



International EPI Cell Daily Evidence Digest – 14/05/2020

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Please note that we are including preprints (**highlighted in red**), which are preliminary reports of work that have NOT been peer-reviewed.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
12.05.2020	US CDC Real-Time Reverse Transcription PCR Panel for Detection of Severe Acute Respiratory Syndrome Coronavirus 2	Emerging Infectious Diseases / Synopsis	• The CDC rRT-PCR panel for detection of SARS-CoV-2 demonstrated high sensitivity and specificity for detecting 5 RNA copies/reaction with no observed false-positive reactivity, and it facilitated rapid detection of SARS-CoV-2 infections in humans.
11.05.2020	Performance of the rapid Nucleic Acid Amplification by Abbott ID NOW COVID-19 in	bioRxiv (not peer reviewed) / Article	• Present result comparisons between Abbot ID NOW COVID-19 and Cepheid Xpert Xpress SARS-CoV-2 using nasopharyngeal

	nasopharyngeal swabs transported in viral media and dry nasal swabs, in a New York City academic institution		swabs transported in VTM, dry nasal swabs for the Abbott assay. <ul style="list-style-type: none"> • Abbot ID NOW COVID-19 missed a third of samples detected positive by Cepheid Xpert Xpress when using NP swabs in VTM and over 48% when using dry nasal swabs.
13.05.2020	Saliva as a non-invasive sample for the detection of SARS-CoV-2: a systematic review	medRxiv (not peer reviewed) / Review	<ul style="list-style-type: none"> • 10 publications fit the criteria for review. Saliva was positive in 31-92% of patients depending on the cohort and length of hospitalization. • Viral loads in saliva are comparable to those in NPS and ranged from 9.9×10^2 to 1.2×10^8 copies/mL during the first week of symptoms and decrease over time. Saliva can be positive up to 20 days post-symptom onset with viral loads correlating with symptom severity and degree of tissue damage.
13.05.2020	Coronavirus: the first seroprevalence data estimates that 5% of the population has been infected, with variability according to provinces	Instituto de salud Carlos III / News	<ul style="list-style-type: none"> • The first data from the ENECOV19 study , the seroprevalence survey that tries to estimate the percentage of the population that has developed antibodies against the new SARS-Cov-2 coronavirus after passing the infection, have been presented. • According to the preliminary results of the first wave of the survey, 5% of the Spanish population has been infected and has developed antibodies.
06.05.2020	Repeated seroprevalence of anti-SARS-CoV-2 IgG antibodies in a population-based sample from Geneva, Switzerland	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • Study consisting of 8 weekly serosurveys among 1335 participants coming from 633 households, with 16% <20 years of age and 53.6% female. • 1st week, estimated a seroprevalence of 3.1% (95% CI 0.2-5.99, n=343). Week 2: increased to 6.1% (95% CI 2.6-9.33, n=416). Week 3: increased to 9.7% (95% CI 6.1-13.11, n=576). • 5-19 year-olds (6.0%, 95% CI 2.3-10.2%) had similar seroprevalence to 20-49 year olds (8.5%, 95%CI 4.99-11.7). Significantly lower seroprevalence in those 50 and older (3.7%, 95% CI 0.99-6.0, p=0.0008). • Assuming presence of IgG antibodies associated with (short term) immunity, epidemic far from burning out due to herd immunity. Further, no differences in seroprevalence between children and middle age adults are observed.
08.05.2020	Evidence of a significant secretory-IgA-dominant SARS-CoV-2 immune response in human milk following recovery from COVID-19	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • In this preliminary report, 15 milk samples obtained from donors previously-infected with SARS-CoV-2 as well as 10 negative control samples obtained prior to Dec 2019 were tested for reactivity to the Receptor Binding Domain (RBD) of the SARS-CoV-2 Spike protein by ELISAs measuring IgA, IgG, IgM, and

			<p>secretory Ab.</p> <ul style="list-style-type: none"> • Eighty percent of samples obtained post-COVID-19 exhibited IgA reactivity, and all these samples were also positive for secretory Ab reactivity, suggesting the IgA is predominantly sIgA. • Overall, these data indicate that there is strong sIgA-dominant SARS-CoV-2 immune response in human milk after infection in the majority of individuals, and that a comprehensive study of this response is highly warranted.
12.05.2020	Symptom Criteria for COVID-19 Testing of Health Care Workers	Academic Emergency Medicine / Article	<ul style="list-style-type: none"> • An evidence based approach to COVID-19 testing which at least includes fever and loss of taste or smell should be utilized when determining which health care workers should be tested.

