Public Health England

COVID-19 Literature Digest – 30/09/2020

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a report three times per week (Mon, Wed, Fri), which includes both preliminary reports of work (preprints) that have NOT been peer-reviewed and research that has been subject to peer review and wider scrutiny.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 wncov.behaviour@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Report for 30.09.2020 (please note that papers that have **NOT been peer-reviewed** are highlighted in red).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
29.09.2020	Safety and Immunogenicity of SARS-CoV-2 mRNA-1273 Vaccine in Older Adults	N Engl J Med / Article	• In this small study involving older adults, adverse events associated with the mRNA-1273 vaccine were mainly mild or moderate. • The 100-µg dose induced higher binding- and neutralizing-antibody titres than the 25-µg dose, which supports the use of the 100-µg dose in a phase 3 vaccine trial.
22.09.2020	Reinfection with SARS-CoV-2 and Failure of Humoral Immunity: a case report	medRxiv (non-peer reviewed) / Article	• The authors sequenced viruses from two distinct episodes of symptomatic COVID-19 separated by 144 days in a single patient, to describe reinfection with a new strain harboring the spike variant D614G. • Demonstrates correlates of adaptive immunity, including a differential response to D614G. • Implications for vaccine programs and benchmarks for protection against reinfection from SARS-CoV-2 are discussed.
28.09.2020	T cell assays differentiate clinical and subclinical SARS-CoV-2 infections from cross-reactive antiviral responses	medRxiv (non-peer reviewed) / Article	• Characterised SARS-CoV-2 T cell immune responses in 168 PCR-confirmed SARS-CoV-2 infected subjects and 118 seronegative subjects without known SARS-CoV-2 exposure. • Concluded that the detection of T cell responses to SARS-CoV-2 is critically dependent on the choice of assay and antigen. Memory responses to specific non-spike proteins provides a method to distinguish recent infection from pre-existing immunity in exposed populations.
29.09.2020	Seroprevalence of SARS CoV-2 antibodies in healthcare workers and administration employees: a prospective surveillance study at a 1,400-bed university hospital in Germany	medRxiv (non-peer reviewed) / Article	• Study comparing SARS-CoV-2 IgG seroprevalence and compliance to wear personal protective equipment (PPE) between HCWs working within (high-risk) or outside (intermediate-risk) units treating suspected or confirmed COVID-19 patients, as well as administration staff (low-risk), in a German hospital. A total of 660 employees were analysed out of 3,228 (20.4%). • 18 participants (2.7%) had SARS-CoV-2 antibodies in at least one immunoassay. 13 (72.2%) of them were not aware of direct COVID-19 exposure and 9 (50.0%) did not report any clinical symptoms. • No evidence was observed for association between seroprevalence and risk area (high-risk: 2 of 137 HCWs (1.5%), intermediate-risk: 10 of 343 HCWs (2.9%), low-risk: 6 of 180 administration employees (3.3%); p=0.574). • Reported compliance to wear PPE differed (p<0.001) between working in high-risk (98.3%) and in intermediate-risk areas (69.8%).
25.09.2020	SARS-CoV-2 Uses CD4 to Infect T Helper Lymphocytes	medRxiv (non-peer reviewed) / Article	• The authors demonstrate that SARS-CoV-2 spike glycoprotein (S) directly binds to the CD4 molecule, which in turn mediates the entry of SARS- CoV-2 in T helper cells in a mechanism that also requires ACE2 and TMPRSS2.

			• Once inside T helper cells, SARS-CoV-2 assembles viral factories, impairs cell function and may cause cell death. • SARS-CoV-2 infected T helper cells express higher amounts of IL-10, which is associated with viral persistence and disease severity. • Suggests CD4-mediated SARS-CoV-2 infection of T helper cells may explain the poor adaptive immune response of many COVID- 19 patients.
28.09.2020	Prime-boost vaccination of mice and Rhesus macaques with two novel adenovirus vectored COVID-19 vaccine candidates	bioRxiv (non-peer reviewed) / Article	• Constructed two novel adenovirus vectored COVID-19 vaccine candidates on simian adenovirus serotype 23 (Sad23L) and human adenovirus serotype 49 vectors (Ad49L) carrying the full-length gene of SARS-CoV-2 spike protein (S), designated Sad23L-nCoV-S and Ad49L-nCoV-S vaccines. • Results suggest that prime-boost immunization with Sad23L-nCoV-S and Ad49L-nCoV-S vaccines can safely elicit strong immunity in mice and macaques.

