



## International EPI Cell Daily Evidence Digest – 28/05/2020

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
- Genomics
- Epidemiology and clinical - children and pregnancy
- Epidemiology and clinical - risk factors
- Epidemiology and clinical - other
- Infection control
- Treatment
- Social sciences
- 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Please note that we are including preprints (**highlighted in red**), which are preliminary reports of work that have NOT been peer-reviewed.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
23.05.2020	<a href="#">Correlation between viral RNA shedding and serum antibodies in COVID-19 patients</a>	Clin Microbiol Infect / Letter	<ul style="list-style-type: none"><li>• Study provided a correlation between viral RNA shedding and serum antibodies. Older age and hypertension may lead to prolonged viral RNA shedding. IgM can be reactive up to week 8 after symptom onset and the response may be stronger in patients with prolonged viral RNA shedding.</li><li>• While larger studies to confirm these findings are needed, these findings might improve our understanding about dynamics of serum antibody response and viral shedding in COVID-19.</li></ul>

27.05.2020	<a href="#">Development and validation of IMMUNO-COV: a high-throughput clinical assay for detecting antibodies that neutralize SARS-CoV-2</a>	bioRxiv (non-peer reviewed) / article	<ul style="list-style-type: none"> <li>Describe the development and validation of IMMUNO-COV, a high-throughput clinical test to quantitatively measure SARS-CoV-2-neutralizing antibodies.</li> <li>The test measures the capacity of serum or purified antibodies to neutralize a recombinant Vesicular Stomatitis Virus (VSV) encoding the SARS-CoV-2 spike glycoprotein.</li> </ul>
27.05.2020	<a href="#">Different pattern of pre-existing SARS-COV-2 specific T cell immunity in SARS-recovered and uninfected individuals</a>	bioRxiv (non-peer reviewed) / article	<ul style="list-style-type: none"> <li>Epitope characterization of NSP7-specific T cells showed recognition of protein fragments with low homology to "common cold" human coronaviruses but conserved among animal betacoronaviruses.</li> <li>Thus, infection with betacoronaviruses induces strong and long-lasting T cell immunity to the structural protein NP.</li> <li>Understanding how pre-existing ORF-1-specific T cells present in the general population impact susceptibility and pathogenesis of SARS-CoV-2 infection is of paramount importance for the management of the current COVID-19 pandemic.</li> </ul>
27.05.2020	<a href="#">Single-cell RNA-seq and V(D)J profiling of immune cells in COVID-19 patients</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>Enriched CD3+ and CD19+ lymphocytes from peripheral blood mononuclear cells of COVID-19 patients (severe patients and recovered patients at early or late stages) and healthy people (SARS-CoV-2 negative) and revealed transcriptional profiles and changes in these lymphocytes by comprehensive single-cell transcriptome and V(D)J recombination analyses.</li> </ul>

## Genomics

Publication Date	Title/URL	Journal/ Article type	Digest
27.05.2020	<a href="#">SARS-CoV-2 Phylogenetic Analysis, Lazio Region, Italy, February-March 2020</a>	Emerg Infect Dis / article	<ul style="list-style-type: none"> <li>Report of the phylogenetic and mutational analysis of SARS-CoV-2 virus strains from the Lazio region of Italy and dynamics of virus spread.</li> <li>Data suggest effective containment of clade V strains, but subsequently, multiple waves of clade G strains were circulating widely in Europe.</li> </ul>
23.05.2020	<a href="#">The emergence of SARS-CoV-2 in Europe and the US</a>	bioRxiv (non-peer reviewed) / article	<ul style="list-style-type: none"> <li>The authors elucidate when, where and how the earliest sustained SARS-CoV-2 transmission networks became established in Europe and the US.</li> <li>The results refute prior findings linking cases in January 2020 with outbreaks that occurred weeks later. Instead, rapid interventions successfully prevented onward transmission of those early cases in Germany and Washington State.</li> <li>Other, later introductions of the virus from China to both Italy and Washington State founded the earliest sustained European and US</li> </ul>

			<p>transmission networks.</p> <ul style="list-style-type: none"> <li>Analyses reveal an extended period of missed opportunity when intensive testing and contact tracing could have prevented SARS-CoV-2 from becoming established in the US and Europe.</li> </ul>
27.05.2020	<a href="#">Crystallographic and electrophilic fragment screening of the SARS-CoV-2 main protease</a>	bioRxiv (non-peer reviewed) / article	<ul style="list-style-type: none"> <li>Authors performed a large-scale screen of electrophile and non-covalent fragments through a combined mass spectrometry and X-ray approach against SARS-CoV-2 main protease, one of two cysteine viral proteases essential for viral replication.</li> <li>Crystallographic screen identified 71 hits that span entire active site, and 3 hits at dimer interface. These structures reveal routes to rapidly develop more potent inhibitors through merging of covalent and non-covalent fragment hits; one series of low-reactivity, tractable covalent fragments was progressed to discover improved binders.</li> <li>These combined hits offer unprecedented structural and reactivity information for on-going structure-based drug design against SARS-CoV-2 main protease.</li> </ul>