Genomics

Publication Date	Title/URL	Journal/ Article type	Digest
07.05.2020	A mouse-adapted SARS-CoV-2 model for the evaluation of COVID-19 medical countermeasures	bioRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • This mouse-adapted SARS-CoV-2 model demonstrates age-related disease pathogenesis and supports the clinical use of IFN lambda-1a treatment in human COVID-19 infections.
13.05.2020	Characterization of SARS-CoV-2 viral diversity within and across hosts	bioRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • Analysed 621 bulk RNA sequencing samples and 7,540 consensus sequences from COVID-19 patients; identify multiple strains of SARS-CoV-2, in four major clades that are prevalent within and across hosts. • Evidence for: (i) within-host diversity across phylogenetic clades; (ii) putative cases of recombination, multi-strain and/or superinfections; (iii) distinct strain profiles across geographical locations and time. • Findings and algorithms will facilitate more detailed evolutionary analyses and contact tracing that specifically account for within-host viral diversity in this and future pandemics.
12.05.2020	SARS-CoV-2 ORF3b is a potent interferon antagonist whose activity is further increased by a naturally occurring elongation variant	bioRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • Show that SARS-CoV-2 ORF3b is a potent interferon antagonist, suppressing the induction of type I interferon more efficiently than its SARS-CoV ortholog. • Analyses of more than 15,000 SARS-CoV-2 sequences identified a natural variant, in which a longer ORF3b reading frame was reconstituted. This variant was isolated from two

			<p>patients with severe disease and further increased the ability of ORF3b to suppress interferon induction.</p> <ul style="list-style-type: none"> • The findings not only help to explain the poor interferon response in COVID-19 patients, but also describe a possibility of the emergence of natural SARS-CoV-2 quasispecies with extended ORF3b that may exacerbate COVID-19 symptoms.
12.05.2020	Mutation landscape of SARS-CoV-2 reveals three mutually exclusive clusters of leading and trailing single nucleotide substitutions	bioRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • Analysed 480 full-length (>29000 nt) sequences from the 1575 SARS-CoV-2 sequences available and identified 37 single-nucleotide substitutions occurring in >1% of the genomes. • Clustering analysis revealed unique geographical distribution of SARS-CoV-2 variants defined by their mutation profile. • Observed several co-occurring mutations that almost never occur individually. Define 3 mutually exclusive lineages (A1, B1 and C1) of SARS-CoV-2 which account for about three quarters of the genomes analysed.
13.05.2020	Androgen regulates SARS-CoV-2 receptor levels and is associated with severe COVID-19 symptoms in men	bioRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • Established a high-throughput drug screening strategy to identify therapeutic candidates that reduce ACE2 levels in human embryonic stem cell (hESC) derived cardiac cells. • 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.
13.05.2020	ChAdOx1 nCoV-19 vaccination prevents SARS-CoV-2 pneumonia in rhesus macaques	bioRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • Show that the adenovirus-vectored vaccine ChAdOx1 nCoV-19, encoding the spike protein of SARS-CoV-2, is immunogenic in mice, eliciting a robust humoral and cell-mediated response. • A single vaccination with ChAdOx1 nCoV-19 induced a humoral and cellular immune response in rhesus macaques. No evidence of immune-enhanced disease following viral challenge in vaccinated animals was observed. ChAdOx1 nCoV-19 is currently under investigation in a phase I clinical trial. <p><i>Authors have competing Interest.</i></p>
13.05.2020	An integrated in silico immuno-genetic analytical platform provides insights into COVID-19 serological and vaccine targets	bioRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • Developed 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. • The tool can be accessed online (http://genomics.lshtm.ac.uk/immuno)

13.05.2020	Rapid isolation and profiling of a diverse panel of human monoclonal antibodies targeting the SARS-CoV-2 spike protein	bioRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • Used a rapid antibody discovery platform to isolate hundreds of human monoclonal antibodies (mAbs) against the SARS-CoV-2 spike (S) protein. • Stratified these mAbs into five major classes based on their reactivity to subdomains of S protein as well as their cross-reactivity to SARS-CoV. Many of these mAbs inhibit infection of authentic SARS-CoV-2 virus, with most neutralizing mAbs recognizing the receptor-binding domain (RBD) of S.
13.05.2020	ReScan, a Multiplex Diagnostic Pipeline, Pans Human Sera for SARS-CoV-2 Antigens	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • Built a pan-human coronavirus proteome-wide programmable phage display assay (VirScan) to profile coronavirus antigens specifically enriched by 20 COVID-19 patient serum IgG. • Identified 9 candidate antigens from a library of 534 SARS-CoV-2 peptides. These arrays could form the basis of a multiplexed COVID-19 serologic assay with enhanced specificity.

