



International EPI Cell Daily Evidence Digest – 24/04/2020

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Please note that we are including preprints (**highlighted in red**), which are preliminary reports of work that have NOT been peer-reviewed.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
23.04.2020	Serological assays for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), March 2020	Eurosurveillance / Article	<ul style="list-style-type: none">• The authors describe development of an ELISA to detect IgG and IgM antibodies to the receptor-binding domain (RBD) of the spike protein of SARS-CoV-2• Highlights include that using IgG ELISA based on the RBD of the

			spike protein to screen sera for SARS-CoV-2 antibody, followed by confirmation using PRNT90, is a valid approach for large-scale sero-epidemiology studies.
23.04.2020	Rapid and sensitive detection of anti-SARS-CoV-2 IgG using lanthanide-doped nanoparticles-based lateral flow immunoassay	Analytical chemistry / Accepted manuscript	<ul style="list-style-type: none"> This assay can achieve rapid and sensitive detection of anti-SARS-CoV-2 IgG in human serum and allow positive identification in suspicious cases; it can also be useful for monitoring the progression COVID-19 and evaluating patients' response to treatment.
15.04.2020	Neutralizing Antibodies Responses to SARS-CoV-2 in COVID-19 Inpatients and Convalescent Patients	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> The neutralizing antibodies were detected even at the early stage of disease, and a significant response showed in convalescent patients. Moreover, changes on antibody levels were individual specific.
18.04.2020	Laboratory data analysis of novel coronavirus (COVID-19) screening in 2510 patients	Clin Chim Acta Clinica chimica acta / Article	<ul style="list-style-type: none"> Collected nucleic acid and haematology data from 2510 patients for COVID-19 infection for retrospective analysis. Concluded that the positive rate of influenza A and B infection was higher than that of COVID-19. Evaluation of pharyngeal swab and faecal samples can improve the positive rate of nucleic acid detection. COVID-19 can cause some haematological indices changes.
22.04.2020	Characteristic CT findings distinguishing 2019 novel coronavirus disease (COVID-19) from influenza pneumonia	European radiology / Research article	<ul style="list-style-type: none"> Although viral pneumonias generally show similar imaging features, there are some characteristic CT findings which may help differentiating COVID-19 from influenza pneumonia.
23.04.2020	Acute Pulmonary Embolism Associated with COVID-19 Pneumonia Detected by Pulmonary CT Angiography	Radiology / Research letter	<ul style="list-style-type: none"> In patients with severe clinical features of COVID-19 infection, the proportion of patients with acute pulmonary embolus was 23% (95% CI: 15%, 33%) on pulmonary CT angiography.
23.04.2020	The laboratory tests and host immunity of COVID-19 patients with different severity of illness	JCI insight / In press preview	<ul style="list-style-type: none"> The number and function of T cells are inconsistent in COVID-19 patients. The hyperfunction of CD4+ and CD8+ T cells is associated with the pathogenesis of extremely severe SARS-CoV-2 infection.
23.04.2020	Diagnosis, Prevention, and Treatment of Thromboembolic Complications in COVID-19: Report of the National Institute for Public Health of the Netherlands	Radiology / Special report	<ul style="list-style-type: none"> This report summarizes evidence for thromboembolic disease, potential diagnostic and preventive actions as well as recommendations for patients with COVID-19 infection.
19.04.2020	Augmented Curation of Unstructured Clinical Notes from a Massive EHR System Reveals Specific Phenotypic Signature of Impending COVID-19 Diagnosis	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> This study introduces an Augmented Intelligence platform for the real-time synthesis of institutional knowledge captured in Electronic Health Record (EHRs). By contrasting the EHR-derived clinical phenotypes of COVID-19-positive (COVIDpos, n=272) versus COVID-19-negative (COVIDneg, n=14,695) patients over each day of the week preceding the PCR testing date, they identify diarrhoea (2.8-fold), change in appetite (2-fold), anosmia/dysgeusia (28.6-fold), and respiratory failure (2.1-fold)

			as significantly amplified in COVIDpos over COVIDneg patients. The specific combination of cough and diarrhoea has a 4-fold amplification in COVIDpos patients during the week prior to PCR testing, and along with anosmia/dysgeusia, constitutes the earliest EHR-derived signature of COVID-19.
23.04.2020	TARGETED PROTEOMICS FOR THE DETECTION OF SARS-COV-2 PROTEINS	bioRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> Here, the authors exploit the potential of targeted mass spectrometry based proteomic technologies to solve the current issue of insufficient SARS-CoV-2 diagnostic testing capacity.

