



## COVID-19 Literature Digest – 11/11/2020

Dear all,

Please find [today's report](#) below.

PHE's COVID-19 Literature Digest has been produced since February 2020. A selection of our previous Digests [can be found here](#). This resource aims to highlight a small selection of recent COVID-19 papers that are relevant to UK settings, contain new data, insights or emerging trends. The Digest Team generate a report three times per week (Mon, Wed, Fri). The reports include both preprints, which should be treated with caution as they are NOT peer-reviewed and may be subject to change, and also research that has been subject to peer review and wider scrutiny. The Digest is very rapidly produced and does not claim to be a perfect product; the inclusion or omission of a publication should not be viewed as an endorsement or rejection by PHE. We do not accept responsibility for the availability, reliability or content of the items included in this resource.

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Best wishes,

Bláthnaid Mahon, Emma Farrow, James Robinson  
*On behalf of the PHE COVID-19 Literature Digest Team*

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**Report for 11.11.2020** (please note that papers that have **NOT been peer-reviewed** are highlighted in red).

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### Serology and immunology

Publication Date	Title / URL	Journal / Article type	Digest
06.11.2020	<a href="#">Preexisting and de novo humoral immunity to SARS-CoV-2 in humans</a>	Science / Report	<ul style="list-style-type: none"><li>• SARS-CoV-2 spike glycoprotein (S)-reactive antibodies were detectable by a flow cytometry-based method in SARS-CoV-2-uninfected individuals and were particularly prevalent in children and adolescents. They were predominantly of the IgG class and targeted the S2 subunit.</li><li>• By contrast, SARS-CoV-2 infection induced higher titres of SARS-CoV-2 S-reactive IgG antibodies, targeting both the S1 and S2 subunits, and concomitant IgM and IgA antibodies, lasting throughout the observation period.</li><li>• Notably, SARS-CoV-2-uninfected donor sera exhibited specific neutralizing activity against SARS-CoV-2 and SARS-CoV-2 S pseudotypes.</li><li>• Distinguishing pre-existing and de novo immunity will be critical for our understanding of susceptibility to and the natural course of SARS-CoV-2 infection.</li></ul>
28.10.2020	<a href="#">Public health antibody screening indicates a six-fold higher SARS-CoV-2 exposure rate than reported cases in children</a>	Med (N Y) / Clinical advances	<ul style="list-style-type: none"><li>• Antibodies were measured by immuno-precipitation assays in capillary blood from 15,771 children aged 1 to 18 years living in Bavaria, Germany, and participating in a public health type 1 diabetes screening program, in 1,916 dried blood spots from neonates in a Bavarian screening study, and in 75 SARS-CoV-2 positive individuals.</li><li>• Dual-antibody positivity was detected in none of 3887 children in 2019 (100% specificity) and 73 of 75 SARS-CoV-2 positive individuals (97.3% sensitivity).</li><li>• Antibody prevalence from Apr 2020 was six-fold higher than the incidence of authority-reported cases (156 per 100,000 children), showed marked variation between the seven Bavarian regions (<math>P &lt; 0.0001</math>), and was not associated with age or sex.</li></ul>
09.11.2020	<a href="#">Proinflammatory IgG Fc structures in patients with severe COVID-19</a>	Nat Immunol / Article	<ul style="list-style-type: none"><li>• Patients with severe COVID-19 produced a unique serologic signature, including an increased likelihood of IgG1 with afucosylated Fc glycans.</li><li>• This Fc modification on SARS-CoV-2 IgGs enhanced interactions with the activating Fc<math>\gamma</math> receptor Fc<math>\gamma</math>RIIIa; when incorporated into immune complexes, Fc afucosylation enhanced production of inflammatory cytokines by monocytes, including interleukin-6 and tumour necrosis factor.</li></ul>

