



## COVID-19 Literature Digest – 17/08/2020

This Daily Evidence Digest is produced by the PHE COVID-19 Literature Digest Team as a resource for professionals working in public health. We do not accept responsibility for the availability, reliability or content of the items included in this resource and do not necessarily endorse the views expressed within them. The papers are organised under the following themes:

- Serology and immunology
- Diagnostics
- Genomics
- Epidemiology and clinical - risk factors
- Epidemiology and clinical - other
- Infection control
- Miscellaneous
- Overviews, comments and editorials (no digest)

Please note that we are including preprints (**highlighted in red**), which are preliminary reports of work that have NOT been peer-reviewed. They should not be relied on to guide clinical practice or health-related behaviour and should NOT be reported in news media as established information.

### Serology and immunology

Publication Date	Title / URL	Journal / Article type	Digest
13.08.2020	<a href="#">Neutralizing antibodies correlate with protection from SARS-CoV-2 in humans during a fishery vessel outbreak with high attack rate</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"><li>• Describe an outbreak of SARS-CoV-2 on a fishing vessel associated with a high attack rate. Predeparture serological and viral RT-PCR testing along with repeat testing after return to shore was available for 120/122 persons on board over a median follow-up of 32.5 days.</li><li>• A total of 104 individuals had an RT-PCR positive viral test, yielding an attack rate on board of 85.2% (104/122 individuals). Metagenomic sequencing of 39 viral genomes suggested the</li></ul>

			<p>outbreak originated largely from a single viral clade.</p> <ul style="list-style-type: none"> <li>• 3 crew members tested seropositive prior to the boat's departure and also had neutralizing and spike-reactive antibodies in follow-up assays. None of these crew members with neutralizing antibody titers showed evidence of viral infection or experienced any symptoms during the outbreak. Presence of neutralizing antibodies from prior infection was significantly associated with protection against re-infection (Fisher's exact test, <math>p=0.002</math>).</li> </ul>
11.08.2020	<a href="#">Functional SARS-CoV-2-specific immune memory persists after mild COVID-19</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• A longitudinal assessment of individuals recovered from mildly symptomatic COVID-19 to determine if they develop and sustain immunological memory against the virus.</li> <li>• Recovered individuals developed COVID-19-specific IgG antibody and neutralizing plasma, as well as virus-specific memory B and T cells that not only persisted, but in some cases increased numerically over three months following symptom onset.</li> <li>• The COVID-19-specific memory lymphocytes exhibited characteristics associated with potent antiviral immunity: memory T cells secreted IFN-<math>\gamma</math> and expanded upon antigen re-encounter, while memory B cells expressed receptors capable of neutralizing virus when expressed as antibodies.</li> <li>• Findings demonstrate that mild COVID-19 elicits memory lymphocytes that persist and display functional hallmarks associated with antiviral protective immunity.</li> </ul>
14.08.2020	<a href="#">Robust T cell immunity in convalescent individuals with asymptomatic or mild COVID-19</a>	Cell / Article	<ul style="list-style-type: none"> <li>• Authors systematically mapped the functional and phenotypic landscape of SARS-CoV-2-specific T cell responses in unexposed individuals, exposed family members, and individuals with acute or convalescent COVID-19.</li> <li>• Collective dataset shows that SARS-CoV-2 elicits robust, broad and highly functional memory T cell responses, suggesting natural exposure or infection may prevent recurrent episodes of severe COVID-19.</li> </ul> <p><i>Previously included in the digest as a preprint.</i></p>
27.07.2020	<a href="#">Evaluation of the immunogenicity of prime-boost vaccination with the replication-deficient viral vectored COVID-19 vaccine candidate ChAdOx1 nCoV-19</a>	NPJ Vaccines / Brief communication	<ul style="list-style-type: none"> <li>• Authors compared the immunogenicity of one or two doses of the COVID-19 vaccine candidate ChAdOx1 nCoV-19 in both mice and pigs.</li> <li>• Whilst a single dose induced antigen-specific antibody and T cells responses, a booster immunisation enhanced antibody</li> </ul>

responses, particularly in pigs, with a significant increase in SARS-CoV-2 neutralising titres.