Genomics

Publication Date	Title/URL	Journal/ Article type	Digest
20.04.2020	Bayesian phylodynamic inference on the temporal evolution and global transmission of SARS-CoV-2	Journal of infection / Letter	<ul style="list-style-type: none"> Continuous evolution is occurring in almost all regions of the SARS-CoV-2 genome and potentially in a country-specific manner. Further efforts on monitoring the genomic mutations are needed.
22.04.2020	Emerging SARS-CoV-2 mutation hot spots include a novel RNA-dependent-RNA polymerase variant	Journal of translational medicine / Research article	<ul style="list-style-type: none"> The findings suggest that the virus is evolving and European, North American and Asian strains might coexist, each of them characterized by a different mutation pattern. The contribution of the mutated RdRp to this phenomenon needs to be investigated.
17.04.2020	A single-cell atlas of the peripheral immune response to severe COVID-19	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> Provide the most thorough cell atlas to date of the peripheral immune response to severe COVID-19.
22.04.2020	Functional and Genetic Analysis of Viral Receptor ACE2 Orthologs Reveals Broad Potential Host Range of SARS-CoV-2	bioRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> In this study, the authors aimed to characterize ACE2 from a diversity of species for its ability to support viral entry. They found that ACE2 is expressed in a wide range of host species, with high conservation especially in mammals.
22.04.2020	Heterogeneous expression of the SARS-Coronavirus-2 receptor ACE2 in the human respiratory tract	bioRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> The authors systematically examined human upper and lower respiratory tract cells using single-cell RNA sequencing and immunohistochemistry to determine where the receptor is expressed. The results reveal that ACE2 expression is highest within the sinonasal cavity and pulmonary alveoli, sites of presumptive viral transmission and severe disease development, respectively. In the lung parenchyma where severe disease occurs, ACE2 was found on the apical surface of a small subset of alveolar type II cells. They saw no increase of receptor expression in the presence of known risk factors for severe coronavirus disease 2019.

21.04.2020	TMPRSS2 and TMPRSS4 mediate SARS-CoV-2 infection of human small intestinal enterocytes	bioRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • Here, the authors demonstrate productive infection of SARS-CoV-2 in ACE2+ mature enterocytes in human small intestinal enteroids. • The results highlight the intestine as a potential site of SARS-CoV-2 replication, which may contribute to local and systemic illness and overall disease progression.
20.04.2020	SARS-CoV-2 Encodes a PPxY Late Domain Motif that is Known to Enhance Budding and Spread in Enveloped RNA Viruses	bioRxiv (not peer reviewed) / Article	<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 spike protein inside hot disordered loop predicted subject to phosphorylation and binding. 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, hence facilitating new infections.
23.04.2020	Structural and biochemical characterization of nsp12-nsp7-nsp8 core polymerase complex from COVID-19 virus	bioRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • The authors describe the near-atomic resolution structure of COVID-19 virus core polymerase complex, consisting of nsp12 catalytic subunit and nsp7-nsp8 cofactors. This structure highly resembles the counterpart of SARS-CoV with conserved motifs for all viral RNA-dependent RNA polymerases, and suggests the mechanism for activation by cofactors. • These findings provide important insights into RNA synthesis by coronavirus polymerase and indicate a good adaptation of COVID-19 virus towards humans with relatively lower body temperatures than the natural bat hosts.
21.04.2020	Recombinant SARS-CoV-2 spike S1-Fc fusion protein induced high levels of neutralizing responses in nonhuman primates	bioRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • In this study, the authors examined the immunogenicity of CHO-expressed recombinant SARS-CoV-2 S1-Fc fusion protein in mice, rabbits, and monkeys as a potential candidate for a COVID-19 vaccine. • The data strongly suggests that the CHO-expressed SARS-CoV-2 S1-Fc recombinant protein could be a strong candidate for vaccine development against COVID-19.

Epidemiology and clinical - children and pregnancy

Publication Date	Title/URL	Journal/ Article type	Digest
20.04.2020	The profile of peripheral blood lymphocyte subsets and serum cytokines in children with 2019 novel coronavirus pneumonia	Journal of Infection / Article in press	<ul style="list-style-type: none"> • Immune response played a very important role in the development of 2019-nCoV pneumonia. The effective CD8+ T cell response might influence the severity of 2019-nCoV pneumonia. The adaptable

			change in IL-10 level might contribute to the relatively mild pneumonia symptoms in children with 2019-nCoV pneumonia and bacterial co-infection might be a risk factor of severe 2019-nCoV pneumonia.
22.04.2020	COVID-19 and what pediatric rheumatologists should know: a review from a highly affected country	Pediatric rheumatology online journal / Review	<ul style="list-style-type: none"> Some of the drugs mostly used by rheumatologists appear to be promising in critical COVID-19 infected patients, where the hyperinflammation and cytokine storm seem to drive to the multiorgan failure.
23.04.2020	Covid-19 and children with cancer: are they at increased risk of infection?	Pediatric research / Letter	<ul style="list-style-type: none"> No relevant literature available on COVID-19 infection and children with cancer.