			<ul style="list-style-type: none"> <li>• These results show that disease severity in COVID-19 correlates with the presence of proinflammatory IgG Fc structures, including afucosylated IgG1.</li> </ul>
05.11.2020	<a href="#">Symptomatic SARS-CoV-2 re-infection of a health care worker in a Belgian nosocomial outbreak despite primary neutralizing antibody response</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• COVID-19 re-infection was confirmed in a young, immunocompetent Belgian health care worker as viral genomes derived from the first and second episode belonged to different SARS-CoV-2 clades.</li> <li>• Symptomatic re-infection occurred after an interval of 185 days, despite the development of an effective humoral immune response following symptomatic primary infection.</li> <li>• The second episode was milder and characterised by a fast rise in serum IgG and neutralizing antibodies.</li> <li>• Although contact tracing and virus culture remained inconclusive, the health care worker formed a transmission cluster with 3 patients and showed evidence of virus replication but not of neutralizing antibodies in her nasopharyngeal swabs.</li> </ul>
02.11.2020	<a href="#">The duration, dynamics and determinants of SARS-CoV-2 antibody responses in individual healthcare workers</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• Serially measured SARS-CoV-2 anti-nucleocapsid IgG titres from 452 seropositive UK healthcare workers demonstrate levels fall by half in 85 days.</li> <li>• From a peak result at 24 days post-first positive PCR test, detectable antibodies last a mean 137 days.</li> <li>• Levels fell faster in younger adults and following asymptomatic infection.</li> </ul>

### Vaccine development

Publication Date	Title / URL	Journal / Article type	Digest
09.11.2020	<a href="#">Pfizer and BioNTech Announce Vaccine Candidate Against COVID-19 Achieved Success in First Interim Analysis from Phase 3 Study</a>	Pfizer / News	<ul style="list-style-type: none"> <li>• Vaccine candidate was found to be more than 90% effective in preventing COVID-19 in participants without evidence of prior SARS-CoV-2 infection in the first interim efficacy analysis.</li> <li>• Analysis evaluated 94 confirmed cases of COVID-19 in trial participants.</li> <li>• Study enrolled 43,538 participants, with 42% having diverse backgrounds, and no serious safety concerns have been observed; Safety and additional efficacy data continue to be collected.</li> <li>• Submission for Emergency Use Authorization (EUA) to the U.S. Food and Drug Administration (FDA) planned for soon after the required safety milestone is achieved, which is currently expected to occur in the third week of Nov.</li> <li>• Clinical trial to continue through to final analysis at 164 confirmed cases in order to collect further data and characterize the vaccine candidate's performance against other study endpoints.</li> </ul>

09.11.2020	<a href="#">Randomized, double-blinded and placebo-controlled phase II trial of an inactivated SARS-CoV-2 vaccine in healthy adults</a>	Clin Infect Dis / Accepted manuscript	<ul style="list-style-type: none"> <li>• Randomized, double-blinded controlled trial: 742 healthy adults received medium (MD) or high dose (HD) of vaccine at an interval of either 14 days or 28 days.</li> <li>• Neutralizing antibody (NAb) and anti-S and anti-N antibodies were detected at different times, and adverse reactions were monitored for 28 days after full immunization.</li> <li>• Adults vaccinated with inactivated SARS-CoV-2 vaccine had NAb as well as anti-S/N antibody, and had a low rate of adverse reactions.</li> </ul>
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#### Epidemiology and clinical – children / pregnancy

