



## International EPI Cell Daily Evidence Digest – 29/07/2020

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
- 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Please note that we are including preprints (**highlighted in red**), which are preliminary reports of work that have NOT been peer-reviewed.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.

### Serology and immunology

Publication Date	Title / URL	Journal / Article type	Digest
27.07.2020	<a href="#">Longitudinal analyses reveal immunological misfiring in severe COVID-19</a>	Nature / Article	<ul style="list-style-type: none"><li>• A study serially analysed immune responses in 113 COVID-19 patients with moderate (non-ICU) and severe (ICU) disease.</li><li>• Immune profiling revealed overall increase in innate cell lineages with a concomitant reduction in T cell number.</li><li>• Unsupervised clustering analysis identified 4 immune signatures, representing (A) growth factors, (B) type-2/3 cytokines, (C) mixed type-1/2/3 cytokines, and (D) chemokines that correlated with three distinct</li></ul>

			disease trajectories of patients. <ul style="list-style-type: none"> <li>• The immune profile of patients who recovered with moderate disease was enriched in tissue reparative growth factor signature (A), while the profile for those with worsened disease trajectory had elevated levels of all four signatures.</li> </ul>
28.07.2020	<a href="#">Evaluation of the mRNA-1273 Vaccine against SARS-CoV-2 in Nonhuman Primates</a>	New England Journal of Medicine / Article	<ul style="list-style-type: none"> <li>• Vaccination of nonhuman primates with either 10 µg (n=8) or 100 µg (n=8) of mRNA-1273 induced robust SARS-CoV-2 neutralizing activity, rapid protection in the upper and lower airways, and no pathologic changes in the lung.</li> </ul>

### Diagnostics

Publication Date	Title / URL	Journal / Article type	Digest
25.07.2020	<a href="#">SARS-CoV-2 viral load dynamics, duration of viral shedding and infectiousness: a living systematic review and meta-analysis</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• A systematic review to characterise viral load dynamics, duration of viral RNA, and viable virus shedding of SARS-CoV-2 in various body fluids</li> <li>• Data suggests SARS-CoV-2 RNA shedding in respiratory fluids and stool can be prolonged, although duration of viable virus is relatively short-lived.</li> <li>• Authors therefore suggest detection of viral RNA cannot be used to infer infectiousness.</li> <li>• High SARS-CoV-2 titres were detectable in the first week of illness with an early peak observed at symptom onset to day 5 of illness.</li> </ul>

### Epidemiology and clinical - risk factors

Publication Date	Title / URL	Journal / Article type	Digest
27.07.2020	<a href="#">Incidence and mortality of pulmonary embolism in COVID-19: a systematic review and meta-analysis</a>	Crit Care / Article	<ul style="list-style-type: none"> <li>• Systematic review examining pulmonary embolism (PE) incidence and mortality in COVID-19 patients</li> <li>• 19 articles, mostly from Europe (84%), met the criteria.</li> <li>• Overall, incidence and mortality rate of COVID-19 patients developing PE was 15.3% (95%: 9.8–21.9) and 45.1% (95%: 22.0–69.4) respectively.</li> <li>• Some evidence of statistical heterogeneity among the studies</li> </ul>