Epidemiology and clinical - risk factors

Publication Date	Title/URL	Journal/ Article type	Digest
22.04.2020	Prevalence of malnutrition and analysis of related factors in elderly patients with COVID-19 in Wuhan, China	European journal of clinical nutrition / Article	<ul style="list-style-type: none"> The prevalence of malnutrition in elderly patients with COVID-19 was high, and nutritional support should be strengthened during treatment, especially for those with diabetes mellitus, low calf circumference, or low albumin.
23.04.2020	Does high cardiorespiratory fitness confer some protection against pro-inflammatory responses after infection by SARS-CoV-2?	Obesity / Review article	<ul style="list-style-type: none"> Preliminary evidence suggests that the severity of symptoms associated with Covid-19 and the eventual outcome of being infected with the virus are associated with the health status of individuals prior to infection.
19.04.2020	Obesity as a risk factor for greater severity of COVID-19 in patients with metabolic associated fatty liver disease	Metabolism: clinical and experimental / article	<ul style="list-style-type: none"> Of 214 COVID-19 patients aged between 18 and 75 years from three hospitals in Wenzhou, China, the presence of obesity in metabolic associated fatty liver disease MAFLD patients was associated with a ~ 6-fold increased risk of severe COVID-19 illness.
23.04.2020	Association of Renin-Angiotensin System Inhibitors With Severity or Risk of Death in Patients With Hypertension Hospitalized for Coronavirus Disease 2019 (COVID-19) Infection in Wuhan, China	JAMA cardiology / Brief report	<ul style="list-style-type: none"> This study provides clinical data on the association between ACEIs/ARBs and outcomes in patients with hypertension hospitalized with COVID-19 infections, suggesting that ACEIs/ARBs are not associated with the severity or mortality of COVID-19 in such patients. These data support current guidelines and societal recommendations for treating hypertension during the COVID-19 pandemic.
19.04.2020	Impaired type I interferon activity and exacerbated inflammatory responses in severe Covid-19 patients	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> The authors propose that type-I IFN deficiency in the blood is a hallmark of severe Covid-19 and could identify and define a high-risk population. The study provides a rationale for testing IFN

administration combined with adapted anti-inflammatory therapy targeting IL-6 or TNF- α in most severe patients. These data also raise concern for utilization of drugs that interfere with the IFN pathway.

Epidemiology and clinical – other

Publication Date	Title/URL	Journal/ Article type	Digest
23.04.2020	Clinical characteristics of coronavirus disease (COVID-19) early findings from a teaching hospital in Pavia, North Italy, 21 to 28 February 2020	Eurosurveillance / Rapid communication	<ul style="list-style-type: none"> • Authors describe clinical characteristics, treatments and outcomes of 44 Caucasian patients with COVID-19 at a single hospital in Pavia, Italy, from 21–28 February 2020. • Of 17 patients with severe disease, 2 died, after a median of 6 days, 14 patients were discharged from hospital. • Predictors of lower odds of discharge were age > 65 years, antiviral treatment and for severe disease, lactate dehydrogenase > 300 mg/dL.
23.04.2020	Epidemiological characteristics of the first 53 laboratory-confirmed cases of COVID-19 epidemic in Hong Kong, 13 February 2020	Eurosurveillance / Article	<ul style="list-style-type: none"> • The authors extracted data of confirmed COVID-19 cases and their close contacts from the publicly available information released by the Hong Kong Centre for Health Protection • The study highlights that with a considerable containment delay and short serial interval, contact-tracing effectiveness may not be optimised to halt the transmission with rapid generations replacement.
23.04.2020	Strong associations and moderate predictive value of early symptoms for SARS-CoV-2 test positivity among healthcare workers, the Netherlands, March 2020	Eurosurveillance / Rapid communication	<ul style="list-style-type: none"> • Healthcare workers (n = 803) with mild symptoms were tested for SARS-CoV-2 (n = 90 positive) and asked to complete a symptom questionnaire. • Anosmia, muscle ache, ocular pain, general malaise, headache, extreme tiredness and fever were associated with positivity. • A predictive model based on these symptoms showed moderate discriminative value (sensitivity: 91.2%; specificity: 55.6%).
23.04.2020	National COVID-19 surveillance report: 23 April 2020 (week 17)	Public health england / Report	<ul style="list-style-type: none"> • This report summarises the information from the surveillance systems which are used to monitor the COVID-19 pandemic in England. • The report is based on week 16 (data between 13 April and 19 April 2020) and where available daily data up to 22 April 2020.
23.04.2020	Epidemiological Assessment of Imported Coronavirus Disease 2019 (COVID-19) Cases in the	JAMA Network Open / Research Letter	<ul style="list-style-type: none"> • All confirmed COVID-19 cases reported to the Municipal Health Commission of Wenzhou (n=482) from January 21 to February 15,