#### Epidemiology and clinical – children and pregnancy

Publication Date	Title/URL	Journal/ Article type	Digest
26.05.2020	<a href="#">COVID-19 in Children and the Dynamics of Infection in Families</a>	Pediatrics / Article	<ul style="list-style-type: none"> <li>This study describes the clinical presentation of the first 40 paediatric cases of COVID-19 in the authors city (Geneva) and the dynamics of their familial clusters.</li> <li>In 79% of households, at least one adult family member was suspected or confirmed for COVID-19 prior to symptom onset in the study child, confirming that children are infected mainly inside familial clusters.</li> <li>In only 8% of households did a child develop symptoms prior to any other household contact, which is in line with previous data showing that children are index cases in less than 10% of SARS CoV-2 familial clusters; however, the study design cannot confirm that child-to-adult transmission occurred.</li> </ul>

## Epidemiology and clinical - risk factors

Publication Date	Title/URL	Journal/ Article type	Digest
28.05.2020	<a href="#">Asthma and COVID-19: risks and management considerations</a>	Oxford COVID-19 Evidence Service / COVID-19	<ul style="list-style-type: none"> <li>• It is unclear if people with asthma (PWA) are at increased risk of contracting COVID-19 or of worse outcomes from COVID-19 infection.</li> <li>• The evidence available is limited with some sources suggesting an underrepresentation of PWA in hospitalised cases, and others showing an increased risk of worse outcomes in PWA which may be associated with disease severity.</li> <li>• Consensus broadly holds that asthma medications should be continued as usual. Asthma care may be disrupted during the pandemic; self-management and remote interventions may be of benefit but have not been tested in this context.</li> </ul>
27.05.2020	<a href="#">Hospitalization and Mortality among Black Patients and White Patients with Covid-19</a>	New England Journal of Medicine / Article	<ul style="list-style-type: none"> <li>• In a large cohort in Louisiana, 76.9% of the patients who were hospitalized with Covid-19 and 70.6% of those who died were black, whereas blacks comprise only 31% of the Ochsner Health population.</li> <li>• Black race was not associated with higher in-hospital mortality than white race, after adjustment for differences in sociodemographic and clinical characteristics on admission.</li> </ul>
25.05.2020	<a href="#">Increased risk for COVID-19 among Migrants from Latin-America, Caribbean, and Sub-Saharan Africa living in Spain</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• Population-based cohort analysis of cumulative incidence of PCR-confirmed COVID-19 cases until April 25 (2020) among 152018 residents of Alcorcon (Spain) attended hospital.</li> <li>• Marked increased risk for COVID-19 among migrants from Sub-Saharan Africa (RR 3.66, 95% confidence interval (CI) 1.42-9.41, p=0.007), Caribbean (RR 6.35, 95% CI 3.83-10.55, p&lt;0.001) and Latin-America (RR 6.92, 95% CI 4.49-10.67, p &lt;0.001) residing in Spain.</li> </ul>
26.05.2020	<a href="#">Neutrophil to Lymphocyte Ratio as Prognostic and Predictive Factor in Patients with Coronavirus Disease 2019: A Retrospective Cross-sectional Study</a>	J Med Virol / Article	<ul style="list-style-type: none"> <li>• Retrospective study with 1004 covid-19 patients found: a mortality rate of 4.0% (40 cases); that the median age of non-survivors (68 years) was significantly older than survivors (62 years); and male sex was more predominant in non-survival group than in the survival group.</li> <li>• Neutrophil to lymphocyte ratio (NLR) value of non-survival group was higher than that of survival group, and after adjusting for confounding factors, NLR &gt; 11.75 was significantly correlated with all-cause in-hospital mortality.</li> <li>• These results suggest that the NLR at hospital admission is associated in-hospital mortality among patients with covid-19.</li> </ul>