Epidemiology and clinical – risk factors

Publication Date	Title / URL	Journal / Article type	Digest
20.09.2020	The spectrum of biochemical alterations associated with organ dysfunction and inflammatory status and their association with disease outcomes in severe COVID-19: A longitudinal cohort and time-series design study	EClinicalMedicine / Article	• On 162 studied patients, 1151 biochemical explorations were carried out for up to 59 biochemical markers. • Only CRP >90 mg/L (odds ratio [OR] 6·87, 95% CI, 2·36–20·01) and urea nitrogen >0·36 g/L (OR 3·91, 95% CI, 1·15–13·29) were independently associated with risk of acute respiratory failure (ARF). Urea nitrogen >0·42 g/L was only marker associated with the risk of COVID-19 related death. • Results point out lack of association between inflammatory markers and risk of death; highlight a significant association between renal dysfunction and risk of COVID-19 related acute respiratory failure and death.
24.09.2020	Assessing the age specificity of infection fatality rates for COVID-19: systematic review, meta-analysis, and public policy implications	medRxiv (non-peer reviewed) / Article	• Study assessing the age specificity of the infection fatality rate (IFR) for COVID-19 using results from 28 seroprevalence studies, as well as five countries that have engaged in comprehensive tracing of COVID-19 cases (Australia, Iceland, Lithuania, New Zealand and South Korea). • Estimated IFR is close to zero for children and younger adults but rises exponentially with age, reaching 0.4% at age 55, 1.3% at age 65, 4.2% at age 75, and 14% at age 85. • Differences in the age structure of the population and the age-specific prevalence of COVID-19 explain nearly 90% of the geographical variation in population IFR.

Epidemiology and clinical – other

Publication Date	Title / URL	Journal / Article type	Digest
28.09.2020	Coronavirus (COVID-19) Infection Survey: characteristics of people testing positive for COVID-19 in England, September 2020	Gov.uk / Official statistics	• Latest estimates show that COVID-19 infections have increased in recent weeks; in this article the authors provide more analysis on the characteristics and behaviours of those testing positive in England between 23 July and 10 Sept. • Positivity rates have increased over time amongst those aged under 35 years who had socially-distanced direct contact with six or more people aged 18 to 69 years, suggesting socially-distanced direct contact in younger age groups is an increasingly important factor in contracting COVID-19. • In recent weeks, COVID-19 positivity rates have been higher amongst people who have travelled abroad, although increases are seen in both those who have and have not travelled.
24.09.2020	Gastrointestinal Complications in Critically Ill Patients With and Without COVID-19	JAMA / Research letter	• 92 patients with COVID-19 and ARDS were propensity score matched to 92 patients with non–COVID-19 ARDS admitted in 2018-2019. • Higher rate of gastrointestinal complications, including mesenteric ischemia, in critically ill COVID-19 patients suggesting a distinct phenotype for COVID-19 compared with conventional ARDS. Differences in duration of illness did not seem to explain the differences in gastrointestinal complications. • Further translational studies are warranted to examine the pathophysiology of these findings.
28.09.2020	Modeling lung perfusion abnormalities to explain early COVID-19 hypoxemia	Nat Commun / Article	• Mathematical model demonstrates that the large amount of pulmonary venous admixture observed in patients with early COVID-19 can be reasonably explained by a combination of pulmonary embolism, ventilation-perfusion mismatching in the noninjured lung, and normal perfusion of the relatively small fraction of injured lung. • Although underlying perfusion heterogeneity exacerbates existing shunt and ventilation-perfusion mismatch in the model, the reported hypoxemia severity in early COVID-19 patients is not replicated without either extensive perfusion defects, severe ventilation-perfusion mismatch, or hyperperfusion of nonoxygenated regions.
20.09.2020	Retinal findings in patients with COVID-19: Results from the SERPICO-19 study	EClinicalMedicine / Article	• Authors screened fundus of 55 COVID-19 patients (and 133 unexposed subjects) to detect alterations of retina and its vasculature. • Retinal findings included: haemorrhages (9·25%), cotton wools spots (7·4%), dilated veins (27·7%), tortuous vessels (12·9%). • Mean arteries diameter (MAD) and mean veins diameter (MVD) higher in COVID-19 patients vs. unexposed subjects (98·3 ± 15·3 µm vs 91·9 ± 11·7 µm, p = 0.006 and 138·5 ± 21·5 µm vs 123·2 ± 13·0 µm, p<0.0001, respectively).

