



International EPI Cell Daily Evidence Digest – 22/04/2020

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Please note that we are including preprints (**highlighted in red**), which are preliminary reports of work that have NOT been peer-reviewed.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
21.04.2020	Connecting clusters of COVID-19: an epidemiological and serological investigation	The Lancet Infectious Diseases / Article	<ul style="list-style-type: none">• Development and application of a serological assay has helped to establish connections between COVID-19 clusters in Singapore.• Serological testing can have a crucial role in identifying

			convalescent cases or people with milder disease who might have been missed by other surveillance methods.
21.04.2020	What is the efficacy and safety of rapid exercise tests for exertional desaturation in covid-19?	CEBM Research / Rapid review	<ul style="list-style-type: none"> • Two tests have potential: the 1-minute sit-to-stand test (in which the patient goes from sit to stand as many times as they can in one minute) and the 40-step test (in which the patient takes 40 steps on a flat surface). • There is no evidence of harm (e.g. precipitation of cardiopulmonary compromise) from either test, but neither is there firm confirmation of their safety. • Neither test has been studied in the context of covid-19; they were validated on patients with chronic interstitial lung disease and airways obstruction.
21.04.2020	Viral load dynamics and disease severity in patients infected with SARS-CoV-2 in Zhejiang province, China, January-March 2020: retrospective cohort study	BMJ / Article	<ul style="list-style-type: none"> • The duration of SARS-CoV-2 is significantly longer in stool samples than in respiratory and serum samples, highlighting the need to strengthen the management of stool samples in the prevention and control of the epidemic • The virus persists longer with higher load and peaks later in the respiratory tissue of patients with severe disease • To prevent transmission of SARS-CoV-2 it is therefore necessary to carry out strict management during each stage of severe disease
21.04.2020	Host, Viral, and Environmental Transcriptome Profiles of the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)	bioRxiv (not peer reviewed) / New results	<ul style="list-style-type: none"> • The authors designed a fast (30 minute) colorimetric test to identify SARS-CoV-2 infection and simultaneously developed a large-scale shotgun meta transcriptomic profiling platform for nasopharyngeal swabs. • Both technologies were used to profile 338 clinical specimens tested for SARS-CoV-2 and 86 NYC subway samples, creating a broad molecular picture of the COVID-19 epidemic in NYC. • The results nominate a novel, NYC-enriched SARS-CoV-2 subclade, reveal specific host responses in ACE pathways, and find mediation risks associated with SARS-CoV-2 infection and ACE inhibitors.
22.04.2020	One-pot Detection of COVID-19 with Real-time Reverse-transcription Loop-mediated Isothermal Amplification (RT-LAMP) Assay and Visual RT-LAMP Assay	bioRxiv (not peer reviewed) / New results	<ul style="list-style-type: none"> • Study describing a one-pot real-time reverse-transcription loop-mediated isothermal amplification (RT-LAMP) assay and one-pot visual RT-LAMP assay for the detection of COVID-19.
22.04.2020	Molecular Detection of SARS-CoV-2 in Formalin Fixed Paraffin Embedded Specimens	bioRxiv (not peer reviewed) / New results	<ul style="list-style-type: none"> • This study describes the identification and evaluation of commercially available reagents and assays for the molecular

			<p>detection of SARS-CoV-2 in infected formalin fixed paraffin embedded (FFPE) cell pellets.</p> <ul style="list-style-type: none"> • The authors developed a dual staining assay using IHC and ISH to detect SARS-CoV-2 antigen and RNA in the same FFPE section. These reagents and assays will accelerate COVID-19 pathogenesis studies in humans and in COVID-19 animal models.
22.04.2020	COVID-19 diagnosis and study of serum SARS-CoV-2 specific IgA, IgM and IgG by a quantitative and sensitive immunoassay	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • This article describes an immunoassay measuring SARS-CoV-2 specific antibodies IgM and IgG, as well as IgA, which provides a better serological testing with improved sensitivity and specificity. • Data of IgA, IgM, and IgG responses in blood of COVID-19 patients may provide novel insight for the monitoring and treatments of COVID-19. • The kits are also suitable for epidemiological studies and vaccine validations.
22.04.2020	Presence of SARS-CoV-2 reactive T cells in COVID-19 patients and healthy donors	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • The authors describe an assay that allows direct detection and characterization of SARS-CoV-2 spike glycoprotein (S)-reactive CD4+ T cells in peripheral blood.
20.04.2020	Chest CT Findings of Early and Progressive Phase COVID-19 Infection from a US Patient	Radiol Case Rep / Case report	<ul style="list-style-type: none"> • Case report discusses the relevant imaging findings of a 60-year-old man who presented with fever, dyspnoea, and cough for 1 week and subsequently tested positive for COVID-19. • Here, stages of imaging findings in COVID-19 are considered along with the implications of fibrosis throughout the stages. • Future considerations include using artificial intelligence algorithms to distinguish between community acquired pneumonias and COVID-19 infection.
21.04.2020	Variable computed tomography appearances of COVID-19	Singapore Med J	<ul style="list-style-type: none"> • Case series of three COVID-19 pneumonia patients highlights the variable chest CT features during the acute and convalescent phases - its use as a first-line diagnostic modality to replace RT-PCR is not certain. • Larger scale studies with longitudinal follow-up would shed light on the evolution of CT findings and the functional sequela of COVID-19 pneumonia.
21.04.2020	CT imaging features of 4,121 patients with COVID-19: a meta-analysis	J Med Virol / Research article	<ul style="list-style-type: none"> • Authors reviewed the CT imaging features of COVID-19; 34 retrospective studies (total 4,121 COVID-19 patients) included and findings shared. • Lung lesions mostly bilateral lungs or multilobar involved. Most common chest CT findings were patchy and ground-glass

