



## International EPI Cell Daily Evidence Digest – 13/05/2020

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:

- Diagnostics
- Genomics
- Epidemiology and clinical - children and pregnancy
- Epidemiology and clinical - risk factors
- Epidemiology and clinical - other
- Infection control
- Treatment
- Social sciences
- Miscellaneous
- 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Please note that we are including preprints (**highlighted in red**), which are preliminary reports of work that have NOT been peer-reviewed.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.

### Diagnostics

Publication Date	Title/URL	Journal/Article type	Digest
02.05.2020	<a href="#">A new role for Biofoundries in rapid prototyping, development, and validation of automated clinical diagnostic tests for SARS-CoV-2</a>	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"><li>• The authors present a reagent-agnostic automated SARS-CoV-2 testing platform that can be quickly deployed and scaled, and that accepts a diverse range of reagents, validated in collaboration with an NHS diagnostic testing lab.</li></ul>

- The validated RNA extraction and RT-qPCR platform has been installed in NHS diagnostic labs with a testing capacity of 1000 samples per day and now contributes to increased patient sample processing in the UK while they continue to refine and develop novel high-throughput diagnostic methods.

## Genomics

Publication Date	Title/URL	Journal/Article type	Digest
12.05.2020	<a href="#">Immune response to SARS-CoV-2 and mechanisms of immunopathological changes in COVID-19</a>	Allergy/ review	<ul style="list-style-type: none"> <li>• Review of the immune response and immunopathological changes in patients linked to deteriorating clinical conditions such as, cytokine storm, acute respiratory distress syndrome, autopsy findings and changes in acute phase reactants and serum biochemistry in COVID-19.</li> </ul>
11.05.2020	<a href="#">Children's Hospital Los Angeles COVID-19 Analysis Research Database (CARD) - A Resource for Rapid SARS-CoV-2 Genome Identification Using Interactive Online Phylogenetic Tools</a>	bioRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> <li>• The Children's Hospital, Los Angeles (CHLA) COVID-19 Analysis Research Database (CARD) (<a href="https://covid19.cpmbiodev.net/">https://covid19.cpmbiodev.net/</a>) is a comprehensive genomic resource that provides access to full-length SARS-CoV-2 viral genomes and associated meta-data for over 18,000 (as of May 10, 2020) isolates collected from global sequencing repositories and the sequencing performed at the Centre for Personalized Medicine (CPM) at CHLA.</li> </ul>
11.05.2020	<a href="#">An integrated in silico immuno-genetic analytical platform provides insights into COVID-19 serological and vaccine targets</a>	bioRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> <li>• Study from LSHTM describing the development of an online tool for SARS-CoV-2 research, which combines an extensive epitope mapping and prediction meta-analysis, with an updated variant database (55,944 non-synonymous mutations) based on 16,087 whole genome sequences, and an analysis of human coronavirus homology.</li> <li>• The tool can be accessed online (<a href="http://genomics.lshtm.ac.uk/immuno">http://genomics.lshtm.ac.uk/immuno</a>) and will serve as a useful tool for biological discovery in the fight against SARS-CoV-2. Further, it may be adapted to inform on biological targets in future outbreaks, including new human coronaviruses that spill over from animal hosts.</li> </ul>
12.05.2020	<a href="#">Meta-analysis of transcriptomes of SARS-Cov2 infected human lung epithelial cells identifies transmembrane serine proteases co-expressed with ACE2 and biological</a>	bioRxiv (not peer reviewed) / Meta-analysis	<ul style="list-style-type: none"> <li>• Meta-analysis of RNA-sequencing data from three studies employing human lung epithelial cells and aiming to identify genes co-expressed with angiotensin I converting enzyme 2 (ACE2).</li> </ul>

[processes related to viral entry, immunity, inflammation and cellular stress](#)

• Several genes correlated or inversely correlated with high significance, among the most significant of these was the transmembrane serine protease 4 (TMPRSS4) - serine proteases are known to be involved in the infection process by priming the virus spike protein.

