an indoor sporting activity where intense physical activity is occurring.
29.10.2020	Estimated Association of Construction Work With Risks of COVID-19 Infection and Hospitalization in Texas	JAMA Netw Open / Original investigation	<ul style="list-style-type: none"> • Assesses the association between construction work during the COVID-19 pandemic and hospitalisation rates for construction workers and the surrounding community, focussing on the Austin-Round Rock metropolitan area in Texas, USA. • Unrestricted construction work was associated with an increase of COVID-19 hospitalisation rates through mid-Aug 2020, from 0.38 per 1000 residents to 1.5 per 1000 residents and from 0.22 per 1000 construction workers to 9.3 per 1000 construction workers. • Safety measures (such as equipment cleaning, wearing PPE, limits on the number of workers at a worksite, and increased health surveillance) were associated with a 50% decrease in transmission. • Observed relative risk of hospitalisation among construction workers aged 18-64 years, compared with other occupational categories, was 4.9 (95% CI, 3.8-6.2).
28.10.2020	Risk of hospital admission with coronavirus disease 2019 in healthcare workers and their households: nationwide linkage cohort study	BMJ / Article	<ul style="list-style-type: none"> • Study of a cohort of healthcare workers (HCW) (N=158,445) in Scotland, with most being patient-facing (n=90,733; 57.3%), and 229,905 household members. • HCW or their households made up 17.2% (360/2097) of all hospital admissions for COVID-19 in the working age population. • Risk of admission due to COVID-19 in non-patient facing HCW and their households was similar to the general population (hazard ratio 0.81 (95% confidence interval 0.52 to 1.26) and 0.86 (0.49 to 1.51), respectively) after adjustment for age, sex, ethnicity, socioeconomic deprivation, and comorbidity. • However, patient-facing HCW were at higher risk (hazard ratio 3.30, 2.13 to 5.13), as were household members of patient-facing HCW (1.79, 1.10 to 2.91). • For most patient-facing HCW and their households, the estimated absolute risk of hospital admission with COVID-19 was less than 0.5%, but it was 1% and above in older men with comorbidity.

30.10.2020	SARS-CoV-2 Exposure and Infection Among Health Care Personnel - Minnesota, March 6-July 11, 2020	MMWR Morb Mortal Wkly Rep / Report	<ul style="list-style-type: none"> • Among 21,406 Minnesota SARS-CoV-2 Health care personnel (HCP) exposures, 5,374 (25%) were higher-risk (within 6 feet, ≥15 minutes, or during an aerosol-generating procedure); exposures involved patient care (66%) and nonpatient contacts (34%). • Compared with HCP working in acute care settings, those working in congregate living and long-term care more often worked while symptomatic and received positive SARS-CoV-2 test results. • Suggests HCP in congregate living and long-term care settings experience considerable risk and pose a transmission risk to residents.
28.10.2020	Investigating the association between ethnicity and health outcomes in SARS-CoV-2 in a London secondary care population	PLoS One / Article	<ul style="list-style-type: none"> • Retrospective analysis of hospitalised SARS-CoV-2 patients (N=645) across two London teaching hospitals from 1 Mar - 30 Apr 2020. • The BAME population were relatively younger than the white population (61.70 years, 95% CI 59.70-63.73 versus 69.3 years, 95% CI 67.17-71.43, p<0.001). • When adjusted for age, sex and comorbidity, ethnicity was not a predictor for ICU admission. • Mean age at death was lower in the BAME population compared to the white population (71.44 years, 95% CI 69.90-72.90 versus, 77.40 years, 95% CI 76.1-78.70 respectively, p<0.001). • When adjusted for age, sex and comorbidities, Asian patients had higher odds of death (OR 1.99: 95% CI 1.22-3.25, p<0.006).
27.10.2020	Cardiovascular comorbidities as predictors for severe COVID-19 infection or death	Eur Heart J Qual Care Clin Outcomes / Accepted manuscript	<ul style="list-style-type: none"> • A nationwide Danish cohort of hospital-screened COVID-19 patients (N=4,090) aged 40 or over, to investigate if pre-existing cardiovascular diseases (CVDs) predict the 30-day risk of i) severe COVID-19 or ii) mortality. • Amongst the cohort 22.1% had ≥ 1 CVD, 23.7% had severe infection within 30 days, and 12.6% died. • Predicted risks of both outcomes at age 75 among men with single CVD comorbidities did not differ in clinically meaningful amounts compared to men with no comorbidities risks for the composite outcome of severe infection; women with heart failure (28.2%; 95% CI 21.1%-37.0%) or atrial fibrillation (30.0%; 95% CI: 24.2%-36.9%) showed modest increases compared to women with no comorbidities (24.0%; 95% CI: 21.4%-26.9%).