	Most Affected City Outside of Hubei Province, Wenzhou, China		<p>2020, were included in this analysis.</p> <ul style="list-style-type: none"> • The basic reproduction number, R0 was estimated as 2.9. • The authors highlight that the timely community containment approaches implemented in Wenzhou were associated with the end of the COVID-19 epidemic in early March 2020.
22.04.2020	Alterations in Smell or Taste in Mildly Symptomatic Outpatients With SARS-CoV-2 Infection	Jama / Research letter	<ul style="list-style-type: none"> • Short report of a small study which evaluated prevalence, intensity, and timing of an altered sense of smell or taste in patients with SARS-CoV-2 infections. • Alterations in smell or taste were frequently reported by mildly symptomatic patients with SARS-CoV-2 infection and often were the first apparent symptom. The results must be interpreted with caution due to study limitations.
14.04.2020	Prevalence and severity of corona virus disease 2019 (COVID-19): A systematic review and meta-analysis	Journal of clinical virology / Review	<ul style="list-style-type: none"> • Fever and cough are the most common symptoms in patients with COVID-19. • The most prevalent comorbidities are hypertension and diabetes which are associated with the severity of COVID-19. • ARDS and ACI may be the main obstacles to treatment recovery for patients. • The case severe rate and mortality is lower than that of SARS and MERS.
18.04.2020	Clinical Characteristics of 20,662 Patients with COVID-19 in mainland China: A Systemic Review and Meta-analysis	medRxiv (not peer reviewed) / Systematic review	<ul style="list-style-type: none"> • The mean age of patients with COVID-19 (n=20,662) was 49.40 years, 53.45% were male, and 38.52% had at least one comorbidity. • Fever and cough were the most common symptoms, followed by fatigue, expectoration, and shortness of breath. Most patients with COVID-19 had abnormal chest CT findings with ground glass opacity (70.70%) or consolidation (29.91%). Laboratory findings shown lymphopenia, increased lactate dehydrogenase, increased infection-related indicators, and fibrinolytic hyperactivity. • Antiviral therapy, antibiotic therapy, and corticosteroids were administered to 89.75%, 79.13%, and 35.64% of patients, respectively.
19.04.2020	Clinical characteristics of imported and second-generation COVID-19 cases outside Wuhan, China: A multicenter retrospective study	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • This study aimed to clarify the clinical characteristics of imported and second-generation cases. This retrospective, multicentre cohort study included 134 confirmed COVID-19 cases from 9 cities outside Wuhan. • Concluded that imported and second-generation cases outside Wuhan had a better prognosis than initial cases in Wuhan. Lymphocyte count and IL-6 level could be used for evaluating

			prognosis. Pulmonary fibrosis as the sequelae of COVID-19 should be taken into account.
22.04.2020	Achieving a Popliteal Venous Access for RRT in Critically Ill COVID-19 Patient in Prone position	Journal of vascular surgery cases and innovative techniques / Case report	<ul style="list-style-type: none"> • This case report outlines a possible challenging scenario that may be encountered when dealing with COVID-19 patients with respiratory compromise in prone position.
23.04.2020	COVID-19 infection and treatment with hydroxychloroquine cause severe haemolysis crisis in a patient with glucose-6-phosphate dehydrogenase deficiency	European journal of haematology / Case report	<ul style="list-style-type: none"> • Case report of severe haemolytic crisis in a patient with G6PD deficiency, initiated by severe COVID-19 infection and hydroxychloroquine use.
18.04.2020	Coronavirus Disease 2019 Pneumonia in Immunosuppressed Renal Transplant Recipients: A Summary of 10 Confirmed Cases in Wuhan, China	Eur Urol European urology / Article	<ul style="list-style-type: none"> • A total of 10 renal transplant recipients with laboratory-confirmed COVID-19 pneumonia were enrolled in this retrospective study. In addition, 10 of their family members diagnosed with COVID-19 pneumonia were included in the control group. • Kidney transplant recipients had more severe COVID-19 pneumonia than the general population, but most of them recovered after a prolonged clinical course and virus shedding.
18.04.2020	A Single Mass Gathering Resulted in Massive Transmission of COVID-19 Infections in Malaysia with Further International Spread	J Travel Med / Article	<ul style="list-style-type: none"> • Malaysia has recorded the highest number of COVID-19 cases in Southeast Asia with more than 35% of new COVID-19 cases linked to the Sri Petaling gathering, a Moslem missionary movement attended by more than 19 000 people of different nationalities, in March 2020 in Kuala Lumpur. • From this cluster, 1701 samples have been tested positive out of 21 920 tests carried out. Thus, mass gathering during COVID-19 pandemic period should be banned to curb disease transmission.
20.04.2020	Characteristics, symptom management and outcomes of 101 patients with COVID-19 referred for hospital palliative care	Journal of Pain and Symptom Management / Article	<ul style="list-style-type: none"> • This article identifies symptom burden, management, response to treatment, and outcomes for a case series of 101 in-patients with confirmed COVID-19 referred to hospital palliative care.
20.04.2020	Gastrointestinal symptoms as Covid-19 onset in hospitalized Italian patients	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • Assessed the prevalence of gastrointestinal symptoms and their correlation with need of non-invasive ventilatory support, intensive care unit admission and death in hospitalized SARS-CoV-2 patients. • GI symptoms were the main presentation in 42 (10.2%) of 411 patients, with a mean onset 4.9 +/- days before admission. In 5 (1.2%) patients GI symptoms have not been associated with respiratory symptoms or fever. They found an inverse trend for ICU admission and death as compared with patients without GI symptoms. • Concluded that GI symptoms can be an early and not negligible