			opacities. Some patients had air bronchogram, spider web sign and cord-like. Lymphadenopathy and pleural effusion were rare.
21.04.2020	Mediastinal lymphadenopathy in patients with severe COVID-19	The Lancet Infectious Diseases / Correspondence	<ul style="list-style-type: none"> • Further studies are needed to better characterise the CT features of patients with COVID-19, in order to establish a possible link between the presence of specific radiological signs and the severity of the disease.

Genomics

Publication Date	Title/URL	Journal/Article type	Digest
21.04.2020	Comparative tropism, replication kinetics, and cell damage profiling of SARS-CoV-2 and SARS-CoV with implications for clinical manifestations, transmissibility, and laboratory studies of COVID-19: an observational study	The Lancet Microbe / Article	<ul style="list-style-type: none"> • This study presents the first quantitative data for tropism, replication kinetics, and cell damage of SARS-CoV-2. • These data provide novel insights into the lower incidence of diarrhoea, decreased disease severity, and reduced mortality in patients with COVID-19, with respect to the pathogenesis and high transmissibility of SARS-CoV-2 compared with SARS-CoV.
21.04.2020	Understanding evolution of SARS-CoV-2: a perspective from analysis of genetic diversity of RdRp gene	J Med Virol / Research article	<ul style="list-style-type: none"> • The study was designed to understand evolution of Betacoronaviruses and in particular diversification of SARS-CoV-2 using RdRp gene, a stable genetic marker. • Population-based analyses of Betacoronaviruses using RdRp, revealed that SARS-CoV-2 is a homogeneous population. SARS-CoV-2 appears to have evolved from Bat-CoV isolate RaTG13, which diversified from a common ancestor from which Pangolin-CoVs have also evolved.
21.04.2020	Possible Bat Origin of Severe Acute Respiratory Syndrome Coronavirus 2	Emerg Infect Dis / Dispatch	<ul style="list-style-type: none"> • Authors showed that severe acute respiratory syndrome coronavirus 2 is probably a novel recombinant virus. • Its genome is closest to that of severe acute respiratory syndrome-related coronaviruses from horseshoe bats, and its receptor-binding domain is closest to that of pangolin viruses. Its origin and direct ancestral viruses have not been identified.
21.04.2020	Synonymous mutations and the molecular evolution of SARS-Cov-2 origins	bioRxiv (not peer-reviewed) / New results	<ul style="list-style-type: none"> • This study describes a detailed analysis of the synonymous divergence, which is less likely to be affected by selection than amino acid divergence, between human SARS-CoV-2 and related strains.
21.04.2020	Elucidating the differences in the molecular mechanism of receptor binding between 2019-	bioRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • These results show major mutations in the 2019-nCoV RBD with respect to the SARS-CoV RBD occurring at the interface of