26.05.2020	<a href="#">The association of low serum albumin level with severe COVID-19: a systematic review and meta-analysis</a>	Crit Care / Research letter	<ul style="list-style-type: none"> <li>• Given the unclear association of hypoalbuminemia and severe COVID-19, the authors conducted a systematic review and meta-analysis to answer this.</li> <li>• A total of 11 studies (with 910 patients, mean age 47.6 ± 8.2 years and 47.0% females) were included.</li> <li>• Demonstrated the association of hypoalbuminemia and severe COVID-19. A low albumin level can potentially lead to early recognition of severe disease and assist clinicians in making informed decision for their patients.</li> </ul>
27.05.2020	<a href="#">Angiotensin-2 as a marker of endothelial activation is a good predictor factor for intensive care unit admission of COVID-19 patients</a>	Angiogenesis / article	<ul style="list-style-type: none"> <li>• Study enrolled 40 consecutive COVID-19 patients admitted to emergency department, half of whom were admitted in conventional wards without any ICU transfer during hospitalization; whereas the 20 others were directly transferred to ICU.</li> <li>• ROC curve analysis identified an Angiotensin-2 cut-off of 5000 pg/mL as the best predictor for ICU outcome, further confirmed in multivariate analysis after adjustment for creatinine, CRP or D-dimers.</li> </ul>
27.05.2020	<a href="#">Seek COVER: Development and validation of a personalized risk calculator for COVID-19 outcomes in an international network</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• Developed and externally validated COVID-19 Estimated Risk (COVER) scores that quantify a patient's risk of hospital admission (COVER-H), requiring intensive services (COVER-I), or fatality (COVER-F) in the 30-days following COVID-19 diagnosis.</li> <li>• The model was validated on patients with a GP, ER, or OP visit in 2020 with a confirmed or suspected COVID-19 diagnosis across four databases from South Korea, Spain and the United States.</li> <li>• Identified 7 predictors (history of cancer, chronic obstructive pulmonary disease, diabetes, heart disease, hypertension, hyperlipidaemia, and kidney disease) which combined with age and sex could discriminate which patients would experience any of their three outcomes.</li> <li>• The models could aid in providing reassurance for low risk patients and shield high risk patients from COVID-19 during de-confinement to reduce the virus' impact on morbidity and mortality.</li> </ul>
21.05.2020	<a href="#">Smoking-Mediated Upregulation of the Androgen Pathway Leads to Increased SARS-CoV-2 Susceptibility</a>	Int J Mol Sci / article	<ul style="list-style-type: none"> <li>• The authors analysed sequencing data from lung and oral epithelial samples obtained from The Cancer Genome Atlas (TCGA) and found that the receptor and transmembrane protease necessary for SARS-CoV-2 entry into host cells, ACE2 and TMPRSS2, respectively, were upregulated in smoking samples from both lung and oral epithelial tissue.</li> <li>• ACE2 and TMPRSS2 upregulation were both correlated to androgen pathway enrichment and the specific upregulation of central pathway</li> </ul>

			<p>regulatory genes.</p> <ul style="list-style-type: none"> <li>• These data provide a potential model for the increased susceptibility of smoking patients to COVID-19 and encourage further exploration into the androgen and tobacco upregulation of ACE2.</li> </ul>
26.05.2020	<a href="#">Hypertension and renin-angiotensin system blockers are not associated with expression of Angiotensin Converting Enzyme 2 (ACE2) in the kidney</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• Examine effect of RAS-inhibition on ACE2 expression in human tissues of key relevance to blood pressure regulation and COVID-19 infection, using information from up to 436 patients whose kidney transcriptomes were characterised by RNA-sequencing.</li> <li>• Data indicate that neither hypertension nor antihypertensive treatment are likely to alter individual risk of SARS-CoV-2 infection or influence clinical outcomes in COVID-19 through changes of ACE2 expression.</li> <li>• Suggest in absence of COVID-19, kidney ACE2 most likely nephro-protective but age-related increase in its expression within lungs and kidneys may be relevant to risk of COVID-19.</li> </ul>

#### Epidemiology and clinical – other

Publication Date	Title/URL	Journal/ Article type	Digest
15.05.2020	<a href="#">Novelty in the gut: a systematic review and meta-analysis of the gastrointestinal manifestations of COVID-19</a>	BMJ Open Gastroenterol / review	<ul style="list-style-type: none"> <li>• Pooled data from 2477 patients with a reverse transcription-PCR-positive COVID-19 infection across 17 studies were analysed.</li> <li>• The review found that diarrhoea (7.8%) followed by nausea and/or vomiting (5.5 %) were the most common GI symptoms.</li> <li>• A meta-analysis found no significant difference in the incidence of diarrhoea or nausea and/or vomiting in severe versus non-severe COVID-19-positive patients, however, there was seven times higher odds of having abdominal pain in patients with severe illness.</li> </ul>