			reporting PE incidence (I2: 92.0%, $p < 0.001$ ) and mortality (I2: 78.6%, $p < 0.001$ ) in COVID-19 was observed.
Ju27.07.2020	<a href="#">Association between NSAIDs use and adverse clinical outcomes among adults hospitalized with COVID-19 in South Korea: A nationwide study</a>	Clin Infect Dis / Article	<ul style="list-style-type: none"> <li>• Conducted a cohort study using South Korea's nationwide healthcare database, which contains data of all subjects who received a test for COVID-19 (n=69,793) as of Apr 8, 2020. We identified adults hospitalized with COVID-19, where cohort entry was the date of hospitalization. NSAIDs users were those prescribed NSAIDs in the 7 days before and including cohort entry and non-users were those not prescribed NSAIDs during this period.</li> <li>• Of 1,824 adults hospitalized with COVID-19 (mean age 49.0 years; female 59%), 354 were NSAIDs users and 1,470 were non-users. Compared with non-use, NSAIDs use was associated with increased risks of the primary composite outcome (OR 1.54 [95% CI 1.13-2.11]) but insignificantly associated with cardiovascular complications (1.54 [0.96-2.48]) or acute renal failure (1.45 [0.49-4.14]).</li> </ul>
21.07.2020	<a href="#">Patient characteristics and predictors of mortality in 470 adults admitted to a district general hospital in England with Covid-19</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• Retrospective analysis of 470 adults (median age = 71; Male = 54.3%) admitted with Covid-19 to Royal Oldham Hospital, of whom 169 (36%) died.</li> <li>• The most common comorbidities were hypertension (n=218, 46.4%), diabetes (n=143, 30.4%) and chronic neurological disease (n=123, 26.1%).</li> <li>• The most frequent complications were acute kidney injury (n=157, 33.4%) and myocardial injury (n=21, 4.5%).</li> <li>• 43 (9.1%) patients required intubation and ventilation, and 39 (8.3%) received non-invasive ventilation.</li> <li>• Independent risk factors for death were increasing age, hypertension, cancer, platelets <math>&lt; 150 \times 10^3</math>/microlitre, C-reactive protein <math>&gt; 100</math> micrograms/mL, <math>&gt; 50\%</math> chest radiograph infiltrates, and acute kidney injury.</li> <li>• No independent association between death and gender, ethnicity, deprivation level, fever, SpO<sub>2</sub>/FiO<sub>2</sub> (oxygen saturation index), lymphopenia or other comorbidities.</li> </ul>
19.07.2020	<a href="#">Mononeuritis multiplex: an unexpectedly common feature of severe COVID-19</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• Among 69 patients with severe COVID-19 discharged from intensive care in a single-hospital study, 11 individuals (16%) had disabling focal neurological deficits relating to an axonal mononeuritis multiplex.</li> <li>• The multi-focal nature of the weakness in these patients was initially unrecognised in many cases as symptoms were wrongly assumed to relate to critical illness neuropathy.</li> </ul>

			<ul style="list-style-type: none"> <li>• Authors suggest mononeuropathy deficits may be common and frequently disabling in patients recovering from COVID-19.</li> </ul>
28.07.2020	<a href="#">Assessment of Community-Level Disparities in Coronavirus Disease 2019 (COVID-19) Infections and Deaths in Large US Metropolitan Areas</a>	JAMA Netw Open / Research Letter	<ul style="list-style-type: none"> <li>• Cross-sectional study examined the association of neighbourhood race/ethnicity and poverty with COVID-19 infections and related deaths in 158 urban US counties</li> <li>• Amongst poorer counties, those with substantially non-White populations had an infection rate nearly 8 times that of counties with substantially White populations (RR, 7.8; 95% CI, 5.1-12.0) and a death rate more than 9 times greater (RR, 9.3; 95% CI, 4.7-18.4).</li> <li>• In all counties, those with substantially non-White or more diverse populations had higher expected cumulative COVID-19 incident infections compared with counties with substantially White or less-diverse populations (e.g. more diverse counties with less poverty: RR, 3.2; 95% CI, 2.3-4.6).</li> <li>• Similar associations were observed for deaths (e.g. more diverse counties with less poverty: RR, 3.8; 95% CI, 2.2-6.7).</li> <li>• Lack of access to disaggregated data precluded further exploration of causal mechanisms.</li> </ul>

#### Epidemiology and clinical – other

Publication Date	Title / URL	Journal / Article type	Digest
28.07.2020	<a href="#">Case characteristics, resource use, and outcomes of 10 021 patients with COVID-19 admitted to 920 German hospitals: an observational study</a>	The Lancet Respiratory Medicine / Article	<ul style="list-style-type: none"> <li>• Of 10,021 hospitalised patients being treated in 920 different hospitals in Germany, 1727 (17%) received mechanical ventilation. The median age was 72 years (IQR 57–82). Men and women were equally represented in the non-ventilated group, whereas twice as many men than women were in the ventilated group.</li> <li>• Most common comorbidities were hypertension (5575 [56%] of 10,021), diabetes (2791 [28%]), cardiac arrhythmia (2699 [27%]), renal failure (2287 [23%]), heart failure (1963 [20%]), and chronic pulmonary disease (1358 [14%]).</li> <li>• In the German health-care system, in which hospital capacities have not been overwhelmed by the COVID-19 pandemic, mortality has been high for patients receiving mechanical ventilation, particularly for patients aged 80 years or older and those requiring dialysis, and has been considerably lower for patients younger than 60 years.</li> </ul>

