



## COVID-19 Literature Digest – 11/09/2020

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:

- Genomics
- Epidemiology and clinical - children and pregnancy
- Epidemiology and clinical - risk factors
- Epidemiology and clinical - other
- Infection control
- Treatment
- Modelling
- Guidance, consensus statements and hospital resources (no digest)
- 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Please note that we are including preprints (**highlighted in red**), which are preliminary reports of work that have NOT been peer-reviewed.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.

### Genomics

Publication Date	Title / URL	Journal / Article type	Digest
09.09.2020	<a href="#">SARS-CoV-2 Polymorphisms and Multisystem Inflammatory Syndrome in Children (MIS-C)</a>	Pediatrics / Article	<ul style="list-style-type: none"><li>• This report compares viral sequences from children diagnosed with MIS-C (n=5) to viral sequences from children without MIS-C (n=8) as well as the wider London community (n=130).</li><li>• Overall, the data suggest that the viruses causing MIS-C in these patients are representative of locally circulating SARS-CoV-2. They found no evidence for an association of MIS-C with the presence of new or unusual sequence polymorphisms.</li></ul>

			<ul style="list-style-type: none"> <li>• This suggests that alternative factors, such as host-genetics, may trigger MIS-C. Further studies are required to address this.</li> </ul>
09.09.2020	<a href="#">The UCSC SARS-CoV-2 Genome Browser</a>	Nat Genet / Comment	<ul style="list-style-type: none"> <li>• The UCSC SARS-CoV-2 Genome Browser (<a href="https://genome.ucsc.edu/covid19.html">https://genome.ucsc.edu/covid19.html</a>) is an adaptation of the authors popular genome-browser visualization tool for this virus, containing many annotation tracks and new features, including conservation with similar viruses, immune epitopes, RT-PCR and sequencing primers and CRISPR guides.</li> </ul>
09.09.2020	<a href="#">Exploring the coronavirus pandemic with the WashU Virus Genome Browser</a>	Nat Genet / Comment	<ul style="list-style-type: none"> <li>• WashU Virus Genome Browser is a web-based portal for efficient visualization of viral ‘omics’ data in the context of a variety of annotation tracks and host infection responses.</li> <li>• Features both a phylogenetic-tree-based view and a genomic-coordinate, track-based view in which users can analyse the sequence features of viral genomes, sequence diversity among viral strains, genomic sites of diagnostic tests, predicted immunogenic epitopes and a continuously updated repository of publicly available genomic datasets.</li> </ul>
09.09.2020	<a href="#">Exploring the structural distribution of genetic variation in SARS-CoV-2 with the COVID-3D online resource</a>	Nat Genet / Comment	<ul style="list-style-type: none"> <li>• To enable easy exploration and spatial visualization of the potential implications of SARS-CoV-2 mutations in infection, host immunity and drug development, the authors have developed COVID-3D (<a href="http://biosig.unimelb.edu.au/covid3d/">http://biosig.unimelb.edu.au/covid3d/</a>).</li> </ul>

### Epidemiology and clinical – children and pregnancy

Publication Date	Title / URL	Journal / Article type	Digest
10.09.2020	<a href="#">Transmission of SARS-CoV-2 in children aged 0 to 19 years in childcare facilities and schools after their reopening in May 2020, Baden-Württemberg, Germany</a>	Eurosurveillance / Rapid communication	<ul style="list-style-type: none"> <li>• Investigated data from SARS-CoV-2 infected 0–19 year olds, who attended schools/childcare facilities, to assess their role in SARS-CoV-2 transmission after these establishments’ reopening in May 2020 in Baden-Württemberg, Germany.</li> <li>• Child-to-child transmission in schools/childcare facilities appeared very uncommon.</li> <li>• The authors anticipate that, with face mask use and frequent ventilation of rooms, transmission rates in schools/childcare facilities would remain low in the next term, even if classes’ group sizes were increased.</li> </ul>