feature of Covid-19, and might be correlated with a more benign disease course.

Infection control

Publication Date	Title/URL	Journal/ Article type	Digest
23.04.2020	Information Technology–Based Tracing Strategy in Response to COVID-19 in South Korea—Privacy Controversies	JAMA / Viewpoint	<ul style="list-style-type: none"> • Viewpoint discussing the privacy concerns of South Korea's advanced information technology (IT) system for tracing individuals suspected to be infected or who had been in contact with an infected person.
22.04.2020	Safer intubation and extubation of patients with COVID-19	Canadian journal of anaesthesia	<ul style="list-style-type: none"> • Illustrated letter describing a technique to potentially reduce contamination from secretions (droplets) and aerosols during intubation and extubation. It assumes that the operator is wearing the recommended personal protective equipment to reduce the risk of contamination, and that the patient is fully paralyzed.
20.04.2020	COVID-19 in cardiac arrest and infection risk to rescuers: a systematic review	Resuscitation / Review	<ul style="list-style-type: none"> • The aim of this review was to identify the potential risk of transmission associated with key interventions (chest compressions, defibrillation, cardiopulmonary resuscitation) to inform international treatment recommendations. • No direct evidence was found, so it is uncertain whether chest compressions or defibrillation cause aerosol generation or transmission of COVID-19 to rescuers.
22.04.2020	Electrostatic Charged Nanofiber Filter for Filtering Airborne Novel Coronavirus (COVID-19) and Nano-aerosols	Separation and purification technology / Article	<ul style="list-style-type: none"> • This study addresses developing novel charged PVDF nanofiber filter technology to effectively capture the deadly airborne coronavirus with the target set at 100nm (nano-aerosol), and not 300nm. • These optimized filters based on rigorous engineering approach provide the badly needed technology for protecting the general public from the deadly airborne COVID-19 and other viruses, and nano-aerosols from air pollution which lead to chronic diseases.
20.04.2020	The risk of SARS-CoV-2 transmission in the healthcare setting and potential impact of cohorting strategies	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • Using stochastic simulations the authors studied the impacts of testing and personal protective equipment (PPE) use. In the base case without testing or PPE, healthcare is rapidly overwhelmed, and becomes a net contributor to the force of infection. • They find that effective use of PPE by both HCW and patients can prevent this situation, while testing alone is less effective. They also

find that even imperfectly effective use of PPE can provide substantial protection and decrease the force of infection. This illustrates the importance of maintaining supplies of PPE throughout healthcare systems.