	nCoV and the SARS-CoV viruses using computational tools		RBD-ACE2 complex. These mutations make the 2019-nCoV RBD protein backbone much more flexible, hydrophobic interactions are reduced and additional polar/charged residues appear at the interface.
21.04.2020	A Computational Approach to Design Potential siRNA Molecules as a Prospective Tool for Silencing Nucleocapsid Phosphoprotein and Surface Glycoprotein Gene of SARS-CoV-2	bioRxiv (not peer-reviewed) / New results	<ul style="list-style-type: none"> In this study, the power of RNA interference technology was harnessed to develop siRNA molecules against specific target genes namely, nucleocapsid phosphoprotein gene and surface glycoprotein gene.
21.04.2020	SARS-CoV-2 Encodes a PPxY Late Domain Motif that is Known to Enhance 1 Budding and Spread in Enveloped RNA Viruses	bioRxiv (not peer-reviewed) / New results	<ul style="list-style-type: none"> Here, analysis of all proteins of SARS-CoV-2 revealed a unique PPxY Late (L) domain motif 25-PPAY-28 in N-terminal of Spike protein. It was demonstrated in enveloped RNA viruses that PPxY motif recruits Nedd4 E3 ubiquitin ligases and ultimately the ESCRT complex to enhance virus budding and release that means a high viral load, thus facilitating new infections.

Epidemiology and clinical - children and pregnancy

Publication Date	Title/URL	Journal/Article type	Digest
20.04.2020	Clinical Manifestation and Laboratory Characteristics of SARS-CoV-2 Infection in Pregnant Women	Viol Sin / Research article	<ul style="list-style-type: none"> Retrospective analysis of eight pregnant cases of SARS-COV-2 found that four were asymptomatic before delivery but became symptomatic post-partum. Correspondingly, white blood cell (WBC) counts increased and lymphocyte (LYMPH) counts decreased. C-reactive protein (CRP) levels in the serum also increased to a higher level than those in general pregnancy. The authors call to closely monitor laboratory parameters: WBC count, LYMPH count, CRP, other imaging features in chest CT scans, to prevent, diagnose, and treat a SARS-CoV-2 infection during pregnancy.
21.04.2020	Varicella-like exanthem associated with COVID-19 in an 8-year-old girl: A diagnostic clue?	Pediatr Dermatol / Brief Report	<ul style="list-style-type: none"> Authors present a case of COVID-19-associated varicella-like exanthem in an 8-year-old girl with mild systemic symptoms.

Epidemiology and clinical - risk factors

Publication Date	Title/URL	Journal/Article type	Digest
21.04.2020	Obesity and SARS-CoV-2: a population to safeguard	Diabetes Metab Res Rev / Article	<ul style="list-style-type: none"> • Evidence of increased risk of SARS-CoV-2 with worse prognosis in patients with obesity, especially among the young. • Underlying pathophysiology likely multi-stranded, from complement system hyperactivation, increased Interleukin-6 secretion, chronic inflammation, presence of comorbidities such as diabetes and hypertension, and a possible local, detrimental effect within the lung.
21.04.2020	Obesity is associated with severe forms of COVID-19	Obesity / Letter	<ul style="list-style-type: none"> • Experience from Lyon University Hospital, France, from 291 consecutive patients admitted to ICU for SARS-CoV-2. • Data confirms the observation from Lille University Centre with higher requirement for IMV in severe obesity ≥ 35 kg/m² compared to lean patients: 81.8% versus 41.9%, p=0.001.
21.04.2020	Is Adipose Tissue a Reservoir for Viral Spread, Immune Activation and Cytokine Amplification in COVID-19	Obesity / Review	<ul style="list-style-type: none"> • Authors posit new obesity-driven predictors of poor COVID-19 outcome, including cardiometabolic disease and hypoventilation syndrome in intensive care patients. • Theoretical mechanistic framework whereby adipose tissue in subjects with obesity may act as a reservoir for more extensive viral spread with increased shedding, immune activation and cytokine amplification. • Recommend studies to test this reservoir concept with a focus on specific cytokine pathways that might be amplified in subjects with obesity and COVID-19.
20.04.2020	COVID-19 infection may cause ketosis and ketoacidosis	Diabetes Obes Metab / Brief report	<ul style="list-style-type: none"> • This study included 658 hospitalized patients with confirmed COVID-19. Forty-two (6.4%) out of 658 patients presented with ketosis on admission with no obvious fever or diarrhoea. • Authors suggest that COVID-19 infection caused ketosis or ketoacidosis, and induced DKA for those patients with diabetes. Ketosis increased the length of hospital stay and mortality. Meanwhile, diabetes increased the length of hospital stay for patients with ketosis but had no effect on their mortality.
21.04.2020	COVID-19 in a High-Risk Dual Heart and Kidney Transplant Recipient	Am J Transplant / Case report	<ul style="list-style-type: none"> • Authors present a dual-organ (heart/kidney) transplant recipient with COVID-19; despite the presence of a number of risk factors for poor outcomes, had a relatively mild clinical course.