Epidemiology and clinical - risk factors

Publication Date	Title/URL	Journal/ Article type	Digest
13.05.2020	Lifestyle Risk Factors for Cardiovascular Disease in Relation to COVID-19 Hospitalization: A Community-Based Cohort Study of 387,109 Adults in UK	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • Conducted the first large scale general population study on lifestyle risk factors for COVID19. Participants were 387,109 men and women (56.4, SD 8.8 yr; 55.1% women) residing in England from UK Biobank study. • There were 760 COVID-19 cases. After adjustment for age, sex and mutually for each lifestyle factor, physical inactivity (Relative risk, 1.32, 95% confidence interval, 1.10, 1.58), smoking (1.42;1.12, 1.79) and obesity (2.05 ;1.68, 2.49) but not heavy alcohol consumption (1.12; 0.93, 1.35) were all related to COVID-19. • Findings suggest that an unhealthy lifestyle synonymous with an elevated risk of non-communicable disease is also a risk factor for COVID-19 hospital admission, accounting for up to half of severe cases. Adopting simple lifestyle changes could lower the risk of severe infection.
13.05.2020	Ethnicity, comorbidity, socioeconomic status, and their associations with COVID-19	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • UK Biobank participants from England linked to Hospital Episode Statistics (HES) and COVID-19 tests until 14 April 2020: 415,582 participants; 2,886 tested and 1,039 positive. Ethnicity

	infection in England: a cohort analysis of UK Biobank data		<p>self-reported and classified using ONS groups.</p> <ul style="list-style-type: none"> • Compared with White participants, Black/Black British participants had adjusted relative risk (RR) of 2.66, Asian/Asian British participants 2.09, Chinese participants 1.72, other ethnicities 1.67, and mixed ethnicities 0.93. • Socioeconomic status (adjusted RR 1.73 (1.43-2.1) for most deprived), also associated with increased risk of COVID-19. • English COVID-19 rates higher in BAME communities / those living in deprived areas.
13.05.2020	Effects of pre-existing morbidities on occurrence of death among COVID-19 disease patients: A systematic review and meta-analysis	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • 42 studies included, comprised of 39,398 samples. Most common pre-existing morbidities in COVID-19 patients: hypertension (36.5%), cardiovascular disease (11.9%), diabetes (22.0%). • Higher likelihood of deaths: pre-existing cardiovascular system diseases (OR: 3.32, 95% CI: 2.79-3.95), immune & metabolic disorders (OR: 2.39, 95% CI: 2.00-2.85), respiratory diseases (OR: 2.02, 95% CI: 1.80-2.26), cerebrovascular system diseases (OR: 4.12, 95% CI: 3.04-5.58), any types of cancers (OR: 2.22, 95% CI: 1.63-3.03), renal (OR: 3.02, 95% CI: 2.60-3.52), and liver system diseases (OR: 1.44, 95% CI: 1.21-1.71).
13.05.2020	Systemic hypoferraemia and severity of hypoxaemic respiratory failure in COVID-19	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • Investigated serum iron concentrations in 30 patients with COVID-19 requiring ICU admission. All patients had low serum iron but patients with severe hypoxemic respiratory failure had more profound hypoferraemia. • Concluded that profound hypoferraemia identifies COVID-19 patients with severe hypoxaemia. Serum iron is a simple biomarker that could be usefully employed to stratify patients and monitor disease. Severe hypoferraemia may plausibly impair critical iron-dependent processes such as lymphocyte responses and hypoxia sensing, contributing to pathology, and is potentially treatable.

Epidemiology and clinical – other

Publication Date	Title/URL	Journal/ Article type	Digest
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13.05.2020	An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study	The Lancet / Article	<ul style="list-style-type: none"> • Evaluated incidence and features of patients with Kawasaki-like disease diagnosed during the SARS-CoV-2 epidemic. • The SARS-CoV-2 epidemic was associated with high incidence of a severe form of Kawasaki disease. A similar outbreak of Kawasaki-like disease is expected in countries involved in the SARS-CoV-2 epidemic.
12.05.2020	Epidemiological, clinical, and virological characteristics of 465 hospitalized cases of coronavirus disease 2019 (COVID-19) from Zhejiang province in China	Influenza Other Respiratory Viruses / Article	<ul style="list-style-type: none"> • SARS-CoV-2 showed virological mutations and more human transmission in Zhejiang province, indicating considerable epidemiological and clinical changes. • Caution in glucocorticoid and antibiotics use is advisable.
13.05.2020	Weather Conditions and COVID-19 Transmission: Estimates and Projections	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • Assembled a dataset that included virus transmission and weather data across 3,739 locations from Dec 12, 2019 to Apr 22, 2020. • The results provide evidence for the relationship between several weather variables and the spread of COVID-19, finding a negative association between temperature and humidity and transmission. However, the (conservatively) estimated effects of summer weather are not strong enough to seasonally control the epidemic in most locations.