Publication Date	Title / URL	Journal / Article type	Digest
09.11.2020	<a href="#">Characteristics and outcomes of neonatal SARS-CoV-2 infection in the UK: a prospective national cohort study using active surveillance</a>	Lancet Child & Adolescent Health / Article	<ul style="list-style-type: none"> <li>• Describe the incidence, characteristics, transmission, and outcomes of SARS-CoV-2 infection in neonates who received inpatient hospital care in the UK.</li> <li>• Identified 66 babies with confirmed SARS-CoV-2 infection (incidence 5.6 [95% CI 4.3–7.1] per 10 000 livebirths), of whom 28 (42%) had severe neonatal SARS-CoV-2 infection (incidence 2.4 [1.6–3.4] per 10 000 livebirths).</li> <li>• Concluded that neonatal SARS-CoV-2 infection is uncommon in babies admitted to hospital. Infection with neonatal admission following birth to a mother with perinatal SARS-CoV-2 infection was unlikely, and possible vertical transmission rare, supporting international guidance to avoid separation of mother and baby. The high proportion of babies from Black, Asian, or minority ethnic groups requires investigation.</li> </ul>

#### Epidemiology and clinical – risk factors

Publication Date	Title / URL	Journal / Article type	Digest
09.11.2020	<a href="#">Association Between Nursing Home Crowding and COVID-19 Infection and Mortality in Ontario, Canada</a>	JAMA Intern Med / Original investigation	<ul style="list-style-type: none"> <li>• In this cohort study that included more than 78 000 residents of 618 nursing homes in Ontario, Canada, COVID-19 mortality in homes with low crowding was less than half (578 of 46 028 residents [1.3%]) than that of homes with high crowding (874 of 32 579 residents [2.7%]).</li> <li>• Shared bedrooms and bathrooms in nursing homes are associated with larger and deadlier COVID-19 outbreaks.</li> </ul>
03.11.2020	<a href="#">An international survey on the impact of COVID-19 in individuals with Down syndrome</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• Analysis of data from the T21RS COVID-19 Initiative, an international survey for clinicians or caregivers/family members on patients with COVID-19 and Down syndrome (DS) (N=1046), and 400 controls.</li> </ul>

		<ul style="list-style-type: none"> <li>• Leading signs/symptoms of COVID-19 and risk factors for severe disease course are broadly similar to the general population.</li> <li>• Mortality rates showed a rapid increase from age 40 and were higher in DS group than for controls (T21RS DS versus controls: risk ratio (RR)=3.5 (95%-CI=2.6;4.4), ISARIC4C DS versus controls: RR=2.9 (95%-CI=2.1;3.8)) even after adjusting for known risk factors for COVID-19 mortality.</li> </ul>
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### Epidemiology and clinical – long term complications / sequelae

Publication Date	Title / URL	Journal / Article type	Digest
09.11.2020	<a href="#">Bidirectional associations between COVID-19 and psychiatric disorder: retrospective cohort studies of 62 354 COVID-19 cases in the USA</a>	Lancet Psychiatry / Article	<ul style="list-style-type: none"> <li>• In patients with no previous psychiatric history, a diagnosis of COVID-19 was associated with increased incidence of a first psychiatric diagnosis in the following 14 to 90 days compared with six other health events (HR 2.1, 95% CI 1.8–2.5 vs influenza; 1.7, 1.5–1.9 vs other respiratory tract infections; 1.6, 1.4–1.9 vs skin infection; 1.6, 1.3–1.9 vs cholelithiasis; 2.2, 1.9–2.6 vs urolithiasis, and 2.1, 1.9–2.5 vs fracture of a large bone; all p&lt;0.0001).</li> <li>• Survivors of COVID-19 appear to be at increased risk of psychiatric sequelae, and a psychiatric diagnosis might be an independent risk factor for COVID-19.</li> </ul>
09.11.2020	<a href="#">Characteristics of Hospitalized COVID-19 Patients Discharged and Experiencing Same-Hospital Readmission — United States, March–August 2020</a>	MMWR Morb Mortal Wkly Rep / Report	<ul style="list-style-type: none"> <li>• Among 126,137 unique patients with an index COVID-19 admission during Mar–July 2020 (US), 15% died during the index hospitalization. Among the 106,543 (85%) surviving patients, 9% (9,504) were readmitted to the same hospital within 2 months of discharge through Aug 2020. More than a single readmission occurred among 1.6% of patients discharged after the index hospitalization.</li> <li>• Risk factors for readmission included age ≥65 years, presence of certain chronic conditions, hospitalization within the 3 months preceding the first COVID-19 hospitalization, and discharge to a skilled nursing facility or with home health care.</li> <li>• These results support recent analyses that found chronic conditions to be significantly associated with hospital readmission and could be explained by the complications of underlying conditions in the presence of COVID-19, COVID-19 sequelae, or indirect effects of the COVID-19 pandemic.</li> </ul>
09.11.2020	<a href="#">Persistent fatigue following SARS-CoV-2 infection is common and independent of severity of initial infection</a>	PLoS One / Article	<ul style="list-style-type: none"> <li>• Of 128 participants (49.5 ± 15 years; 54% female), more than half reported persistent fatigue (67/128; 52.3%) at median of 10 weeks after initial COVID-19 symptoms.</li> <li>• There was no association between COVID-19 severity (need for inpatient admission, supplemental oxygen or critical care) and fatigue following COVID-19.</li> <li>• Additionally, there was no association between routine laboratory markers of</li> </ul>