21.04.2020	COVID-19 Infection in Patients with Sickle Cell Disease	Br J Haematol / Letter	<ul style="list-style-type: none"> • Authors present a case series of four SCD patients who were found to be positive for COVID-19 and describe their approach to management.
21.04.2020	No evidence that androgen regulation of pulmonary TMPRSS2 explains sex-discordant COVID-19 outcomes	bioRxiv (not peer-reviewed) / New results	<ul style="list-style-type: none"> • Higher morbidity and mortality of men with COVID-19 may be explained by androgen-driven mechanisms, including the proposed androgen regulation of pulmonary TMPRSS2, the host co-receptor for SARS-CoV-2. • The authors find no evidence for increased TMPRSS2 mRNA expression in the lungs of males compared to females in humans or mice.
21.04.2020	Integrated analyses of single-cell atlases reveal age, gender, and smoking status associations with cell type-specific expression of mediators of SARS-CoV-2 viral entry and highlights inflammatory programs in putative target cells	bioRxiv (not peer-reviewed) / New results	<ul style="list-style-type: none"> • These analyses suggest that differences in the cell type-specific expression of mediators of SARS-CoV-2 viral entry may be responsible for aspects of COVID-19 epidemiology and clinical course, and point to putative molecular pathways involved in disease susceptibility and pathogenesis
19.04.2020	Coronaviruses and people with intellectual disability: An exploratory data analysis	J Intellect Disabil Res / Review	The COVID-19 open research dataset (CORD-19) was searched for articles mentioning intellectual disability. The authors found few articles (259 out of 26,055) in CORD-19 but plan to run the search weekly. The authors comment on the usefulness of the CORD-19 platform in deciding whether to pursue a systematic or other review.

Epidemiology and clinical – other

Publication Date	Title/URL	Journal/Article type	Digest
21.04.2020	Epidemiological trends of COVID-19 epidemic in Italy during March 2020. From 1,000 to 100,000 cases	J Med Virol	<ul style="list-style-type: none"> • Based on Italian Ministry of Health data, authors reconstructed the daily course of virus-positive cases and deaths during March 2020 for whole Italy, 19 regions and 2 provinces • From February 29 to March 31 there was a 100.9-fold increase in the cumulative number of cases and a 428.6-fold increase in the number of deaths in Italy.
21.04.2020	Ethnicity and COVID-19: an urgent public health research priority	The Lancet / Correspondence	<ul style="list-style-type: none"> • Striking differences between Chinese and Italian mortality indicate ethnicity might affect disease outcome, but there is little to no data to support or refute this. • Only two (7%) of 29 publications reported ethnicity disaggregated data

			<ul style="list-style-type: none"> • None of the ten highest COVID-19 case-notifying countries reported data related to ethnicity; UK mortality reporting, for example, does not require information on ethnicity.
22.04.2020	How many are at increased risk of severe COVID-19 disease? Rapid global, regional and national estimates for 2020	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • Based on current guidelines and prevalence data from GBD, this study estimates that one in five individuals worldwide has a condition that is on the list of those at increased risk of severe COVID-19 disease. • However, for many of these individuals the underlying condition will be undiagnosed or not severe enough to be captured in health systems, and in some cases the increase in risk may be quite modest. • There is an urgent need for robust analyses of the risks associated with different underlying conditions so that countries can develop targeted shielding policies to mitigate the effects of the COVID-19 pandemic.
20.04.2020	A Case Series of Recurrent Viral RNA Positivity in Recovered COVID-19 Chinese Patients	J Gen Intern Med / Article	<ul style="list-style-type: none"> • Small study of 20 discharged patients. Seven days after hospital discharge, 3 patients who initially tested negative at discharge developed positive RT-PCR test results. One tested positive by faecal RNA, while two tested positive by both salivary and faecal RNA tests at 1 week of follow-up. • All 20 patients returning for the week 2 follow-up tested negative for SARS-CoV-2, irrespective of sampling route. Findings suggest that strict self-isolation protocols and extended follow-up periods might be needed for recovered COVID-19 patients
22.04.2020	Epidemiological and clinical characteristics of 26 asymptomatic SARS-CoV-2 carriers	The Journal of Infectious Diseases / Article	<ul style="list-style-type: none"> •The authors retrospectively analysed 26 persistently asymptomatic severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) carriers. •They concluded that in asymptomatic patients, changes in biochemical and inflammatory variables are small and changes on chest CT can occur
21.04.2020	Central Nervous System Involvement by Severe Acute Respiratory Syndrome Coronavirus -2 (SARS-CoV-2)	J Med Virol / Commentary	<ul style="list-style-type: none"> • Authors report the presence of virus in neural and capillary endothelial cells in frontal lobe tissue obtained at post-mortem examination from a COVID-19 infected patient. • Observations of virus in neural tissue, in conjunction with clinical correlates of worsening neurologic symptoms, inform closer understanding of pathogenic mechanisms underlying CNS involvement.