Epidemiology and clinical – risk factors

Publication Date	Title / URL	Journal / Article type	Digest
09.09.2020	<a href="#">Risk stratification of patients admitted to hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: development and validation of the 4C Mortality Score</a>	Bmj / Article	<ul style="list-style-type: none"> <li>• Prospective observational cohort study in which the authors developed and validated a pragmatic risk score to predict mortality in patients admitted to hospital with COVID-19.</li> <li>• 35,463 patients were included in the derivation dataset (mortality rate 32.2%) and 22 361 in the validation dataset (mortality rate 30.1%), from 260 hospitals across England, Scotland, and Wales.</li> <li>• The 4C Mortality Score outperformed existing scores, showed utility to directly inform clinical decision making, and can be used to stratify patients admitted to hospital with COVID-19 into different management groups. The score should be further validated to determine its applicability in other populations.</li> </ul>
09.09.2020	<a href="#">Clinical Outcomes in Young US Adults Hospitalized With COVID-19</a>	JAMA Internal Medicine / Research letter	<ul style="list-style-type: none"> <li>• Investigated the clinical profile and outcomes of 3222 young adults (aged 18-34, non-pregnant) who required hospitalization for COVID-19 in the US.</li> <li>• Experienced substantial rates of adverse outcomes: 21% required intensive care, 10% required mechanical ventilation, and 2.7% died.</li> <li>• Morbid obesity, hypertension, and diabetes were common and associated with greater risks of adverse events. Young adults with more than 1 of these conditions faced risks comparable with those observed in middle-aged adults without them.</li> <li>• More than half of these patients requiring hospitalization were Black or Hispanic, consistent with prior findings of disproportionate illness severity in these demographic groups.</li> </ul>
07.09.2020	<a href="#">COVID-19 in patients with hepatobiliary and pancreatic diseases in East London: A single-centre cohort study</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• A single-centre cohort study (15,586 patients) explored the impact of COVID-19 in patients with pre-existing hepato-pancreato-biliary (HPB).</li> <li>• An increased risk of COVID-19 for men (Relative Risk, RR=1.59; 95% CI 1.21 to 2.09) and Black ethnicity (RR=2.2; 95% CI 1.5 to 3.18) was observed.</li> <li>• Substance mis-users and patients on Vitamin D treatment were both at higher risk of infection.</li> <li>• The higher risks associated with South Asian ethnicity, patients with pre-existing non-malignant pancreatic or liver conditions, age&gt;70, and past smokers were due to co-existing comorbidities.</li> <li>• Increased mortality risk was observed for Black ethnicity (RR=2.4; 95% CI 1.35 to 3.48), and patients with a pre-existing kidney condition (RR=2.13; 95%</li> </ul>

			CI 1.16 to 3.55), particularly when accompanied with an acute episode of renal complications (RR=2.74; 95% CI 1.32 to 5.13).
09.09.2020	<a href="#">Clinical characteristics and outcomes of immunosuppressed patients hospitalized with COVID-19: experience from London</a>	J Intern Med / Article	<ul style="list-style-type: none"> <li>• In this cohort study of 981 confirmed COVID-19 patients consecutively hospitalized at a large North West London hospital, immunosuppressant use was associated with significantly higher mortality rates.</li> </ul>

### Epidemiology and clinical – long term complications / sequelae

Publication Date	Title / URL	Journal / Article type	Digest
10.09.2020	<a href="#">Reduced maximal aerobic capacity after COVID-19 in young adult recruits, Switzerland, May 2020</a>	Eurosurveillance / Rapid communication	<ul style="list-style-type: none"> <li>• In March 2020, the authors observed an outbreak of COVID-19 among a relatively homogenous group of 199 young (median age 21 years; 87% men) Swiss recruits.</li> <li>• By comparing physical endurance before and in median 45 days after the outbreak, they found a significant decrease in predicted maximal aerobic capacity in COVID-19 convalescent but not in asymptotically infected and SARS-CoV-2 naive recruits.</li> <li>• This finding might be indicative of lung injury after apparently mild COVID-19 in young adults.</li> </ul>

### Infection control

Publication Date	Title / URL	Journal / Article type	Digest
09.09.2020	<a href="#">Incidence of Nosocomial COVID-19 in Patients Hospitalized at a Large US Academic Medical Center</a>	JAMA Network Open / Original investigation	<ul style="list-style-type: none"> <li>• The authors investigated the incidence of hospital-acquired COVID-19 at a large US academic medical centre.</li> <li>• In this cohort study of 9149 patients admitted to a large US academic medical centre over a 12-week period, 697 were diagnosed with COVID-19.</li> <li>• In the context of a comprehensive and progressive infection control program, only 2 hospital-acquired cases were detected: 1 patient was likely infected by a pre-symptomatic spouse before visitor restrictions were implemented, and 1 patient developed symptoms 4 days after a 16-day hospitalization but without known exposures in the hospital.</li> <li>• These findings suggest that overall risk of hospital-acquired COVID-19 was low and that rigorous infection control measures may be associated with minimized risk.</li> </ul>