			• COVID-19 can affect the retina. Retinal veins diameter seems directly correlated with the disease severity. Its assessment could have possible applications in the management of COVID-19.
29.09.2020	Clinical criteria for COVID-19-associated hyperinflammatory syndrome: a cohort study	Lancet Rheumatology/ Article	• Proposed and validated criteria for hyperinflammation in COVID-19. • This hyperinflammatory state, cHIS, is commonly associated with progression to mechanical ventilation and death. • External validation is needed. The cHIS scale might be helpful in defining target populations for trials and immunomodulatory therapies.

Infection control

Publication Date	Title / URL	Journal / Article type	Digest
29.09.2020	Multiple COVID-19 Clusters on a University Campus — North Carolina, August 2020	MMWR Morb Mortal Wkly Rep / Report	• A North Carolina university experienced a rapid increase in COVID-19 cases and clusters within 2 weeks of opening the campus to students. Student gatherings and congregate living settings, both on and off campus, likely contributed to the rapid spread of COVID-19 in this setting. • Enhanced measures are needed to reduce transmission at institutes of higher education and could include reducing on-campus housing density, ensuring adherence to masking and other mitigation strategies, increasing testing for SARS-CoV-2, and discouraging student gatherings.
21.09.2020	The characteristics of COVID-19 transmission from case to high-risk contact, a statistical analysis from contact tracing data	EClinicalMedicine / Article	• 1108 high-risk contacts in Phuket, Thailand, analysed to investigate risk factors for transmission from confirmed COVID-19 cases to their high-risk contacts. Impact of quarantine measures (individual isolation in state provided facilities for all high-risk contacts) on contacts' probability of infection was also analysed. • 15.6% found to be infected, accounted for 80% of 214 confirmed cases in Phuket till 29th April 2020. 10.68% infected before quarantine, 4.55% after. • Contact living in same household with a confirmed case was 25% more exposed to infection when compared to a contact who did not share a household. • Sharing accommodation with an infected case / exposure to a case with several documented secondary transmission, generally increased infection probability. • Some confirmed cases exhibit a higher risk of spreading SARS-CoV-2 to their contacts compared to a typical confirmed case. Further studies of high reproduction groups of infected patients are recommended.
28.09.2020	The potential contribution of face coverings to the control of SARS-CoV-2 transmission in schools and broader society in the UK: a modelling study	medRxiv (non-peer reviewed) / Article	• Assuming current test-trace-isolate (TTI) levels, authors assess adoption of masks in secondary schools in addition to community settings can reduce the size of a second wave, but will not prevent it; more testing of symptomatic people, tracing and isolating of their contacts is also needed.

			• To avoid a second wave, with masks mandatory in secondary schools and in certain community settings, 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.
24.09.2020	Face Masks, Public Policies and Slowing the Spread of COVID-19: Evidence from Canada	medRxiv (non-peer reviewed) / Article	• Authors estimate impact of mask mandates on Canadian COVID-19 case growth; exploits 2 month variation in indoor face mask mandates in 34 public health regions in Ontario. • In first few weeks after implementation, mask mandates are associated with a reduction of 25% in the weekly number of new COVID-19 cases. Additional analysis with province-level data provides corroborating evidence. • Counterfactual policy simulations suggest mandating indoor masks nationwide in early July may have reduced weekly new cases by 25-40% mid-August (700 to 1,100 fewer cases per week).