21.04.2020	Long-term Coexistence of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) with Antibody Response in Coronavirus Disease 2019 (COVID-19) Patients	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> • Whether antibodies are important for the adaptive immune responses against SARS-CoV-2 infection needs to be determined. • SARS-CoV-2 could exist in patients who have virus-specific IgG antibodies for a very long period, with two cases for up to 50 days. • Suggestion that without antibody-mediated adaptive immunity, innate immunity may still be powerful enough to eliminate SARS-CoV-2.
21.04.2020	Eosinophil count in severe coronavirus disease 2019 (COVID-19)	QJM / Article	<ul style="list-style-type: none"> • Response to Qian et al. study of epidemiologic and clinical characteristics of 91 hospitalized patients - showed a trend, though nonsignificant, towards eosinopenia in patients with COVID-19. • Results of own literature review and pooled analysis suggest that, despite the still limited volume of data on eosinophil count in patients with COVID-19, eosinopenia may not be associated with unfavourable progression of COVID-19.
21.04.2020	Response letter to Eosinophil count in severe coronavirus disease 2019 (COVID-19)	QJM / Letter	<ul style="list-style-type: none"> • Original authors maintain that early detection of SARS-CoV-2 infection could be based on fever, upper respiratory symptoms, lymphopenia and eosinophilia. However, the relationship between eosinopenia and SARS-CoV-2 infection needs further study.

Infection control

Publication Date	Title/URL	Journal/Article type	Digest
21.04.2020	The impact of COVID-19 on neurosurgeons and the strategy for triaging non-emergent operations: a global neurosurgery study	Acta Neurochir (Wien) / Article	<ul style="list-style-type: none"> • Authors report on the impact of COVID-19 on neurosurgeons around the world. From their ranking of the nine case scenarios (494 respondents to the principal survey from 60 countries), deduced a strategic scheme that can serve as a guideline to triage non-emergent neurosurgical procedures during the pandemic.
21.04.2020	Barriers and facilitators to healthcare workers' adherence with infection prevention and control (IPC) guidelines for respiratory infectious diseases: a rapid qualitative evidence synthesis	Cochrane Database Syst Rev / Review	<ul style="list-style-type: none"> • Rapid review identified 30 studies exploring the views and experiences of nurses, doctors and other healthcare workers when dealing with severe acute respiratory syndrome (SARS), H1N1, MERS (Middle East respiratory syndrome), tuberculosis (TB), or seasonal influenza.

			<ul style="list-style-type: none"> • Factors influencing ability and willingness to follow IPC guidelines include guideline itself and how communicated, support from managers, workplace culture, training, physical space, access to and trust in personal protective equipment, and a desire to deliver good patient care. Importance of including all facility staff, including support staff, when implementing IPC guidelines highlighted.
21.04.2020	A Rapidly Deployable Negative Pressure Enclosure for Aerosol-Generating Medical Procedures	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • Describes an Aerosol Containment Enclosure (ACE) capable of maintaining negative pressure during simulated aerosol-generating medical procedures (AGMPs). • In all cases, containment was improved relative to an identical enclosure with non-occluded ports at ambient pressure. During the current COVID-19 pandemic, the use of such a device may assist in reducing nosocomial infections among healthcare providers.
21.04.2020	Estimates of regional infectivity of COVID-19 in the United Kingdom following imposition of social distancing measures	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> • This paper describes regional variation in the reproduction number of SARS-CoV-2 infections observed using publicly reported data in the UK, with a view to understanding both if there are clear hot spots in viral spread in the country, or if there are any clear spatial patterns. • The authors estimate that the viral replication number remains slightly above 1 overall but that its trend is to decrease, based on case data up to the 8 April. This suggests the peak of the first wave of COVID-19 patients is imminent.

Treatment

Publication Date	Title/URL	Journal/Article type	Digest
21.04.2020	Hospital-based use of thromboprophylaxis in patients with COVID-19	The Lancet / Correspondence	<ul style="list-style-type: none"> • The authors offer further information about thromboprophylaxis that they believe is worth considering when treating patients who have been admitted to hospital with COVID-19.
20.04.2020	Ventilation of COVID-19 patients in intensive care units	Herz / Letter	<ul style="list-style-type: none"> • Review, concludes ventilation of COVID-19 ICU patients is challenging because of heterogeneous lung pathology that requires an individualized lung-protective ventilation strategy to improve outcome.