09.09.2020	<a href="#">Airborne contamination of COVID-19 in hospitals: a scoping review of the current evidence</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• The authors reviewed the current evidence on the air contamination with SARS-CoV-2 in hospital settings, and the factors associated with contamination including the viral load and the particles size (17 articles included).</li> <li>• Overall, 27.5% (68/247) of air sampled from close patients environment were positive for SARS-CoV-2 RNA, without difference according to the setting (ICU: 27/97, 27.8%; non-ICU: 41/150, 27.3%; p=0.93), or the distance from patients (&lt;1 meter: 1/64, 1.5%; 1-5 meters: 4/67, 6%; p=0.4).</li> <li>• In other areas, the positivity rate was 23.8% (5/21) in toilets, 9.5% (20/221) in clinical areas, 12.4% (15/121) in staff areas, and 34.1% (14/41) in public areas.</li> <li>• Concluded that in hospital, the air near and away from COVID-19 patients is frequently contaminated with SARS-CoV-2 RNA, with however, rare proofs of their viability. High viral loads found in toilet/bathrooms, staff and public hallways suggests to carefully consider these areas.</li> </ul>
09.09.2020	<a href="#">Environmental and Aerosolized SARS-CoV-2 Among Hospitalized COVID-19 Patients</a>	Journal of Infectious Diseases / Article	<ul style="list-style-type: none"> <li>• Studied 20 hospitalized COVID-19 patients, their hospital rooms (fomites and aerosols), and their close contacts for molecular and culture evidence of SARS-CoV-2 virus.</li> <li>• Among the more than 400 samples, they found molecular evidence of virus in most sample types, especially the nasopharyngeal (NP), saliva, and faecal samples, but the prevalence of molecular positivity among fomites and aerosols was low.</li> <li>• In summary, the low molecular prevalence and lack of viable SARS-CoV-2 virus in fomites and air samples implied low nosocomial risk SARS-CoV-2 transmission through inanimate objects or aerosols.</li> </ul>

## Treatment

Publication Date	Title / URL	Journal / Article type	Digest
07.09.2020	<a href="#">Combination of tocilizumab and steroids to improve mortality in patients with severe COVID-19 infection: a Spanish, multicenter, cohort study</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• In a retrospective cohort study in 18 Spanish hospitals, patients admitted with severe COVID-19 treated with tocilizumab (n=268) were compared to patients not treated with tocilizumab (n=238). Tocilizumab effect in patients receiving steroids during the 48h following inclusion was also analysed.</li> <li>• Mortality was lower in patients treated with tocilizumab than in controls (16.8% versus 31.5%, HR 0.514 [95CI 0.355-0.744], p&lt;0.001; weighted HR 0.741 [95CI 0.619-0.887], p=0.001).</li> </ul>

			<ul style="list-style-type: none"> <li>• Tocilizumab treatment reduced mortality by 14.7% relative to no tocilizumab treatment (RRR 46.7%).</li> <li>• Among patients treated with steroids, mortality was lower in patients treated with tocilizumab than in those treated with steroids alone (10.9% versus 40.2%, HR 0.511 [95CI 0.352-0.741], p=0.036; weighted HR 0.6 [95CI 0.449-0.804], p&lt;0.001) (Interaction p=0.094).</li> </ul>
04.09.2020	<a href="#">Hydroxychloroquine for prevention of COVID-19 mortality: a population-based cohort study</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• An English cohort study evaluated the effectiveness of hydroxychloroquine for prevention, as opposed to treatment, of COVID-19 mortality.</li> <li>• Of 194,637 patients with rheumatoid arthritis (RA) or systemic lupus erythematosus (SLE), 30,569 (15.7%) received ≥2 prescriptions of hydroxychloroquine in the six months prior to 1 March 2020.</li> <li>• Estimated standardised cumulative COVID-19 mortality was 0.23% (95% CI 0.18-0.29) among users and 0.22% (95% CI 0.20-0.25) among non-users; an absolute difference of 0.008% (95% CI -0.051-0.066).</li> <li>• After accounting for age, sex, ethnicity, use of other immunosuppressives, and geographic region, no association with COVID-19 mortality was observed (HR 1.03, 95% CI 0.80-1.33).</li> </ul>