		inflammation and cell turnover (leukocyte, neutrophil or lymphocyte counts, neutrophil-to-lymphocyte ratio, lactate dehydrogenase, C-reactive protein) or pro-inflammatory molecules and fatigue post COVID-19. <ul style="list-style-type: none"> <li>• Female gender and those with a pre-existing diagnosis of depression/anxiety were over-represented in those with fatigue.</li> </ul>
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### Transmission

Publication Date	Title / URL	Journal / Article type	Digest
10.11.2020	<a href="#">Transmission of SARS-CoV-2 on mink farms between humans and mink and back to humans</a>	Science / Report	<ul style="list-style-type: none"> <li>• Investigation using whole genome sequencing of outbreaks on 16 mink farms and the humans living or working on these farms (Netherlands).</li> <li>• Conclude that the virus was initially introduced from humans and has since evolved.</li> <li>• Despite enhanced biosecurity, early warning surveillance and immediate culling of infected farms, transmission occurred between mink farms in three big transmission clusters with unknown modes of transmission.</li> <li>• Sixty-eight percent (68%) of the tested mink farm residents, employees and/or contacts had evidence of SARS-CoV-2 infection.</li> <li>• Where whole genomes were available, these persons were infected with strains with an animal sequence signature, providing evidence of animal to human transmission of SARS-CoV-2 within mink farms.</li> </ul>

### Infection control / non-pharmaceutical interventions

Publication Date	Title / URL	Journal / Article type	Digest
10.11.2020	<a href="#">New WHO dashboard quantifies and visualizes European countries' COVID-19 measures</a>	WHO Europe / News	<ul style="list-style-type: none"> <li>• WHO/Europe has just launched its Public Health and Social Measures (PHSM) Severity Index to provide standardized data on the ways in which countries in the WHO European Region have sought to slow or stop community spread of COVID-19. This latest tool systematically captures and analyses individual governmental PHSM responses to COVID-19 in the 53 countries of the Region.</li> <li>• It captures 6 types of public health measures: the wearing of masks; closure of schools; closure of offices, businesses, institutions and operations; restrictions on gatherings; restrictions on domestic movement; and limitations to international travel.</li> </ul>
09.11.2020	<a href="#">Real-time, interactive website for US-county-level COVID-19 event risk assessment</a>	Nat Hum Behav / Article	<ul style="list-style-type: none"> <li>• Authors provide real-time, geolocalized risk information that estimates risk that at least one individual with SARS-CoV-2 is present in U.S gatherings of different</li> </ul>