*Previously included in the digest as a preprint.*

## Diagnostics

Publication Date	Title / URL	Journal / Article type	Digest
13.08.2020	<a href="#">CovidNudge: diagnostic accuracy of a novel lab-free point-of-care diagnostic for SARS-CoV-2</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• The authors describe the development and diagnostic accuracy assessment of a novel, rapid point-of-care RT-PCR test, the DnaNudge platform CovidNudge test, which requires no laboratory handling or sample pre-processing.</li> <li>• Of 386 paired samples tested across all groups, 67 tested positive on the CovidNudge platform and 71 with standard laboratory RT-PCR.</li> <li>• Test sensitivity varied by group (Group 1 93% [84-98%], Group 2 100% [48-100%] and Group 3 100% [29-100%], giving an average sensitivity of 94.4% (95% confidence interval 86-98%) and an overall specificity of 100% (95%CI 99-100%).</li> <li>• Amplification of the viral nucleocapsid (n1, n2, n3) targets were most sensitive for detection of SARS-CoV2, with the assay able to detect 1x10<sup>4</sup> viral particles in a single swab.</li> </ul>

## Genomics

Publication Date	Title / URL	Journal / Article type	Digest
22.07.2020	<a href="#">Geographic and Genomic Distribution of SARS-CoV-2 Mutations</a>	Frontiers in microbiology / Research article	<ul style="list-style-type: none"> <li>• Authors gathered the 48,635 SARS-CoV-2 complete genomes currently available; then analysed and annotated all SARS-CoV-2 mutations compared with the reference Wuhan genome NC_045512.2, observing an average of 7.23 mutations per sample.</li> <li>• Their analysis shows the prevalence of single nucleotide transitions as the major mutational type across the world. There exist at least three clades characterized by geographic and genomic specificity. In particular, clade G, prevalent in Europe, carries a D614G mutation in the Spike protein, which is</li> </ul>

responsible for the initial interaction of the virus with the host human cell.

### Epidemiology and clinical - risk factors

Publication Date	Title / URL	Journal / Article type	Digest
12.08.2020	<a href="#">OpenSAFELY: Do adults prescribed Non-steroidal anti-inflammatory drugs have an increased risk of death from COVID-19?</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>Assessed the association between NSAID use and deaths from COVID-19 using OpenSAFELY, a secure analytical platform. Working on behalf of NHS England, the authors used routine clinical data from &gt;17 million patients in England linked to death data from the Office for National Statistics.</li> <li>In Study 1, they included 535,519 current NSAID users and 1,924,095 non-users in the general population. In Study 2, they included 1,711,052 people with rheumatoid arthritis/osteoarthritis, of whom 175,631 (10%) were current NSAID users.</li> <li>Found no evidence of a harmful effect of NSAIDs on COVID19 related deaths. Risks of COVID-19 do not need to influence decisions about therapeutic use of NSAIDs.</li> </ul>

### Epidemiology and clinical – other

Publication Date	Title / URL	Journal / Article type	Digest
14.08.2020	<a href="#">Robust, reproducible clinical patterns in hospitalised patients with COVID-19</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>Obtained structured clinical data on 68,914 patients in the UK and used a principled, unsupervised clustering approach to partition the first 33,468 cases according to symptoms reported at recruitment.</li> <li>Core symptom set of fever, cough, and dyspnoea co-occurred with additional symptoms in three patterns: fatigue and confusion, diarrhoea and vomiting, or productive cough. Presentations with a single reported symptom of dyspnoea or confusion were common, and a subgroup of patients reported few or no symptoms.</li> <li>Symptom clusters were highly consistent in replication analysis</li> </ul>