21.04.2020	Fast Identification of Possible Drug Treatment of Coronavirus Disease -19 (COVID-19) Through Computational Drug Repurposing Study	J Chem Inf Model	<ul style="list-style-type: none"> • Authors applied computer-aided drug design techniques to quickly identify promising drug repurposing candidates. 2-4 known drugs stand out as potential inhibitors of SARS-Cov-2 main protease, including Carfilzomib, Eravacycline, Valrubicin, Lopinavir and Elbasvir. • Detailed receptor-ligand interactions were analysed and hot spots for the receptor-ligand binding identified. One hotspot residue HIS41, is a conserved residue across many viruses including SARS-Cov, SARS-Cov-2, MERS-Cov, and HCV.
19.04.2020	PAK1-blockers: Potential Therapeutics against COVID-19	Med Drug Discov / Review	<ul style="list-style-type: none"> • Review of the current evidence of natural and synthetic PAK1-blockers such as propolis, melatonin, ciclesonide, hydroxy chloroquine (HQ), ivermectin, and ketorolac, as treatment for COVID-19.
20.04.2020	Nafamostat mesylate blocks activation of SARS-CoV-2: New treatment option for COVID-19	Antimicrob Agents Chemother / Letter	<ul style="list-style-type: none"> • In the light of the global impact of COVID-19 on human health, the proven safety of nafamostat mesylate and its increased antiviral activity as compared to camostat mesylate, authors argue that this compound should be evaluated in clinical trials as COVID-19 treatment.
21.04.2020	Human iPSC-Derived Cardiomyocytes are Susceptible to SARS-CoV-2 Infection	bioRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • This study reports that SARS-CoV-2 can infect human induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CMs) in vitro, establishing a model for elucidating the mechanisms of infection and potentially a cardiac-specific antiviral drug screening platform.
21.04.2020	Inhibition of PIKfyve kinase prevents infection by EBOV and SARS-CoV-2	bioRxiv (not peer-reviewed) / New results	<ul style="list-style-type: none"> • This article describes potent inhibitory effects on content release and infection by chimeric VSV containing the envelope proteins of EBOV (VSV-EBOV) or SARS-CoV-2 (VSV-SARS-CoV-2) elicited by Apilimod and Vacuolin-1, small molecule inhibitors of the main endosomal Phosphatidylinositol-3-Phosphate/Phosphatidylinositol 5-Kinase, PIKfyve. • It also describes potent inhibition of SARS-CoV-2 strain 2019-nCoV/USA-WA1/2020 by Apilimod.
21.04.2020	Letter to the Editor: Acute hypertriglyceridemia in patients with COVID-19 receiving tocilizumab	J Med Virol / Letter	<ul style="list-style-type: none"> • Two cases of acute hypertriglyceridemia in patients with COVID-19 treated with tocilizumab: one with elevated biomarkers consistent with acute pancreatitis the other without. • Observations highlight the complex, not fully elucidated interrelationship between elevated IL-6 and pharmacologic interventions impacting this pathway. Clinicians should consider monitoring for hypertriglyceridemia and acute pancreatitis as