			<p>sizes.</p> <ul style="list-style-type: none"> <li>• Website combines county level documented case reports and ascertainment bias information obtained via population-wide serological surveys to estimate real-time circulating, per-capita infection rates.</li> <li>• Provides data-driven information to help individuals / policy makers make prudent decisions that could help control spread, particularly in hard-hit regions.</li> </ul>
09.11.2020	<a href="#">The impact of COVID-19 nonpharmaceutical interventions on the future dynamics of endemic infections</a>	Proc Natl Acad Sci U S A / Article	<ul style="list-style-type: none"> <li>• Nonpharmaceutical interventions (NPIs), e.g. social distancing, reduce COVID-19 cases / other circulating infections like respiratory syncytial virus (RSV) and seasonal influenza.</li> <li>• Susceptible population for these infections will increase while NPIs are in place. Authors project large future outbreaks of both following a period of extended NPIs.</li> <li>• These outbreaks, which may reach peak numbers in the winter, could increase the burden to healthcare systems.</li> </ul>

#### Treatment

Publication Date	Title / URL	Journal / Article type	Digest
05.11.2020	<a href="#">De novo design of potent and resilient hACE2 decoys to neutralize SARS-CoV-2</a>	Science / Report	<ul style="list-style-type: none"> <li>• Authors describe design, validation, and optimization of de novo hACE2 decoys to neutralize SARS-CoV-2. Best decoy, CTC-445.2, binds with low nanomolar affinity and high specificity to the RBD of the spike protein.</li> <li>• Cryo-EM shows that the design is accurate and can simultaneously bind to all three RBDs of a single spike protein. Because the decoy replicates the spike protein target interface in hACE2, it is intrinsically resilient to viral mutational escape.</li> <li>• A bivalent decoy, CTC-445.2d, shows ~10-fold improvement in binding. CTC-445.2d potentially neutralizes SARS-CoV-2 infection of cells in vitro and a single intranasal prophylactic dose of decoy protected Syrian hamsters from a subsequent lethal SARS-CoV-2 challenge.</li> </ul>
09.11.2020	<a href="#">COVID-19 treatments and pathogenesis including anosmia in K18-hACE2 mice</a>	Nature / Article	<ul style="list-style-type: none"> <li>• Using K18-hACE2 mice, authors show that infection with SARS-CoV-2 causes severe disease in the lung, and in some mice, the brain.</li> <li>• Evidence of thrombosis and vasculitis was detected in mice with severe pneumonia.</li> <li>• Mice developed anosmia at early times after infection. Pre-treatment with convalescent plasma prevented notable clinical disease, but did not prevent anosmia.</li> </ul>

## Modelling

Publication Date	Title / URL	Journal / Article type	Digest
03.11.2020	<a href="#">COVID-19 reopening strategies at the county level in the face of uncertainty: Multiple Models for Outbreak Decision Support</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"><li>• Models seventeen reopening strategies for a mid-sized county in the United States, in a novel process designed to fully express scientific uncertainty while reducing linguistic uncertainty and cognitive biases.</li><li>• Suggests that a second outbreak will occur within 6 months of reopening, unless schools and non-essential workplaces remain closed; up to half the population could be infected with full workplace reopening; and non-essential business closures reduced median cumulative infections by 82%.</li><li>• Intermediate reopening interventions identified no win-win situations.</li></ul>

## Guidance and consensus statements

Publication Date	Title / URL	Journal / Article type
11.11.2020	<a href="#">Heating, ventilation and air-conditioning systems in the context of COVID-19: first update</a>	European Centre for Disease Prevention and Control / Technical report
09.11.2020	<a href="#">COVID-19: investigation and management of travellers returning from Denmark and their household contacts</a>	Gov.uk / Guidance

## Overviews, comments and editorials

Publication Date	Title / URL	Journal / Article type
09.11.2020	<a href="#">The UK needs a sustainable strategy for COVID-19</a>	Lancet / Correspondence
01.11.2020	<a href="#">Care home staff and residents on the pandemic front line</a>	Lancet Healthy Longevity / Editorial

## Produced by the PHE COVID-19 Literature Digest Team

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