### Epidemiology and clinical - children and pregnancy

Publication Date	Title/URL	Journal/Article type	Digest
08.05.2020	<a href="#">Placental pathology in COVID-19</a>	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"><li>• 16 placentas from patients with SARS-CoV-2 were examined (15 with live birth in the 3rd trimester 1 delivered in the 2nd trimester after intrauterine fetal demise).</li><li>• Relative to controls, COVID-19 placentas show increased prevalence of features of maternal vascular malperfusion (MVM), a pattern of placental injury reflecting abnormalities in oxygenation within the intervillous space associated with adverse perinatal outcomes.</li><li>• Only 1 COVID-19 patient was hypertensive despite the association of MVM with hypertensive disorders and preeclampsia. These changes may reflect a systemic inflammatory or hypercoagulable state influencing placental physiology.</li></ul>

### Epidemiology and clinical - risk factors

Publication Date	Title/URL	Journal/Article type	Digest
12.05.2020	<a href="#">Manifestations and prognosis of gastrointestinal and liver involvement in patients with COVID-19: a systematic review and meta-analysis</a>	The Lancet Gastroenterology & Hepatology / Systematic review	<ul style="list-style-type: none"><li>• The authors aimed to quantify the effects of COVID-19 on the digestive system, by analysing findings from 35 studies, including 6686 patients with COVID-19, that met inclusion criteria.</li><li>• 29 studies (n=6064) reported gastrointestinal symptoms in patients with COVID-19 at diagnosis and the pooled prevalence of digestive system comorbidities was 4%.</li><li>• The pooled prevalence of digestive symptoms was 15% with nausea or vomiting, diarrhoea, and loss of appetite being the three most common symptoms.</li></ul>

12.05.2020	<a href="#">Development and Validation of a Clinical Risk Score to Predict the Occurrence of Critical Illness in Hospitalized Patients With COVID-19</a>	JAMA Internal Medicine / Original investigation	<ul style="list-style-type: none"> <li>• In this study with a development cohort of 1590 patients and a validation cohort of 710 patients, a risk score was developed and validated to predict development of critical illness.</li> <li>• The authors identified 10 independent predictors and developed a risk score (COVID-GRAM) that predicts development of critical illness.</li> <li>• The risk score predictors included: chest radiography abnormality, age, haemoptysis, dyspnoea, unconsciousness, number of comorbidities, cancer history, neutrophil-to-lymphocyte ratio, lactate dehydrogenase, and direct bilirubin.</li> </ul>
11.05.2020	<a href="#">COVID-19 in people living with human immunodeficiency virus: a case series of 33 patients</a>	Infection / Article	<ul style="list-style-type: none"> <li>• This preliminary case series does not support excess morbidity and mortality among symptomatic COVID-19 PLWH and with viral suppression on antiretroviral treatment (ART).</li> <li>• SARS-CoV-2 infections may occur during boosted darunavir-based and/or on tenofovir-containing ART.</li> </ul>
12.05.2020	<a href="#">Rapid Review: Diabetic retinopathy screening during the COVID-19 pandemic</a>	Oxford COVID-19 Evidence Service / Rapid Review	<ul style="list-style-type: none"> <li>• This rapid review addresses options for retinal screening programmes for people with diabetes (PWD) during the COVID-19 pandemic</li> </ul>
12.05.2020	<a href="#">Androgen regulates SARS-CoV-2 receptor levels and is associated with severe COVID-19 symptoms in men</a>	bioRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> <li>• Study describing a high-throughput drug screening strategy to identify therapeutic candidates that reduce ACE2 levels in human embryonic stem cell (hESC) derived cardiac cells.</li> <li>• Additionally, clinical data on COVID-19 patients demonstrated that abnormal androgen states are significantly associated with severe disease complications and cardiac injury as measured by blood troponin T levels.</li> <li>• These findings provide important insights on the mechanism of increased disease susceptibility in male COVID-19 patients and identify androgen receptor inhibition as a potential therapeutic strategy.</li> </ul>
07.04.2020	<a href="#">ACE-inhibitors and Angiotensin-2 Receptor Blockers are not associated with severe SARS- COVID19 infection in a multi-site UK acute Hospital Trust</a>	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> <li>• UK cohort study of 1200 patients, evaluating the hypothesis that ACE- inhibitors (ACEi) and Angiotensin-2 Blockers (ARB), commonly used in patients with hypertension or diabetes, may raise ACE2 levels and increase the risk of severe COVID19 infection.</li> <li>• There was no evidence for increased severity of COVID19 disease in hospitalised patients on chronic treatment with ACEi or ARB. A trend towards a beneficial effect of ACEi/ARB requires further evaluation in larger meta-analyses and randomised clinical trials.</li> </ul>
05.05.2020	<a href="#">Elevated RDW is Associated with Increased Mortality Risk in COVID-19</a>	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> <li>• Retrospective study of the relationship between Red blood cell distribution width (RDW) and COVID19 mortality risk for 1198 adult</li> </ul>