			described with chronic tocilizumab use for rheumatoid arthritis in those receiving it for COVID-19.
22.04.2020	Interleukin-6 blockade for severe COVID-19	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> The authors demonstrate that, in highly selected patients, IL6 blockade could curb the "cytokine storm", prevent ICU admission and the requirement for mechanical ventilation.
22.04.2020	Effectiveness and Safety of Glucocorticoids to Treat COVID-19: A Rapid Review and Meta-Analysis	medRxiv (not peer-reviewed) / Rapid review	<ul style="list-style-type: none"> One RCT and 22 cohort studies were included in this review. Glucocorticoid therapy was found to reduce the duration of fever, but not mortality, duration of hospitalization or lung inflammation absorption. Long-term use of high-dose glucocorticoids increased the risk of adverse reactions such as coinfections, so routine use of systemic glucocorticoids for patients with COVID-19 cannot be recommend.
21.04.2020	Cross-reactive neutralization of SARS-CoV-2 by serum antibodies from recovered SARS patients and immunized animals	bioRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> This study found that a palm civet SARS-CoV-derived RBD elicited more potent cross-neutralizing responses in immunized animals than the RBD from a human SARS-CoV strain, informing a strategy to develop a universal vaccine against emerging CoVs.
20.04.2020	A short review on antibody therapy for COVID-19	New Microbes New Infect / Article	<ul style="list-style-type: none"> The authors review the antibody therapy that might be an immediate strategy for emergency prophylaxis and SARS-CoV-2 therapy
21.04.2020	Artificial intelligence predicts the immunogenic landscape of SARS-CoV-2: toward universal blueprints for vaccine designs	bioRxiv (not peer-reviewed) / New results	<ul style="list-style-type: none"> The authors describe the profile of the entire SARS-CoV-2 proteome and identify a subset of epitope hotspots that could be harnessed in a vaccine formulation to provide a broad coverage across the global population.
21.04.2020	Melatonin: Roles in influenza, Covid-19, and other viral infections	Rev Med Virol / Review	<ul style="list-style-type: none"> Review of the melatonergic pathway role in viral infections, emphasizing influenza and covid-19 infections. A number of factors can act to inhibit the key cellular changes upon which viruses act, with melatonin being one such factor. The utility of melatonin is paradoxically under-appreciated, if not suppressed, by its ready availability, low cost, and very high safety profile.
20.04.2020	Salvage use of tissue plasminogen activator (tPA) in the setting of acute respiratory distress syndrome (ARDS) due to COVID-19 in the USA: a Markov decision analysis	World J Emerg Surg	<ul style="list-style-type: none"> Systemic tissue plasminogen activator (tPA) has been previously demonstrated to improve PaO₂/FiO₂ (mmHg) when given to critically ill patients with acute respiratory distress syndrome (ARDS). A decision analytic Markov state transition model was created to simulate critically ill COVID-19 patients as they transitioned to either recovery or death. Two patient groups were simulated

			<p>(50,000 patients in each group); (1) Patients received tPA immediately upon diagnosis of ARDS and (2) patients received standard therapy for ARDS.</p> <ul style="list-style-type: none"> • Salvage use of tPA may improve recovery of ARDS patients, thereby reducing COVID-19-related mortality and ensuring sufficient resources to manage this pandemic.
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Social sciences

Publication Date	Title/URL	Journal/Article type	Digest
21.04.2020	The implications of COVID-19 for the care of children living in residential institutions	The Lancet Child & Adolescent Health / Correspondence	<ul style="list-style-type: none"> • Numerous residential institutions for children are being closed as a result of COVID-19 and children appear to be being sent back to their communities without proper consideration of where they will reside, how their transition will be supported, and whether their safety will be monitored. • The authors view that although a shift from institutional to family based care is a priority, these transitions need to be carefully planned and managed, with effective and sustained family preparation, strengthening, monitoring, and other support
20.04.2020	Elder Abuse in the COVID-19 Era	J Am Geriatr Soc / Article	<ul style="list-style-type: none"> • In order to better understand the complex dynamics that lead to elder abuse, this group developed a theoretical model called the Abuse Intervention/Prevention Model (AIM [5]). • This model focuses on three core and intersecting considerations: (1) the vulnerable older adult, (2) the trusted other, and (3) the context in which the abuse occurs. • The authors consider each of these in relation to the COVID-19 pandemic and end with suggested ways to mitigate the risks
21.04.2020	Psychological stress of medical staffs during outbreak of COVID-19 and adjustment strategy	J Med Virol / Article	<ul style="list-style-type: none"> • Random sample questionnaire survey was conducted among 2110 medical staffs and 2158 college students in China. • The emotion, cognition, physical and mental response of front-line medical staff showed obvious "exposure effect", and psychological crisis intervention strategy can be helpful.