			<p>using a further 35446 individuals subsequently recruited to ISARIC-4C. Similar patterns were externally verified in 4445 patients from a study of self-reported symptoms of mild disease.</p> <ul style="list-style-type: none"> <li>• Authors propose that four patterns are usefully distinct from the core symptom groups: gastro-intestinal disease, productive cough, confusion, and pauci-symptomatic presentations. Importantly, each is associated with an in-hospital mortality which differs from that of patients with core symptoms.</li> </ul>
12.08.2020	<a href="#">Place and underlying cause of death during the COVID19 pandemic: retrospective cohort study of 3.5 million deaths in England and Wales, 2014 to 2020</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• Describe the place and cause of death during the COVID-19 pandemic. This national death registry included all adult (<math>\geq 18</math> years) deaths in England and Wales between 1st Jan 2014 and 30th June 2020.</li> <li>• Between 2nd Mar and 30th June 2020, there was an excess mortality of 57860 (a proportional increase of 35%) compared with the expected deaths, of which 50603 (86.2%) were COVID-19 related.</li> <li>• Almost half the excess deaths occurred in care homes (25611 deaths) where deaths were 55% higher than expected. One fifth of the excess deaths occurred in hospital (15938 deaths; a proportional increase of 21%) with the remainder occurring at home (16190 deaths; a proportional increase of 39%).</li> </ul>
12.08.2020	<a href="#">Patient outcomes after hospitalisation with COVID-19 and implications for follow-up; results from a prospective UK cohort</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• Consecutive patients hospitalised with COVID19 were prospectively recruited to an observational cohort with outcomes recorded at 28 days. All were invited to a systematic follow up at 12 weeks, including chest radiograph, spirometry, exercise test, blood tests, and health-related quality of life (HRQoL) questionnaires. Findings: Between 30th March and 3rd June 2020, 163 patients with COVID19 were recruited.</li> <li>• Patients with COVID 19 remain highly symptomatic at 12 weeks, however, clinical abnormalities requiring action are infrequent, especially in those without a supplementary oxygen requirement during their acute illness. This has significant implications for physicians assessing patients with persistent symptoms, suggesting that a more holistic approach focussing on rehabilitation and general wellbeing is paramount.</li> </ul>
12.08.2020	<a href="#">Obesity, old age and frailty are the true risk factors for COVID-19 mortality and</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• Observational study retrospectively reviewed hospital electronic medical records of 466 consecutive patients who were admitted to Croydon University Hospital confirmed positive by rapid PCR</li> </ul>

	<a href="#">not chronic disease or ethnicity in Croydon</a>		test from 11th Mar 2020 to 9th Apr 2020. <ul style="list-style-type: none"> <li>• Found no significant effect of ethnicity and chronic diseases as independent risk factors on COVID-19 mortality in Croydon population whereas male sex, high BMI, old age and frailty were found to be independent risk factors.</li> </ul>
13.08.2020	<a href="#">Hepatic pathology in patients dying of COVID-19: a series of 40 cases including clinical, histologic, and virologic data</a>	Mod Pathol / Article	<ul style="list-style-type: none"> <li>• Authors report clinical and histologic findings related to the liver in 40 patients who died of complications of COVID-19.</li> <li>• Macrovesicular steatosis was the most common finding, involving 30 patients (75%). Mild lobular necroinflammation and portal inflammation were present in 20 cases each (50%). Vascular pathology, including sinusoidal microthrombi, was infrequent, seen in six cases (15%). PCR of liver tissue was positive in 11 of 20 patients tested (55%).</li> <li>• Patients dying of COVID-19 had biochemical evidence of hepatitis (of variable severity) and demonstrated histologic findings of macrovesicular steatosis and mild acute hepatitis (lobular necroinflammation) and mild portal inflammation. Viral RNA also identified in a sizeable subset of liver tissue samples.</li> </ul>

## Infection control

Publication Date	Title / URL	Journal / Article type	Digest
13.08.2020	<a href="#">Face mask use in the general population and optimal resource allocation during the COVID-19 pandemic</a>	Nat Commun / Article	<ul style="list-style-type: none"> <li>• Used mathematical modelling to examine the epidemiological impact of face masks, considering resource limitations and a range of supply and demand dynamics.</li> <li>• Face mask use, particularly for a pathogen with relatively common asymptomatic carriage, is an effective intervention strategy, while optimized distribution is important when resources are limited.</li> </ul> <p><i>Previously included in the digest as a preprint.</i></p>
01.06.2020	<a href="#">Should individuals in the community without respiratory symptoms wear facemasks to reduce the spread of COVID-19?</a>	Norwegian Institute of Public Health / Rapid review	<ul style="list-style-type: none"> <li>• This is a rapid review of the knowledge base for the use of face masks by people in the community to reduce the spread of covid-19.</li> <li>• If a recommendation to wear face masks is made: medical masks or quality controlled non-medical masks with a documented filtration effect should be used; the community should be given</li> </ul>