27.07.2020	<a href="#">Prevalence of SARS-CoV-2 Infection Among Asymptomatic Health Care Workers in the Greater Houston, Texas, Area</a>	JAMA Network Open / Research letter	<ul style="list-style-type: none"> <li>• Houston Methodist initiated a COVID-19 surveillance program among asymptomatic HCWs and expanded to asymptomatic community residents. Reports the prevalence of SARS-CoV-2 among the first group tested.</li> <li>• A total of 2872 individuals, including 2787 HCWs and 85 community residents, were included; the mean (SD) age was 40.9 (11.7) years and 73% (95% CI, 71.6%-74.9%) were women.</li> <li>• Report a 4.8% difference between COVID-19-facing (5.4%) and non-COVID-19-facing (0.6%) HCWs, potentially indicating transmission from patients or co-workers. All nonclinical HCWs and community residents had RT-PCR test results negative for SARS-CoV-2.</li> <li>• Nonclinical HCWs worked in buildings with separate entrances and heating, ventilation, and air conditioning systems, with lower population density due to remote working policies. Comparison across job categories of COVID-19-facing HCWs did not yield significant differences between presumably high and low exposures, supporting the need for uniform infection control practices within patient care units.</li> </ul>
27.07.2020	<a href="#">Nosocomial spread of COVID-19: lessons learned from an audit on a stroke/neurology ward in a UK district general hospital</a>	Clin Med (Lond) / Article	<ul style="list-style-type: none"> <li>• Describes a COVID-19 outbreak in a 25-bed neurology/stroke ward in the early phase of the pandemic (Mar to May 2020).</li> <li>• Twenty-one of 133 admissions (16%) tested positive for COVID-19 and of those, 8 (6% of admissions) were determined to be nosocomial. Thus 38% (8/21) of COVID-19 infections were hospital-acquired.</li> <li>• Ten of the patients that contracted COVID-19 died; of these three were hospital-acquired cases.</li> <li>• Five of the 21 patients had negative swabs prior to receiving a positive test result.</li> <li>• Authors highlight the importance of appropriate use of personal protective equipment with high-risk patients and the difficulties of COVID-19 management in a high-risk patient population.</li> </ul>
22.07.2020	<a href="#">The best COVID-19 predictor is recent smell loss: a cross-sectional study</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• A cross-sectional study quantified changes in chemosensory abilities using 0-100 visual analog scales (VAS) for participants reporting a positive (C19+; n=4148) or negative (C19-; n=546) COVID-19 laboratory test outcome.</li> <li>• Both C19+ and C19- groups exhibited smell loss, but it was significantly larger in C19+ participants (mean = 82.5, SD = 27.2)</li> </ul>

		<p>points).</p> <ul style="list-style-type: none"> <li>• Smell loss during illness was best predictor of COVID-19 in both single and cumulative feature models (ROC AUC=0.72).</li> <li>• VAS ratings of smell loss were more predictive than binary chemosensory yes/no-questions or other cardinal symptoms, such as fever or cough.</li> <li>• Olfactory recovery within 40 days was reported for ~50% of participants and best predicted by time since illness onset.</li> </ul>
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## Infection control

Publication Date	Title / URL	Journal / Article type	Digest
27.07.2020	<a href="#">Estimation of Viral Aerosol Emissions From Simulated Individuals With Asymptomatic to Moderate Coronavirus Disease 2019</a>	JAMA Network Open / Original investigation	<ul style="list-style-type: none"> <li>• In this mathematical modelling study, breathing and coughing by a simulated individual with COVID-19 were estimated to release large numbers of viruses in a poorly ventilated room with a coughing person. However, the estimated infectious risk posed by a person with typical viral load who breathes normally was low, and only few people with very high viral load posed an infection risk in a poorly ventilated closed environment.</li> <li>• These results may partially explain the observed rates of transmission and suggest that there is a need for strict respiratory protection when people are in the same room with an individual with COVID-19.</li> </ul>