#### Infection control

Publication Date	Title/URL	Journal/ Article type	Digest
26.05.2020	<a href="#">Combining fine-scale social contact data with epidemic modelling reveals interactions between contact tracing, quarantine, testing</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• Authors simulated control strategies for SARS-CoV-2 in a real-world social network generated from high resolution GPS data.</li> <li>• Tracing contacts-of-contacts reduced size of simulated outbreaks more</li> </ul>

	<a href="#">and physical distancing for controlling COVID-19</a>		<p>than tracing only contacts, but resulted in almost one third of local population being quarantined at a single point in time. Test and release of non-infectious individuals reduced numbers quarantined without large increase in outbreak, but high testing rates required to be effective.</p> <ul style="list-style-type: none"> <li>• If testing availability constrained, estimated that combining physical distancing with contact tracing could control epidemic while reducing number of quarantined individuals.</li> <li>• Their approach highlights the importance of network structure and social dynamics in evaluating the potential impact of SARS-CoV-2 control.</li> </ul>
27.05.2020	<a href="#">The Potential Impact of Intensified Community Hand Hygiene Interventions on Respiratory tract Infections: A Modelling Study</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• Developed a simple model-based framework for understanding the key determinants of the effectiveness of changes in hand hygiene behaviour in reducing transmission and used it to explore the potential impact of interventions aimed at achieving large-scale population-wide changes in hand hygiene behaviour.</li> <li>• Analyses showed that the effect of hand hygiene is highly dependent on the duration of viral persistence on hands and that hand washing needs to be performed very frequently or immediately after hand contamination events in order to substantially reduce the probability of infection.</li> </ul>

## Treatment

Publication Date	Title/URL	Journal/ Article type	Digest
27.05.2020	<a href="#">Remdesivir for 5 or 10 Days in Patients with Severe Covid-19</a>	New England Journal of Medicine / Article	<ul style="list-style-type: none"> <li>• Reports a randomized, open-label, phase 3 trial involving hospitalized patients with confirmed SARS-CoV-2 infection, oxygen saturation of 94% or less while they were breathing ambient air, and radiologic evidence of pneumonia.</li> <li>• The trial did not show a significant difference in efficacy between a 5-day course and a 10-day course of intravenous remdesivir treatment in patients with severe Covid-19 due to SARS-CoV-2 who did not require mechanical ventilation at baseline.</li> </ul>
26.05.2020	<a href="#">Simeprevir suppresses SARS-CoV-2 replication and synergizes with remdesivir</a>	bioRxiv (non-peer reviewed) / article	<ul style="list-style-type: none"> <li>• By in vitro screening and biochemical characterization, authors identified hepatitis C virus (HCV) protease inhibitor simeprevir as an especially promising repurposable drug for treating COVID-19.</li> <li>• Simeprevir synergizes with RNA-dependent RNA polymerase (RdRP) inhibitor remdesivir to suppress replication of SARS-CoV-2 in vitro.</li> <li>• Their results provide preclinical rationale for the combination treatment</li> </ul>

			of simeprevir and remdesivir for the pharmacological management of COVID-19 patients.
26.05.2020	<a href="#">Efficacy and harms of remdesivir for the treatment of COVID-19: a systematic review and meta-analysis</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• Paucity of adequately powered and fully reported RCTs evaluating effects of remdesivir in adult, hospitalized COVID-19 patients. Remdesivir should not be recommended for the treatment of severe COVID-19. <i>Similar to SR included in yesterday's Digest with the addition of two case series.</i></li> </ul>
27.05.2020	<a href="#">Hydroxychloroquine or Chloroquine for Treatment or Prophylaxis of COVID-19: A Living Systematic Review</a>	Ann Intern Med / review	<ul style="list-style-type: none"> <li>• Four randomized controlled trials, 10 cohort studies, and 9 case series assessed treatment effects of the medications, but no studies evaluated prophylaxis.</li> <li>• Evidence was conflicting and insufficient regarding the effect of hydroxychloroquine on such outcomes as all-cause mortality, progression to severe disease, clinical symptoms, and upper respiratory virologic clearance with antigen testing.</li> </ul>
23.05.2020	<a href="#">Herbal Medicine for the Treatment of Coronavirus Disease 2019 (COVID-19): A Systematic Review and Meta-Analysis of Randomized Controlled Trials</a>	J Clin Med / Systematic review	<ul style="list-style-type: none"> <li>• Seven RCTs with a total of 855 patients were included. All included trials compared the combined therapy of herbal medicine with Western medicine to Western medicine alone.</li> <li>• The combined therapy significantly improved the total effective rate (RR 1.23, 95% CI 1.13 to 1.34, <math>p &lt; 0.001</math>), cough symptom disappearance rate (RR 1.45, 95% CI 1.12 to 1.89, <math>p = 0.005</math>), and sputum production symptom disappearance rate (RR 1.73, 95% CI 1.19 to 2.50, <math>p = 0.004</math>).</li> <li>• Significant effects of the combined therapy of herbal medicine with Western medicine were found, and revealed the potential role of herbal medicine in treating COVID-19. More high-quality RCTs are needed to further validate the effectiveness and adverse events of herbal medicine in the treatment of COVID-19.</li> </ul>