Treatment

Publication Date	Title/URL	Journal/ Article type	Digest
23.04.2020	Use of glucocorticoids in patients with adrenal insufficiency and COVID-19 infection	The Lancet Diabetes & Endocrinology / Correspondence	<ul style="list-style-type: none"> • Authors comment that tailoring of glucocorticoid stress regimens in COVID-19 requires a more evidence-based approach. • The pathophysiology of immune response and the systemic complications associated with a SARS-CoV-2 infection set the pace, and the protocol should be adapted to the patient's clinical stage.
23.04.2020	Incidence of Adverse Drug Reactions in COVID-19 patients in China: an active monitoring study by Hospital Pharmacovigilance System	Clinical pharmacology and therapeutics / Article	<ul style="list-style-type: none"> • Results showed that the prevalence of adverse drug reactions was 37.8% in patients, which was predominated by drug-induced gastrointestinal disorders and liver system disorders (23.0% vs. 13.8%). The ADR could be explained by the use of lopinavir/ ritonavir and umifenovir by 63.8% and 18.1%, respectively.
21.04.2020	Efficacy of glutathione therapy in relieving dyspnea associated with COVID-19 pneumonia: A report of 2 cases	Respiratory medicine case reports / Case report	<ul style="list-style-type: none"> • Oral and IV glutathione, glutathione precursors (N-acetyl-cysteine) and alpha lipoic acid may represent a novel treatment approach for blocking NFKappaB and addressing "cytokine storm syndrome" and respiratory distress in patients with COVID-19 pneumonia.
23.04.2020	Covid-19 pneumonia in a kidney transplant recipient successfully treated with Tocilizumab and Hydroxychloroquine	American journal of transplantation / Case report	<ul style="list-style-type: none"> • Case report: a 61-year-old kidney transplant recipient with several co-morbidities who was hospitalized and later received a diagnosis of Covid-19 pneumonia; the infection was successfully managed with the use of hydroxychloroquine and a single administration of Tocilizumab, after immunosuppression reduction; the patient did not require mechanical ventilation.
21.04.2020	Identification of potential treatments for COVID-19 through artificial intelligence-enabled phenomic analysis of human cells infected with SARS-CoV-2	bioRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • Remdesivir was the only antiviral tested with strong efficacy, neither chloroquine nor hydroxychloroquine had any beneficial effect in this human cell model, and a small number of compounds not currently being pursued clinically for SARS-CoV-2 have efficacy.
23.04.2020	Is Low Alveolar Type II Cell SOD3 in the Lungs of Elderly Linked to the Observed Severity of COVID-19?	Antioxidants & redox signaling / Just accepted	<ul style="list-style-type: none"> • The findings of this work propose the hypotheses that lung-specific delivery of SOD3/ATF4 related antioxidants may work in synergy with promising anti-viral drugs such as remdesivir to further improve COVID-19 outcomes in the elderly.

22.04.2020	Potential use of hydroxychloroquine, ivermectin and azithromycin drugs in fighting COVID-19: trends, scope and relevance	New microbes and new infections / Mini review	<ul style="list-style-type: none"> Hydroxychloroquine and ivermectin were known to act by creating the acidic environment and inhibiting the importin (IMPα/β1) mediated viral import. Azithromycin was found to act similar to the hydroxychloroquine as an acidotropic lipophilic weak base. All the three categories of drugs seemed to potentially act against novel coronavirus infection. However, their efficacies need to be studied in detail individually and in combination in-vivo in order to combat COVID-19 infection.
20.04.2020	Darunavir does not prevent SARS-CoV-2 infection in HIV patients	Pharmacological research / Research article	<ul style="list-style-type: none"> Given the structural similarity with lopinavir, darunavir is a potentially effective treatment against SARS-CoV-2 and is currently under investigation in phase III clinical trials. However, this study provides preliminary evidence that darunavir, at least at the currently adopted dosage of 800 mg, did not prevent SARS-CoV-2 infection in people living with HIV and, at least in one case, did not protect from the worsening of respiratory function.
22.04.2020	Structure-based design of antiviral drug candidates targeting the SARS-CoV-2 main protease	Science (New York, N.Y.) / Research article	<ul style="list-style-type: none"> The authors designed and synthesized two lead compounds targeting M(pro) Both exhibited excellent inhibitory activity and potent anti-SARS-CoV-2 infection activity. Both compounds showed good PK properties in vivo, and 11a also exhibited low toxicity, suggesting that these compounds are promising drug candidates.
21.04.2020	Hispidin and Lepidine E: two Natural Compounds and Folic acid as Potential Inhibitors of 2019-novel coronavirus Main Protease (2019-nCoVMPpro), molecular docking and SAR study	Current computer-aided drug design / Research article	<ul style="list-style-type: none"> By screening several molecules, the authors identified three candidate agents that inhibit the main protease of coronavirus. Hispidin, lepidine E, and folic acid bound tightly in the enzyme, strong hydrogen bonds have been formed (1.69-1.80Å) with the active site residues. This study provides a possible therapeutic strategy for CoVID-19.
23.04.2020	Operational protocol for donation of anti-COVID-19 convalescent plasma in Italy	Vox sanguinis / Letter	<ul style="list-style-type: none"> Describes a protocol for donation of anti-COVID-19 convalescent plasma.

Social sciences

Publication Date	Title/URL	Journal/ Article type	Digest
24.04.2020	Coronavirus and the social impacts on disabled people in Great Britain	Office for National Statistics / Report	<ul style="list-style-type: none"> Indicators from the Opinions and Lifestyle Survey covering the period 27 March 2020 to 13 April 2020 on the impact of the