Modelling

Publication Date	Title/URL	Journal/Article type	Digest
21.04.2020	Effect of changing case definitions for COVID-19 on the epidemic curve and transmission parameters in mainland China: a modelling study	The Lancet Public Health / Article	<ul style="list-style-type: none"> • This study aimed to assess whether changes in case definitions affected inferences on the transmission dynamics of coronavirus disease 2019 (COVID-19) in China.
21.04.2020	Estimation of Coronavirus Disease Case-Fatality Risk in Real Time	Emerg Infect Dis / Research Letter	<ul style="list-style-type: none"> • Authors hypothesise that the time-varying number of cumulative cases and deaths should be considered in the epidemic profile. • They ran a simulation comparing 3 methods to calculate case-fatality risk for coronavirus disease using parameters described in previous studies. Case-fatality risk calculated from these methods all are biased at the early stage of the epidemic. When comparing real-time case-fatality risk, the current trajectory of the epidemic should be considered.
21.04.2020	Applying the unified models of ecology to forecast epidemics, with application to Covid-19	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> • An ecological model is described that includes a biological pathogen-growth factor and an ecological social-response factor. • All parameters in the model are designed to be measurable from publicly available data. • The model was used to successfully predict the outcome of the 2014-15 Ebola outbreak, and is here applied to COVID-19.
21.04.2020	Effects of medical resource capacities and intensities of public mitigation measures on outcomes of COVID-19 outbreaks	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> • Multiple data sources and cross validation of a COVID-19 epidemic model, coupled with a medical resource logistic model, are used to look at factors that affect epidemic progressions in different countries. • Key factors included the type of emergency medical responses, especially improved detection rates, the ability to promote public health measures, and the synergistic effects of combinations of multiple prevention and control strategies.
20.04.2020	Predicting turning point, duration and attack rate of COVID-19 outbreaks in major Western countries	Chaos Solitons Fractals / Article	<ul style="list-style-type: none"> • The authors employed a model to analyse the available daily new cases data of the COVID-19 outbreaks in six Western countries, Canada, France, Germany, Italy, UK and USA. • They took the governments' interventions (stay-at-home advises/orders, lockdowns, quarantines and social distancing) against COVID-19 into consideration. • The analysis allows a statistical prediction to be made on the turning point (the time that the daily new cases peak), the duration (the period that the outbreak lasts) and the attack rate

		(the percentage of the total population that will be infected over the course of the outbreak) for these countries.
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Guidance, consensus statements and hospital resources

Publication Date	Title/URL	Journal/Article type
20.04.2020	Managing COVID-19 symptoms (including at the end of life) in the community: summary of NICE guidelines	BMJ / Guidance
22.04.2020	Multicenter initial guidance on use of antivirals for children with COVID-19/SARS-CoV-2	Journal of the Pediatric Infectious Diseases Society / Article
21.04.2020	The Obstacle Course of Reperfusion for STEMI in the COVID-19 Pandemics	Circulation
21.04.2020	Recommendation of a practical guideline for safe tracheostomy during the COVID-19 pandemic	Eur Arch Otorhinolaryngol / Review Article
20.04.2020	COVID-19 patients and the radiology department - advice from the European Society of Radiology (ESR) and the European Society of Thoracic Imaging (ESTI)	Eur Radiol
21.04.2020	Flexible Laryngoscopy and COVID-19	Otolaryngol Head Neck Surg / Correspondence

Overviews, comments and editorials

Publication Date	Title/URL	Journal/Article type
21.04.2020	Preparing for COVID-19's aftermath: simple steps to address social determinants of health	J R Soc Med / Editorial review
19.04.2020	2019 Novel coronavirus (COVID-19) overview	Journal of Public Health / Review
21.04.2020	A Frail Health Care System for an Old Population: Lesson form the COVID-19 Outbreak in Italy	J Gerontol A Biol Sci Med Sci / Editorial
22.04.2020	A case series of children with Coronavirus Disease 2019: what have we learned?	Clinical Infectious Diseases / Editorial
20.04.2020	Rituximab for granulomatosis with polyangiitis in the pandemic of covid-19: lessons from a case with severe pneumonia	Ann Rheum Dis / Correspondence
21.04.2020	Targeting the Adipose Tissue in COVID-19	Obesity / Review
21.04.2020	Response of a tertiary dermatology department to COVID-19 / Letter	Australas J Dermatol
21.04.2020	Challenges in Heart Transplantation in the Era of COVID-19	Circulation / Article
21.04.2020	Rapid detection of COVID-19 coronavirus using a reverse transcriptional loop-mediated isothermal amplification (RT-LAMP) diagnostic platform	Clin Chem / Letter to the editor
20.04.2020	Faecal calprotectin indicates intestinal inflammation in COVID-19	Gut / Letter

21.04.2020	Peritoneal Dialysis in the time of COVID-19	Perit Dial Int / Commentary
19.04.2020	Abortion in the context of COVID-19: a human rights imperative	Sex Reprod Health Matters / Comment
21.04.2020	Building trust while influencing online COVID-19 content in the social media world	The Lancet Digital Health / Comment
21.04.2020	Targeting COVID-19 interventions towards migrants in humanitarian settings	The Lancet Infectious Diseases / Comment
21.04.2020	The important role of serology for COVID-19 control	The Lancet Infectious Diseases / Comment
22.04.2020	Suicide risk and prevention during the COVID-19 pandemic	The Lancet Psychiatry / Comment
21.04.2020	Comment on "Cutaneous manifestations in COVID-19: a first perspective " by Recalcati S	Journal of the European Academy of Dermatology and Venereology / Comment

Produced by the PHE COVID-19 Literature Digest Team

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