## Social science

Publication Date	Title/URL	Journal/ Article type	Digest
28.04.2020	<a href="#">Adapting IAPT services to support frontline NHS staff during the Covid-19 pandemic: the Homerton Covid Psychological Support (HCPS) pathway</a>	Cogn Behav Therap / Article	<ul style="list-style-type: none"> <li>• Mental health services and psychology professional bodies across the UK have issued guidance to meet the needs of frontline staff. An attempt has been made to translate these sets of guidance into clinical provisions via the recently established Homerton Covid Psychological Support (HCPS) pathway delivered by Talk Changes (Hackney &amp; City IAPT).</li> <li>• This article describes the phased, stepped-care and evidence-based</li> </ul>

			<p>approach that has been adopted by the service to support local frontline NHS staff.</p> <ul style="list-style-type: none"> <li>• The authors wish to share their service design and pathway of care with other Improving Access to Psychological Therapies (IAPT) services who may also seek to support hospital frontline staff within their associated NHS Trusts and in doing so, lay the foundations of a coordinated response.</li> </ul>
27.05.2020	<a href="#">COVID-19-related anxiety predicts somatic symptoms in the UK population</a>	Br J Health Psychol / article	<ul style="list-style-type: none"> <li>• Results from a large, representative sample (N = 2,025) of the UK adult population showed that moderate to high levels of anxiety associated with COVID-19 were significantly associated with general somatic symptoms and in particular with gastrointestinal and fatigue symptoms.</li> <li>• This pattern of associations remained significant after controlling for generalized anxiety disorder (GAD), pre-existing health problems, age, gender, and income.</li> <li>• This is the first evidence that anxiety associated with COVID-19 makes a unique contribution to somatization, above and beyond the effect of GAD.</li> </ul>

#### Guidance, consensus statements

Publication Date	Title/URL	Journal/ Article type
22.05.2020	<a href="#">Position paper on the preparation of immune plasma to be used in the treatment of patients with COVID-19</a>	Blood Transfus / Position paper

#### Overviews, comments and editorials

Publication Date	Title/URL	Journal/ Article type
27.05.2020	<a href="#">A view from UK public health registrars on the challenges of COVID-19</a>	The Lancet / Correspondence
27.05.2020	<a href="#">Minimise, manage, and modify: the UK must create and use time</a>	The Lancet / Correspondence
27.05.2020	<a href="#">COVID-19 testing delays and pathology services in the UK</a>	The Lancet / Correspondence
27.05.2020	<a href="#">The early landscape of COVID-19 vaccine development in the UK and rest of the world</a>	Immunology / article
26.05.2020	<a href="#">Pandemic Preparedness: Developing Vaccines and Therapeutic Antibodies For COVID-19</a>	Cell / Perspective
27.05.2020	<a href="#">Molecular, serological, and biochemical diagnosis and monitoring of COVID-19: IFCC taskforce evaluation of the latest evidence</a>	Clin Chem Lab Med / review

27.05.2020	<a href="#">Type I and Type III Interferons - Induction, Signaling, Evasion, and Application to Combat COVID-19</a>	Cell Host & Microbe / Review
26.05.2020	<a href="#">Is It Safe for Me to Go to Work? Risk Stratification for Workers during the Covid-19 Pandemic</a>	New England Journal of Medicine / Perspective
27.05.2020	<a href="#">Innovative strategies to support physical distancing among individuals with active addiction</a>	The Lancet Psychiatry / Comment
27.05.2020	<a href="#">The COVID-19 MS Coalition - accelerating diagnostics, prognostics, and treatment</a>	The Lancet / Correspondence
27.05.2020	<a href="#">Small droplet aerosols in poorly ventilated spaces and SARS-CoV-2 transmission</a>	The Lancet Respiratory Medicine / Comment

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

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