		<p>patients diagnosed with SARS COV2.</p> <ul style="list-style-type: none"> <li>Elevated RDW at diagnosis and an increase in RDW during admission are both associated with increased mortality risk for adult COVID19 patients at a large academic medical centre network.</li> </ul>
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### Epidemiology and clinical – other

Publication Date	Title/URL	Journal/Article type	Digest
11.05.2020	<a href="#">Real-time tracking of self-reported symptoms to predict potential COVID-19</a>	Nature Medicine / Brief communication	<ul style="list-style-type: none"> <li>Of 2,618,862 participants who reported potential symptoms of COVID-19 on a smartphone-based app, 18,401 had undergone a SARS-CoV-2 test, and those testing positive reported more loss of smell and taste than those with a negative test result.</li> <li>Modelling predicted that 140,312 (17.42%) participants were likely to have COVID-19.</li> </ul>
11.05.2020	<a href="#">Coronavirus (COVID-19) related deaths by occupation, England and Wales: deaths registered up to and including 20 April 2020</a>	UK Office for National Statistics,	<ul style="list-style-type: none"> <li>Provisional analysis of deaths involving the coronavirus (COVID-19), by different occupational groups, among males and females aged 20 to 64 years in England and Wales.</li> </ul>
07.05.2020	<a href="#">Clotting Factors in COVID-19: Epidemiological Association and Prognostic Values in Different Clinical Presentations in an Italian Cohort</a>	Journal of clinical medicine / Article	<ul style="list-style-type: none"> <li>The aim of this study was to describe the basic clotting parameters in 67 COVID-19 patients and their prognostic role in different clinical forms of the disease.</li> <li>Fibrinogen seems to increase early in COVID-19 patients and may be used as a risk stratification marker for the early detection of a subgroup of patients at increased risk to develop SARS, who might benefit from a different and thorough clinical surveillance and treatment.</li> </ul>
30.04.2020	<a href="#">COVID-19 length of hospital stay: a systematic review and data synthesis</a>	medRxiv (not peer reviewed) / Systematic review	<ul style="list-style-type: none"> <li>Systematic review of 52 studies to gather data on length of stay (LoS) of patients with COVID-19 in hospital and in ICU.</li> <li>Median hospital LoS ranged from 4 to 53 days within China, and 4 to 21 days outside of China, across 45 studies. ICU LoS was reported by eight studies - four each within and outside China - with median values ranging from 6 to 12 and 4 to 19 days, respectively.</li> <li>Summary distributions give a median hospital LoS of 14 (IQR: 10-19) days for China, compared with 5 (IQR: 3-9) days outside of China. For ICU, the summary distributions are more similar (median (IQR) of 8 (5-13) days for China and 7 (4-11) days outside of China).</li> </ul>