Epidemiology and clinical – other

Publication Date	Title / URL	Journal / Article type	Digest
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29.10.2020	Unravelling the modes of transmission of SARS-CoV-2 during a nursing home outbreak: looking beyond the church super-spread event	Clin Infect Dis/ Article	<ul style="list-style-type: none"> • Epidemiological investigation of a COVID-19 outbreak in a Dutch nursing home, following an on-site church service held on 8 Mar 2020. • After the church service, 30 of 39 attendees (77%) developed symptoms; 14 were tested and were positive for COVID-19 (11 residents and 3 non-residents). • In the following five weeks, 62 of 300 residents (21%) and 30 of 640 healthcare workers (HCWs) (5%) tested positive for COVID-19; 21 of 62 residents (34%) died. • Although initial investigation suggested the church service as source of the outbreak, detailed analysis showed a more complex picture, most consistent with widespread regional circulation of the virus in the weeks before the outbreak, and multiple introductions into the nursing home before the visitor ban. • The findings underscore the importance of careful outbreak investigations to understand SARS-CoV-2 transmission to develop evidence-based mitigation measures.
30.10.2020	COVID-19 Outbreak at an Overnight Summer School Retreat - Wisconsin, July-August 2020	MMWR Morb Mortal Wkly Rep / Report	<ul style="list-style-type: none"> • From 2 July – 11 Aug 2020, a COVID-19 outbreak at an overnight high-school retreat likely began with a single student who had received a negative SARS-CoV-2 molecular test result <1 week before the retreat and led to 116 (76%) diagnosed COVID-19 cases among attendees.
27.10.2020	Disease burden and clinical severity of the first pandemic wave of COVID-19 in Wuhan, China	Nat Commun / Article	<ul style="list-style-type: none"> • Estimates disease burden and clinical severity by age of COVID-19 in Wuhan from 1 Dec 2019 to 31 Mar 2020, taking into account the sensitivity of laboratory assays, prospective community screenings, and healthcare seeking behaviours. • Rates of symptomatic cases, medical consultations, hospitalizations and deaths were estimated at 796 (95% CI: 703-977), 489 (472-509), 370 (358-384), and 36.2 (35.0-37.3) per 100,000 persons, respectively. • The COVID-19 outbreak in Wuhan had a higher burden than the 2009 influenza pandemic or seasonal influenza in terms of hospitalization and mortality rates, and clinical severity was similar to that of the 1918 influenza pandemic.

Infection control / non-pharmaceutical interventions

Publication Date	Title / URL	Journal / Article type	Digest
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30.10.2020	Facilitators and barriers to engagement with contact tracing during infectious disease outbreaks: A rapid review of the evidence	PLoS One / Article	<ul style="list-style-type: none"> • Rapid systematic review to identify facilitators and barriers to uptake of, and engagement with, contact tracing during infectious disease outbreaks. • Four themes were identified as facilitators: collective responsibility; personal benefit; co-production of contact tracing systems; and the perception of the system as efficient, rigorous and reliable. • Five themes were identified as barriers: privacy concerns; mistrust and/or apprehension; unmet need for more information and support; fear of stigmatization; and mode-specific challenges.
28.10.2020	Evaluating the effect of demographic factors, socioeconomic factors, and risk aversion on mobility during the COVID-19 epidemic in France under lockdown: a population-based study	Lancet Digital Health / Article	<ul style="list-style-type: none"> • Aimed to use mobile phone data to study how mobility in France changed before and during lockdown, breaking down the findings by trip distance, user age and residency, and time of day, and analysing regional data and spatial heterogeneities. • Lockdown was effective in reducing population mobility across scales. Caution should be taken in the timing of policy announcements and implementation, because anomalous mobility followed policy announcements, which might act as seeding events. Conversely, risk aversion might be beneficial in further decreasing mobility in highly affected regions. • Also identified socioeconomic and demographic constraints to the efficacy of restrictions. The unveiled links between geography, demography, and timing of the response to mobility restrictions might help to design interventions that minimise invasiveness while contributing to the current epidemic response.

Treatment

Publication Date	Title / URL	Journal / Article type	Digest
28.10.2020	SARS-CoV-2 Neutralizing Antibody LY-CoV555 in Outpatients with Covid-19	N Engl J Med / Article	<ul style="list-style-type: none"> • In this interim analysis of a phase 2 trial, one (2800 mg) of three doses (700 mg, 2800 mg, or 7000 mg) of neutralizing antibody LY-CoV555 appeared to accelerate the natural decline in viral load over time, whereas the other doses had not by day 11.
28.10.2020	Identification of SARS-CoV-2 Inhibitors using Lung and Colonic Organoids	Nature / Article	<ul style="list-style-type: none"> • Describes a lung organoid model using human pluripotent stem cells (hPSC-LOs) and a complementary model using hPSC-derived colonic organoids (hPSC-COs). • Performed a high throughput screen of FDA-approved drugs and identified entry inhibitors of SARS-CoV-2, including imatinib, mycophenolic acid (MPA), and quinacrine dihydrochloride (QNHC). Treatment at physiologically

			relevant levels of these drugs significantly inhibited SARS-CoV-2 infection of both hPSC-LOs and hPSC-COs.
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Modelling

Publication Date	Title / URL	Journal / Article type	Digest
29.10.2020	Report 34 - COVID-19 Infection Fatality Ratio Estimates from Seroprevalence	Imperial College / Report	<ul style="list-style-type: none"> • After screening 175 studies, the authors identified 10 representative antibody surveys to obtain updated estimates of the IFR using a modelling framework that addresses limitations listed. • Found that that age-specific IFRs follow an approximately log-linear pattern, with the risk of death doubling approximately every eight years of age. • Estimate the overall IFR in a typical low-income country, with a population structure skewed towards younger individuals, to be 0.23% (0.14-0.42 95% prediction interval range). • In contrast, in a typical high income country, with a greater concentration of elderly individuals, they estimate the overall IFR to be 1.15% (0.78-1.79 95% prediction interval range).

Guidance and consensus statements

Publication Date	Title / URL	Journal / Article type
28.10.2020	A guide for health protection teams about interpreting Ct in real-time, reverse transcription polymerase chain reaction (RT-PCR) assays performed for Sars-CoV-2.	Gov.uk / Guidance

Overviews, comments and editorials

Publication Date	Title / URL	Journal / Article type
29.10.2020	COVID-19 transmission—up in the air	Lancet Respiratory Medicine / Editorial
29.10.2020	Dexamethasone in hospitalised patients with COVID-19: addressing uncertainties	Lancet Respiratory Medicine / Comment
27.10.2020	Protection against SARS-CoV-2 by BCG vaccination is not supported by epidemiological analyses	Sci Rep / Article

Produced by the PHE COVID-19 Literature Digest Team

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