			coronavirus (COVID-19) pandemic on disabled people in Great Britain.
23.04.2020	Coronavirus and the social impacts on Great Britain: 23 April 2020	Office for National Statistics / Report	<ul style="list-style-type: none"> Indicators from the Opinions and Lifestyle Survey covering the period 3 to 13 April 2020 to understand the impact of the coronavirus (COVID-19) pandemic on people, households and communities in Great Britain. This bulletin includes new indicators on compliance with the government's Stay at home measures and the impact of home-schooling.
23.04.2020	Challenges and Priorities in Responding to COVID-19 in Inpatient Psychiatry	Psychiatric services / Open forum	<ul style="list-style-type: none"> This Open Forum focuses on specific challenges, contingency planning considerations, and downstream impacts of COVID-19 on inpatient psychiatric care.
20.04.2020	Affective temperament, attachment style, and the psychological impact of the COVID-19 outbreak: an early report on the Italian general population	Brain, behavior, and immunity / Article	<ul style="list-style-type: none"> The outbreak of COVID-19 is severely affecting mental health worldwide, and individual response varies according to background and specific features. Temperament and attachment predict the psychological impact of the COVID-19 pandemic.
23.04.2020	Weight Stigma and the "Quarantine-15"	Obesity / Perspective	<ul style="list-style-type: none"> Due to stay-at-home orders and sudden unemployment, millions have found themselves isolated at home without their usual routines. This rise in unstructured time, combined with the enormous stress of the pandemic and its far-reaching consequences, have led to widespread concerns among the general public about vulnerability to overeating, sedentary behaviour, and weight gain.

Miscellaneous

Publication Date	Title/URL	Journal/ Article type	Digest
25.04.2020	Travel restrictions hampering COVID-19 response	The Lancet / World Report	<ul style="list-style-type: none"> The COVID-19 pandemic has sparked an unprecedented shutdown of borders and airlines, which is severely restricting the movement of essential medical personnel and supplies that are vital to stem the spread of the virus and save lives.
23.04.2020	Coronavirus and the economic impacts on the UK: 23 April 2020	Office for National Statistics / Report	<ul style="list-style-type: none"> The indicators and analysis presented are based on responses from the new voluntary fortnightly business survey, which captures the views of businesses on the impact COVID-19 on turnover, workforce prices, trade and business resilience. These data relate to the period 23 March to 5 April 2020.

23.04.2020	Coronavirus, the UK economy and society, faster indicators: 23 April 2020	Office for National Statistics / Report	<ul style="list-style-type: none"> • New data and experimental indicators on the UK economy and society, including information related to the coronavirus (COVID-19). • Indicators are constructed from rapid response surveys, novel data sources and experimental methods.
24.04.2020	Variation in volumes and characteristics of trauma patients admitted to a level one trauma centre during national level 4 lockdown for COVID-19 in New Zealand	The New Zealand medical journal / Article	<ul style="list-style-type: none"> • Overall there was a reduction of 43% in all injury-related admissions with significant reductions seen in major injury (50% reduction), males (50% reduction) and children aged 0-14 years (48% reduction). Results for ethnicity and persons aged over 14 years were within 3% deviation of this overall 43% reduction. Injuries at home, particularly falls, predominate.
22.04.2020	Defending against the Novel Coronavirus (COVID-19) Outbreak: How Can the Internet of Things (IoT) help to save the World?	Health policy and technology / Article	<ul style="list-style-type: none"> • Considering the present situation in China, IoT based smart disease surveillance systems have the potential to be a major breakthrough in efforts to control the current pandemic. With much of the infrastructure itself in place already (i.e. smartphones, wearable technologies, internet access) the role this technology can have in limiting the spread of the pandemic involves only the collection and analysis of data already gathered.

Modelling

Publication Date	Title/URL	Journal/ Article type	Digest
23.04.2020	Report 16: Role of testing in COVID-19 control	Imperial College / Report 16	<ul style="list-style-type: none"> • A simple mathematical model to investigate the potential effectiveness of alternative testing strategies for COVID-19 control. • Weekly screening of healthcare workers (HCWs) and other at-risk groups using PCR or point-of-care tests for infection irrespective of symptoms is estimated to reduce their contribution to transmission by 25-33%. • Widespread PCR testing in the general population is unlikely to limit transmission more than contact-tracing and quarantine based on symptoms alone, but could allow earlier release of contacts from quarantine.
22.04.2020	Modelling the COVID-19 epidemic and implementation of population-wide interventions in Italy	Nature medicine / Research letter	<ul style="list-style-type: none"> • The authors propose a new model that predicts the course of the epidemic to help plan an effective control strategy. The model considers eight stages of infection: susceptible (S), infected (I), diagnosed (D), ailing (A), recognized (R), threatened (T), healed (H) and extinct (E), collectively termed SIDARTHE.