Treatment

Publication Date	Title / URL	Journal / Article type	Digest
20.09.2020	An open-label, randomized trial of the combination of IFN-κ plus TFF2 with standard care in the treatment of patients with moderate COVID-19	EClinicalMedicine / Article	• Open-label, randomized, clinical trial involving 86 patients with moderate COVID-19: receive either aerosol inhalation treatment with IFN-κ and TFF2 every 24 h for six consecutive dosages in addition to standard care (experimental group) or standard care alone (control group). • The combination treatment is safe and superior to standard care alone in shortening the time up to viral RNA negative conversion in all clinical samples. • In addition, the patients in experimental group had a significantly shortened CT imaging improvement time than those in control group. • Treatment may facilitate clinical improvement (negative for virus, improvement by CT, reduced hospitalization stay) so result in an early release from hospital.
28.09.2020	Anti-C5a antibody IFX-1 (vilobelimab) treatment versus best supportive care for patients with severe COVID-19 (PANAMO): an exploratory, open-label, phase 2 randomised controlled trial	Lancet Rheumatology / Article	• Explored the potential benefit and safety of selectively blocking the anaphylatoxin and complement protein C5a with the monoclonal antibody IFX-1 (vilobelimab), in patients with severe COVID-19. • Concluded that in this small exploratory phase 2 part of the PANAMO trial, C5a inhibition with IFX-1 appears to be safe in patients with severe COVID-19. • The secondary outcome results in favour of IFX-1 are preliminary because the study was not powered on these endpoints, but they support the investigation of C5a inhibition with IFX-1 in a phase 3 trial using 28-day mortality as the primary endpoint.

27.09.2020	Cardiovascular disease and severe hypoxemia associated with higher rates of non-invasive respiratory support failure in COVID-19	medRxiv (non-peer reviewed) / Article	• Retrospective cohort study of hospitalized COVID-19 adults treated with high-flow oxygen delivered through nasal cannula (HFNC - 331 patients) and/or non-invasive positive pressure ventilation (NIPPV - 747 patients) for acute hypoxemic respiratory failure (AHRF). • Significant proportion of patients receiving non-invasive respiratory modalities for COVID-19 AHRF achieved successful discharge without requiring ETI; lower success rates among those with cardiovascular disease or more severe hypoxia. • Role of non-invasive respiratory modalities in COVID-19 related AHRF requires further consideration.

Guidance and consensus statements

Publication Date	Title / URL	Journal / Article type
29.09.2020	Health matters: delivering the flu immunisation programme during the COVID-19 pandemic	Gov.uk / Guidance

Overviews, comments and editorials

Publication Date	Title / URL	Journal / Article type
29.09.2020	Lockdown impact on COVID-19 epidemics in regions across metropolitan France	Lancet / Correspondence
29.09.2020	Low risk of SARS-CoV-2 transmission by fomites in real-life conditions	Lancet Infectious Diseases / Correspondence
29.09.2020	False-positive COVID-19 results: hidden problems and costs	Lancet Respiratory Medicine / Comment
26.09.2020	Models for mortality require tailoring in the context of the COVID-19 pandemic	Lancet / Commentary
29.09.2020	The opening salvo of anti-complement therapy against COVID-19	Lancet Rheumatology / Comment
29.09.2020	Defining the scourge of COVID-19 hyperinflammatory syndrome	Lancet Rheumatology / Comment
25.09.2020	Characterizing COVID-19 maternal-fetal transmission and placental infection using comprehensive molecular pathology	EBioMedicine / Commentary
29.09.2020	Confronting antimicrobial resistance beyond the COVID-19 pandemic and the 2020 US election	Lancet / Comment

Produced by the PHE COVID-19 Literature Digest Team

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