Infection control

Publication Date	Title/URL	Journal/ Article type	Digest
12.05.2020	Measures Undertaken in China to Avoid COVID-19 Infection: Internet-Based, Cross-Sectional Survey Study	Journal of Medical Internet Research / Article	<ul style="list-style-type: none"> • A total of 10,304 participants responded to the survey, with 10,198 valid responses; 74.1% (n=7557) were female and 25.9% (n=2641) were male. • The methods employed by Chinese citizens and authorities have effectively curtailed the spread of COVID-19, demonstrating that this pandemic can be brought under control as long as the right measures are taken.
11.05.2020	Wearable Sensing and Telehealth Technology with Potential Applications in the Coronavirus Pandemic	IEEE Reviews in Biomedical Engineering / Article	<ul style="list-style-type: none"> • The article looks at: 1) wearable devices suitable for monitoring the populations at risk and those in quarantine; 2) unobtrusive sensing systems for detecting the disease; and 3) telehealth technologies for the remote monitoring and diagnosis of COVID-19 and related diseases.

Treatment

Publication Date	Title/URL	Journal/ Article type	Digest
13.05.2020	Should Clinicians Use Chloroquine or Hydroxychloroquine Alone or in Combination With Azithromycin for the Prophylaxis or Treatment of COVID-19?	Annals of Internal Medicine / Article	<ul style="list-style-type: none"> • Current evidence about efficacy and harms for use in the context of COVID-19 is sparse, conflicting, and from low quality studies, increasing the uncertainty and lowering our confidence in the conclusions of these studies when assessing the benefits or understanding the balance when compared with harms. • These interim practice points are based on best available evidence. The authors will maintain these practice points as a living guidance document, updated as new evidence becomes available.
13.05.2020	Drug vignettes: Azithromycin	Oxford COVID-19 Evidence Service / Drug vignette	<ul style="list-style-type: none"> • There have been no reports of the results of well-designed clinical trials of the use of azithromycin in COVID-19. It is more likely to reduce the risk of secondary bacterial infection than to have a direct antiviral effect, but other antibacterial agents are preferable for this purpose. • It should not be used in combination with hydroxychloroquine. • Until the results of adequately powered, double-masked, randomized controlled trials appear, if any, it should not be used to treat COVID-19 except as part of such trials. (This is a non-peer-reviewed article)
11.05.2020	Corticosteroids for critically ill COVID-19 patients with cytokine release syndrome: a limited case series	Canadian Journal of Anaesthesia / Correspondence	<ul style="list-style-type: none"> • The authors describe a case series of 15 COVID-19 patients admitted to ICU who received corticosteroids in the context of cytokine release syndrome (CRS). • They suggest the possibility of short-term clinical improvements with corticosteroids.

Modelling

Publication Date	Title/URL	Journal/ Article type	Digest
12.05.2020	Crowding and the epidemic intensity of COVID-19 transmission	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • Analysed highly-resolved spatial variables for cities in China together with case count data in order to investigate the role of climate, urbanization, and variation in interventions across

		<p>China.</p> <ul style="list-style-type: none"> • Show that the epidemic intensity of COVID-19 is strongly shaped by crowding, such that epidemics in dense cities are more spread out through time, and denser cities have larger total incidence. • Observed differences in epidemic intensity are well captured by a metapopulation model of COVID-19 that explicitly accounts for spatial hierarchies. Densely-populated cities worldwide may experience more prolonged epidemics. Whilst stringent interventions can shorten the time length of these local epidemics, although these may be difficult to implement in many affected settings.
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Guidance, consensus statements and hospital resources

Publication Date	Title/URL	Journal/ Article type
13.05.2020	Infection prevention and control and preparedness for COVID-19 in healthcare settings - third update	European Centre for Disease Control and Prevention / Technical report
12.05.2020	Biosafety measures for preventing infection from COVID-19 in clinical laboratories: IFCC Taskforce Recommendations	Clinical Chemistry and Laboratory Medicine / Taskforce recommendations
01.04.2020	A quality evaluation of guidelines on five different viruses causing public health emergencies of international concern	Annals of Translational Medicine / Review article

Overviews, comments and editorials

Publication Date	Title/URL	Journal/ Article type
13.05.2020	Covid-19 contact tracing: a briefing	British Medical Journal / Feature
13.05.2020	Kawasaki-like disease: emerging complication during the COVID-19 pandemic	The Lancet / Comment
12.05.2020	Self-reported olfactory loss in COVID-19: is it really a favorable prognostic factor?	International Forum of Allergy & Rhinology / Letter to the editor

Produced by the PHE COVID-19 Literature Digest Team

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