## Modelling

Publication Date	Title / URL	Journal / Article type	Digest
09.09.2020	<a href="#">Substantial underestimation of SARS-CoV-2 infection in the United States</a>	Nat Commun / article	<ul style="list-style-type: none"> <li>• Authors use a semi-Bayesian probabilistic bias analysis to account for incomplete testing and imperfect diagnostic accuracy.</li> <li>• Estimate total number of SARS-CoV-2 infections in U.S. by April 18, 2020 was 6,454,951 (19 per 1000)—an estimate nine times larger than the 721,245 confirmed cases (2 per 1000) reported during this period.</li> <li>• Accounting for uncertainty, the number of infections was 3 to 20 times higher than the number of confirmed cases. 86% (simulation interval: 64-99%) of this difference is due to incomplete testing, while 14% (0.3-36%) is due to imperfect test accuracy.</li> <li>• These results imply that 89% of infections in the U.S. were undocumented - consistent with a mathematical modelling study that reported that 86% of infections were undocumented using data from Wuhan, China.</li> </ul>
09.09.2020	<a href="#">Projected health-care resource needs for an effective response to COVID-19 in 73</a>	Lancet Global Health / Article	<ul style="list-style-type: none"> <li>• This study aimed to identify what the additional health-care costs of a strategic preparedness and response plan (SPRP) would be if current transmission levels are maintained in a status quo scenario, or under</li> </ul>

	<a href="#">low-income and middle-income countries: a modelling study</a>		<p>scenarios where transmission is increased or decreased by 50%.</p> <ul style="list-style-type: none"> <li>• The number of COVID-19 cases was projected for 73 low-income and middle-income countries for each of the three scenarios for both 4-week and 12-week timeframes, starting from June 26, 2020.</li> <li>• Concluded that the sizeable costs of a COVID-19 response in the health sector will escalate, particularly if transmission increases. Instituting early and comprehensive measures to limit the further spread of the virus will conserve resources and sustain the response.</li> </ul>
07.09.2020	<a href="#">COVID-19 transmission in a university setting: a rapid review of modelling studies</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• A rapid review and appraisal of the literature on mathematical models investigating COVID-19 infection in a university setting.</li> <li>• All models suggest a significant potential for transmission of COVID-19 in universities.</li> <li>• Testing of symptomatic persons and screening of the university community regardless of symptoms, combined with isolation of infected individuals and effective contact tracing were critical for infection control in the absence of other interventions.</li> <li>• When other interventions were considered (e.g. teaching online, physical distancing, face coverings) the additional value of screening for infection control was limited.</li> </ul>
08.09.2020	<a href="#">COVID-19 Transmission Dynamics and Effectiveness of Public Health Interventions in New York City during the 2020 Spring Pandemic Wave</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• The authors model the transmission dynamics of COVID-19 in New York City during the pandemic and estimate the effectiveness of public health interventions.</li> <li>• The overall R number was estimated as 2.99 at the beginning of the pandemic wave and reduced to 0.93 one week after the stay-at-home mandate. Most age groups experienced similar reductions in transmission.</li> <li>• Interventions reducing contact rates were associated with a 70.7% (95% CI: 65.0 - 76.4%) reduction of transmission overall and &gt;50% for all age groups during the pandemic.</li> <li>• Face covering was associated with a 6.6% (95% CI: 0.8 - 12.4%) reduction of transmission overall and up to 20% for 65+ year-olds during the first month of implementation.</li> <li>• Accounting for the amount of time masks are in use (i.e. mainly outside homes), these findings indicate universal masking could reduce transmission by up to 28-32% when lockdown-like measures are lifted, if the high effectiveness estimated for older adults were achieved for all ages.</li> </ul>

## Guidance and consensus statements

Publication Date	Title / URL	Journal / Article type
10.09.2020	<a href="#">Coronavirus (COVID-19): testing guidance for employers</a>	Gov.uk / Guidance
04.09.2020	<a href="#">Chemoprophylaxis, diagnosis, treatments, and discharge management of COVID-19: An evidence-based clinical practice guideline (updated version)</a>	Mil Med Res / Article

## Overviews, comments and editorials

Publication Date	Title / URL	Journal / Article type
08.09.2020	<a href="#">Testing for SARS-CoV-2 antibodies</a>	Bmj / Practice
10.09.2020	<a href="#">Trained Innate Immunity, Epigenetics, and Covid-19</a>	N Engl J Med / Perspective
10.09.2020	<a href="#">It is time to get serious about vaccine confidence</a>	Lancet / Comment
10.09.2020	<a href="#">Heidi Larson: shifting the conversation about vaccine confidence</a>	Lancet / Perspective
09.09.2020	<a href="#">COVACTA trial raises questions about tocilizumab's benefit in COVID-19</a>	Lancet Rheumatology / News
09.09.2020	<a href="#">Use of "normal" risk to improve understanding of dangers of covid-19</a>	Bmj / Analysis
09.09.2020	<a href="#">Obesity and Hypertension in the Time of COVID-19</a>	JAMA / Editorial

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