08.05.2020	<a href="#">Genetic drift and environmental spreading dynamics of COVID-19</a>	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> <li>• Retrospective case series aiming to delineate the genetic and environmental determinants of COVID-19 spreading, set in Spain, Italy, Sweden, Finland, Norway.</li> <li>• Results suggest dependence of COVID-19 pandemic spreading on wintertime conditions, with expected waning over the summer.</li> <li>• The findings indicate association of COVID-19 to a sharp North/South climate gradient, with faster spreading in southern regions. Thus, warmer climate conditions may not limit SARS-CoV-2 diffusion. Very cold regions may be better spared by recurrent courses of infection.</li> </ul>
24.04.2020	<a href="#">Individual variation in susceptibility or exposure to SARS-CoV-2 lowers the herd immunity threshold</a>	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> <li>• Although estimates vary, simple calculations suggest that herd immunity to SARS-CoV-2 requires 60-70% of the population to be immune.</li> <li>• By fitting epidemiological models that allow for heterogeneity to SARS-CoV-2 outbreaks across the globe, this study shows that variation in susceptibility or exposure to infection reduces these estimates. Accurate measurements of heterogeneity are therefore of paramount importance in controlling the COVID-19 pandemic.</li> </ul>
08.05.2020	<a href="#">A rapid review of available evidence on the serial interval and generation time of COVID-19</a>	medRxiv (not peer reviewed) / Rapid review	<ul style="list-style-type: none"> <li>• Rapid review to advise on appropriate parameter values for serial interval and generation time in national COVID-19 transmission models for Ireland and on methodological issues relating to those parameters.</li> <li>• The values of the estimates for serial interval and generation time are heavily influenced by the contact rates between infectious and susceptible individuals. Mitigation measures that are introduced in a country or region are of paramount importance in this regard.</li> <li>• The serial interval estimate of 6.6 days (95% confidence interval: 0.7, 19.0) from the paper by Cereda et al. is likely to be the most relevant to European countries. National estimates should be obtained as soon as possible.</li> </ul>

## Infection control

Publication Date	Title/URL	Journal/Article type	Digest
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12.05.2020	<a href="#">Personal Protective Equipment (PPE) for Surgeons during COVID-19 Pandemic: A Systematic Review of Availability, Usage, and Rationing</a>	British Journal of Surgery / Review	<ul style="list-style-type: none"> <li>• There is a global effort to overcome shortages by combining the most effective use of existing PPE in combination with innovative strategies to produce more.</li> <li>• Practical advice on all aspects of PPE are detailed in this systematic review.</li> </ul>
07.05.2020	<a href="#">Facemasks prevent influenza-like illness: implications for COVID-19</a>	medRxiv (not peer reviewed) / Meta-analysis	<ul style="list-style-type: none"> <li>• Meta-analysis of 8 RCTs examining the efficacy of wearing facemasks to prevent influenza-like illness (ILI) in community settings, irrespective of confirmatory testing for the causative virus.</li> <li>• Participants wearing facemasks had a significantly lower risk of developing ILI than those not wearing facemasks and there was no heterogeneity. The decreased risk of ILI was more pronounced if everyone wore facemask irrespective of whether they were infected or not, compared to those wearing facemasks when infected or uninfected.</li> <li>• Although there are no RCTs of facemasks for SARS-CoV-2, as with other simple measures such as social distancing and handwashing, these data support the recommendation to wear facemasks in public to further reduce transmission of SARS-CoV-2 and flatten the curve of this pandemic, especially when social distancing is impractical, such as shopping, or travelling with public transport for work that cannot be done from home.</li> </ul>
07.05.2020	<a href="#">Stability of SARS-CoV-2 on environmental surfaces and in human excreta</a>	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> <li>• At room temperature, SARS-CoV-2 was stable on environmental surfaces and remained viable up to 7 days on smooth surfaces.</li> <li>• The virus could survive for several hours in faeces and 3-4 days in urine.</li> </ul>