			training to ensure correct use and the risks should be explained, especially the risks of a false sense of security and contamination of masks; training should be tailored to the needs of different groups, including people with different levels of fluency and different socio-economic circumstances.
14.08.2020	<a href="#">Potential Role of Social Distancing in Mitigating Spread of Coronavirus Disease, South Korea</a>	Emerg Infect Dis / Dispatch	<ul style="list-style-type: none"> <li>• In South Korea, the coronavirus disease outbreak peaked at the end of Feb and subsided in mid-March.</li> <li>• Authors analysed the likely roles of social distancing in reducing transmission. Analysis indicated that although transmission might persist in some regions, epidemics can be suppressed with less extreme measures than those taken by China.</li> </ul>
13.08.2020	<a href="#">A novel approach for evaluating contact patterns and risk mitigation strategies for COVID-19 in English Primary Schools with application of Structured Expert Judgement</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• Conducted a structured expert elicitation of a sample of Primary Headteachers to quantify contact patterns within schools in pre-COVID-19 times and how these patterns were expected to change upon re-opening.</li> <li>• The authors interpret the reduction in children's contacts as a consequence of efforts to reduce mixing with interventions such as forming groups of children (bubbles) who are organized to learn together to limit contacts.</li> <li>• Distributions of contacts for children and adults can be used to inform COVID-19 transmission modelling. Findings suggest that while official DfE guidelines form the basis for risk mitigation in schools, individual schools have adopted their own bespoke strategies, often going beyond the guidelines.</li> </ul>

## Treatment

Publication Date	Title / URL	Journal / Article type	Digest
14.08.2020	<a href="#">Tocilizumab among patients with COVID-19 in the intensive care unit: a multicentre observational study</a>	The Lancet Rheumatology / Article	<ul style="list-style-type: none"> <li>• Retrospective observational cohort study at 13 hospitals - of association between tocilizumab exposure and hospital-related mortality among COVID-19 patients requiring ICU support. 210 (27% of 764 total patients) received tocilizumab.</li> <li>• In the primary multivariable Cox regression analysis with propensity matching, an association was noted between receiving tocilizumab and decreased hospital-related mortality (HR 0.64, 95% CI 0.47–0.87; p=0.0040).</li> </ul>

- Similar associations with tocilizumab were noted among subgroups requiring mechanical ventilatory support and with baseline C-reactive protein of 15 mg/dL or higher.

## Miscellaneous

Publication Date	Title / URL	Journal / Article type	Digest
13.08.2020	<a href="#">COVID-19 vaccination intention in the UK: Results from the COVID-19 Vaccination Acceptability Study (CoVAccS), a nationally representative cross-sectional survey</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• Online cross-sectional survey of 1,500 UK adults to investigate factors associated with intention to be vaccinated against COVID-19.</li> <li>• 64% reported being likely to be vaccinated against COVID-19, 27% were unsure, and 9% reported being unlikely to be vaccinated.</li> <li>• Personal and clinical characteristics, previous influenza vaccination, general vaccination beliefs, and beliefs and attitudes about COVID-19 and a COVID-19 vaccination explained 77% of the variance in vaccination intention.</li> <li>• Intention to be vaccinated was associated with factors such as positive COVID-19 vaccination beliefs, weaker beliefs that the vaccination would cause side effects, greater perceived information sufficiency to make a decision, older age, and having been vaccinated for influenza last winter (2019/20).</li> </ul>

## Overviews, comments and editorials

Publication Date	Title / URL	Journal / Article type
14.08.2020	<a href="#">Influenza in the COVID-19 Era</a>	JAMA / Insights
14.08.2020	<a href="#">Returning to School in the Era of COVID-19</a>	JAMA Pediatrics / Editorial
14.08.2020	<a href="#">The EVALI outbreak and vaping in the COVID-19 era</a>	The Lancet Respiratory Medicine / Editorial
14.08.2020	<a href="#">The conundrum of interleukin-6 blockade in COVID-19</a>	The Lancet Rheumatology / Comment

To sign-up, email [COVID.LitDigest@phe.gov.uk](mailto:COVID.LitDigest@phe.gov.uk)

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