## Treatment

Publication Date	Title / URL	Journal / Article type	Digest
27.07.2020	<a href="#">Characteristics and Strength of Evidence of COVID-19 Studies Registered on ClinicalTrials.gov</a>	JAMA Internal Medicine / Comment	<ul style="list-style-type: none"> <li>• Evaluated the characteristics and expected strength of evidence of COVID-19 studies registered on ClinicalTrials.gov.</li> <li>• Identified 1551 studies registered from Mar 1, 2011, to May 19, 2020, meeting inclusion criteria. Of the 1551 studies, 451 (29.1%) could potentially yield OCEBM level 2 evidence, or the highest level of individual study evidence.</li> <li>• Although a few large multicentre trials may generate high-quality</li> </ul>

evidence, the large proportion of studies with an expected low level of evidence is concerning.

- Limitations: Current regulations only require drug, device, or biological studies to register with ClinicalTrials.gov. Half of non-US studies are estimated to not be registered with ClinicalTrials.gov,<sup>6</sup> and OCEBM is most accurately applied to completed studies.

## Modelling

Publication Date	Title / URL	Journal / Article type	Digest
25.07.2020	<a href="#">Using social contact data to predict and compare the impact of social distancing policies with implications for school re-opening</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• Authors used social contact data from the UK, combined with incidence data and Google Community Mobility Reports, to predict the impact of social distancing policies on the R number.</li> <li>• Data indicates the minimum UK reproduction number that can be achieved without limiting household contacts is 0.45 (95%CI:0.41-0.50).</li> <li>• Preventing leisure contacts has a smaller impact (R=2.0,95%CI:1.8-2.4) than preventing work contacts (R=1.5,95%CI:1.4-1.7).</li> <li>• Post-lockdown opening of primary schools alone has a modest impact (R=0.83, 95%CI:0.77-0.90), but high adherence to other measures is needed.</li> <li>• Opening secondary schools as well as primary school has a larger impact (R=0.95,95%CI:0.85-1.07), however transmission could still be controlled with effective contact tracing.</li> </ul>

## Guidelines, consensus statements

Publication Date	Title / URL	Journal / Article type
24.07.2020	<a href="#">Preventing and managing COVID-19 across long-term care services: Policy brief, 24 July 2020</a>	WHO / Policy Brief
27.07.2020	<a href="#">Infectious Diseases Society of America Guidelines on Infection Prevention for Health Care Personnel Caring for Patients with Suspected or Known COVID-19</a>	Clin Infect Dis / Guidance

## Overviews, comments and editorials

Publication Date	Title / URL	Journal / Article type
27.07.2020	<a href="#">Covid-19: UK Obstetric Surveillance System (UKOSS) study in context</a>	Bmj / Letter
27.07.2020	<a href="#">Assessing the extent of SARS-CoV-2 circulation through serological studies</a>	Nat Med / Comment
27.07.2020	<a href="#">Sampling the host response to SARS-CoV-2 in hospitals under siege</a>	Nat Med / Letter
14.07.2020	<a href="#">Lessons for COVID-19 Immunity from Other Coronavirus Infections</a>	Immunity / Article
27.07.2020	<a href="#">High rates of stillbirth and preterm delivery in women with covid-19 and the efficacy of ECMO in pregnancy</a>	Bmj / Letter
27.07.2020	<a href="#">Illness-Related Work Absence in Mid-April Was Highest on Record</a>	JAMA Internal Medicine / Research letter
28.07.2020	<a href="#">Lung fibrosis: an undervalued finding in COVID-19 pathological series</a>	The Lancet Infectious Diseases / Correspondence
26.07.2020.	<a href="#">Is risk compensation threatening public health in the covid-19 pandemic?</a>	BMJ / Analysis
21.07.2020	<a href="#">Tracking COVID-19 in the United States</a>	Resolve to Save Lives / Report
28.07.2020.	<a href="#">NIH Launches Platform to Serve as Depository for COVID-19 Medical Data</a>	Jama / Health Agencies Update

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