## Treatment

Publication Date	Title/URL	Journal/Article type	Digest
12.05.2020	<a href="#">Respiratory disease in rhesus macaques inoculated with SARS-CoV-2</a>	Nature / Article	<ul style="list-style-type: none"> <li>• The authors establish the rhesus macaque as a model of COVID-19 to understand pathogenesis and aid development and testing of treatments.</li> <li>• Disease is similar to that in humans, lasting 8-16 days with hallmarks of human disease visible in lung radiographs.</li> </ul>
07.05.2020	<a href="#">Remdesivir in treatment of COVID-19: A systematic benefit-risk assessment</a>	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> <li>• The Benefit-Risk Action Team (BRAT) framework was used to assess the overall benefit-risk of the use of remdesivir as a</li> </ul>

			<p>treatment for COVID-19 compared to standard of care, placebo or other treatments.</p> <ul style="list-style-type: none"> <li>• Preliminary clinical trial results suggest a favourable benefit-risk profile for remdesivir compared to placebo, however there is limited safety data available at the current time.</li> <li>• The current framework summarises the key anticipated benefits and risks for which further data are needed.</li> </ul>
07.05.2020	<a href="#">Systematic Review and Meta-analysis of the Effectiveness and Safety of Hydroxychloroquine in COVID-19</a>	medRxiv (not peer reviewed) / Systematic review	<ul style="list-style-type: none"> <li>• Systematic review and meta-analysis of 5 trials involving 677 patients were included.</li> <li>• The use of hydroxychloroquine with or without azithromycin for treatment of COVID-19 patients, seems to be effective. The combination of hydroxychloroquine and azithromycin has shown synergic effects. However, mortality rate was increased when the treatment was conducted with hydroxychloroquine.</li> </ul>
07.05.2020	<a href="#">The British Thoracic Society survey of rehabilitation to support recovery of the Post Covid -19 population</a>	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> <li>• Report on a British Thoracic Society survey to rapidly identify the components of a post-Covid-19 rehabilitation assessment and elements of a successful rehabilitation programme for those post Covid-19 to inform service delivery.</li> <li>• Recommendations for the intervention described a holistic programme focusing on symptom management, return of function and return to employment. The free text comments added depth to the survey and the need not to reinvent the wheel rather adapt well established (pulmonary rehabilitation) services to accommodate the needs of the post Covid-19 population.</li> </ul>

## Social sciences

Publication Date	Title/URL	Journal/Article type	Digest
06.05.2020	<a href="#">Immunity Passports for SARS-CoV-2: an online experimental study of the impact of antibody test terminology on perceived risk and behaviour</a>	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> <li>• 2 by 3 experimental study with 1,204 UK participants to assess the impact of describing an antibody-positive test result using the terms Immunity and Passport or Certificate, alone or in combination, on perceived risk of becoming infected with SARS-CoV-2 and intention to continue protective behaviours.</li> <li>• Using the term Immunity (vs Antibody) to describe antibody tests for SARS-CoV-2 increases the proportion of people believing that an antibody-positive result means they have no risk of catching</li> </ul>

			<p>coronavirus in the future, a perception that may be associated with less frequent hand washing.</p> <ul style="list-style-type: none"> <li>• The way antibody testing is described may have implications for the likely impact of testing on transmission rates.</li> </ul>
06.05.2020	<a href="#">The German COVID-19 Survey on Mental Health: Primary Results</a>	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> <li>• Large cross-sectional survey of 3,545 volunteers to assess mental health in response to the lockdown in Germany.</li> <li>• Participants scored mild severity distress in the PHQ stress module. Depression and anxiety as assessed by PHQ-4 was significantly higher than in reference samples.</li> <li>• 45.3% of participants reported worsened sleep, increased levels of irritation, anger and aggression compared to pre-pandemic times. Most importantly, 5% of all participants reported experiencing interpersonal violence (IPV).</li> </ul>

#### Miscellaneous

Publication Date	Title/URL	Journal/Article type	Digest
12.05.2020	<a href="#">Report 22 - Equity in response to the COVID-19 pandemic: an assessment of the direct and indirect impacts on disadvantaged and vulnerable populations in low- and lower middle-income countries</a>	Imperial College / Report	<ul style="list-style-type: none"> <li>• Results demonstrate clear trends that the probability of death from COVID-19 increases with increasing poverty.</li> <li>• On average, an estimate of 32.0% (2.5th-97.5th centile 8.0%-72.5%) increase in the probability of death in the poorest quintile compared to the wealthiest quintile from three factors: differences in handwashing access, occupation and hospital access.</li> </ul>
07.05.2020	<a href="#">Coronavirus Disease 2019 (COVID-19): An Evidence Map of Medical Literature</a>	medRxiv (not peer reviewed) / Evidence map	<ul style="list-style-type: none"> <li>• Evidence map and bibliometric analysis of the medical literature on COVID-19 between 1 January and 24 March 2020 to systematically identify gaps and propose areas for valuable future research.</li> <li>• The examined COVID-19 medical literature originated primarily from Asia and focussed mainly on clinical features and diagnosis of the disease. Many areas of potential research remain underexplored, such as mental health research, the use of novel technologies and artificial intelligence, research on the pathophysiology of COVID-19 within different body systems, and research on indirect effects of COVID-19 on the care of non-COVID-</li> </ul>

19 patients. • Figures are included showing evidence gaps, country distribution, topics of publication, article type.

## Modelling

Publication Date	Title/URL	Journal/Article type	Digest
12.05.2020	<a href="#">Estimating excess 1-year mortality associated with the COVID-19 pandemic according to underlying conditions and age: a population-based cohort study</a>	The Lancet / Article	<ul style="list-style-type: none"> <li>• Population-based cohort study of 3,862,012 individuals. Linked primary and secondary care electronic health records from England, reporting prevalence of underlying conditions. Estimated 1-year mortality in each condition, developing simple models of excess Covid-19-related deaths.</li> <li>• In a full suppression scenario, the authors estimated two excess deaths with an RR of 1.5, four with an RR of 2.0 and seven with an RR of 3.0.</li> <li>• In a mitigation scenario, the authors estimated 18374 excess deaths with an RR of 1.5, 36749 with an RR of 2.0, and 73498 with an RR of 3.0.</li> <li>• In a do nothing scenario, the authors estimated 146996 excess deaths with an RR of 1.5, 293991 with an RR of 2.0, and 587982 with an RR of 3.0.</li> </ul>
08.05.2020	<a href="#">Significant Relaxation of SARS-CoV-2-Targeted Non-Pharmaceutical Interventions Will Result in Profound Mortality: A New York State Modelling Study</a>	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> <li>• Model developed to estimate the effect of undocumented infections, seasonal infectivity, immunity, and non-pharmaceutical interventions (NPIs), such as social distancing, on the transmission, morbidity, and mortality of SARS-CoV-2 in New York State (NYS).</li> <li>• Simulations revealed dramatic infectivity driven by undocumented infections, and a peak basic reproductive number in NYS of 7.6. NPIs have been effective, and relaxation &gt;50% will result in tens-of-thousands more deaths.</li> <li>• Endemic infection is likely to occur in the absence of profound sustained immunity. As a result, until an effective vaccine or other effective pharmaceutical intervention is developed, it will be critical to not reduce NPIs &gt;50% below current levels.</li> </ul>

## Guidance, consensus statements and hospital resources

Publication Date	Title/URL	Journal/Article type
11.05.2020	<a href="#">A strategic approach to COVID-19 vaccine R&amp;D</a>	Science/Policy forum

#### Overviews, comments and editorials

Publication Date	Title/URL	Journal/Article type
12.05.2020	<a href="#">A wake-up call: COVID-19 and its impact on children's health and wellbeing</a>	The Lancet Global Health / Comment
12.05.2020	<a href="#">Avoiding indirect effects of COVID-19 on maternal and child health</a>	The Lancet Global Health / Comment

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

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