			<ul style="list-style-type: none"> • They compared simulation results with real data on the COVID-19 epidemic in Italy, and modelled possible scenarios of implementation of countermeasures. The results demonstrate that restrictive social-distancing measures will need to be combined with widespread testing and contact tracing to end the ongoing COVID-19 pandemic.
18.04.2020	What are the Underlying Transmission Patterns of COVID-19 Outbreak? - An Age-specific Social Contact Characterization	EClinicalMedicine / Article	<ul style="list-style-type: none"> • Developed a computational model to reveal the interactions in terms of the social contact patterns among the population of different age-groups. • The authors focused their study on 6 representative cities in China: Wuhan, together with Beijing, Tianjin, Hangzhou, Suzhou, and Shenzhen, which are five major cities from three key economic zones. The results show that the social contact-based analysis can readily explain the underlying disease transmission patterns as well as the associated risks (including both confirmed and unconfirmed cases). • With an in-depth characterization of age-specific social contact-based transmission, the retrospective and prospective situations of the disease outbreak, including the past and future transmission risks, the effectiveness of different interventions, and the disease transmission risks of restoring normal social activities, are computationally analysed and reasonably explained.
23.04.2020	The Potential Health Care Costs And Resource Use Associated With COVID-19 In The United States	Health affairs / Research article	<ul style="list-style-type: none"> • The authors developed a Monte Carlo simulation model representing the U.S. population. They estimate resource use and direct medical costs per infection and at the national level, with various “attack rates” to understand the potential economic benefits of reducing the burden of the disease.
16.04.2020	Lessons from mainland China's epidemic experience about the growth rules of infected and recovered cases of COVID-19 worldwide	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • According to the linear connection between the growth rules for infected and recovered cases identified from the Chinese data, they predicted that the semi-saturation period (SSP) of the recovered cases outside China ranges from 82 to 196 days (March 22 to July 8). • They found a strong positive correlation between the SSP of infected cases and the timing of the government's response, providing strong evidence for the effectiveness of rapid epidemic control measures in various countries.
22.04.2020	Optimal control of the COVID-19 pandemic with non-pharmaceutical interventions	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • The authors performed an optimal control analysis of a mathematical model of SARS-CoV-2 transmission. • They found that a major factor that differentiates strategies that prioritize lives saved versus reduced time under control is how quickly control is relaxed once social distancing restrictions expire in

			<p>May 2020. Strategies that maintain control at a high level until summer 2020 allow for tapering of control thereafter and minimal deaths, whereas strategies that relax control in the short term lead to fewer options for control later and a higher likelihood of exceeding hospital capacity.</p>
18.04.2020	Decline in global COVID-19 transmission	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • The authors analysed COVID-19 data through Apr 15, 2020 using a partially observed Markov process. • They found evidence for a declining transmission rate in 42 of the 51 examined countries. Of those 42 countries 34 have significant evidence for subcritical transmission rates, although the decline in new cases are relatively slow compared to the initial growth rates. • This suggests that global scale social distancing efforts to slow the spread of COVID-19 are effective although they need to be strengthened in many regions and maintained in others to avoid further resurgence of COVID-19. The slow decline also suggests alternative strategies to control the virus are needed before social distancing efforts are partially relaxed.
20.04.2020	Climatic factors influence COVID-19 outbreak as revealed by worldwide mortality	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • Here, using data recorded in 208 territories from 88 countries, the authors show that mortality rate is negatively influenced by warmer air temperature and positively affected by higher relative humidity. Each additional Celsius degree decreases mortality rate by ~4%, while a 1% increase in relative humidity raises mortality rate by ~2%. Temperature is positively correlated with UV-index, for which one unit of increase results in a ~15% decrease in the mortality rate. • The authors also show that other factors contribute to the dynamics of the COVID-19 outbreak, such as the proportion of vulnerable age classes in the population, access to a non-overwhelmed health system, as well as governmental travel restrictions for controlling the spread of the disease.
19.04.2020	COVID-19 Asymptomatic Infection Estimation	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • Machine learning based fine-grained simulator (MLSim) showed better forecast accuracy than the SEIR and LSTM-based prediction models. The MLSim learned from the data of China's mainland reveals that there could have been 150,408 (142,178-157,417) asymptomatic and had self-healed patients, which is 65% (64% - 65%) of the inferred total infections including undetected ones. The numbers of asymptomatic but infectious patients on April 15, 2020, were inferred as, Italy: 41,387, Germany: 21,118, USA: 354,657, France: 40,379, and UK: 144,424.

Guidance, consensus statements and hospital resources

Publication Date	Title/URL	Journal/ Article type
23.04.2020	Rapid Risk Assessment: Coronavirus disease 2019 (COVID-19) in the EU/EEA and the UK– ninth update	European Centre for Disease Control and Prevention / Risk assessment
23.04.2020	Practical recommendations for the management of diabetes in patients with COVID-19	The Lancet Diabetes & Endocrinology / Viewpoint
22.04.2020	SAGES and EAES recommendations for minimally invasive surgery during COVID-19 pandemic	Surgical endoscopy / Guidelines
22.04.2020	Solid Organ Transplantation Programs Facing Lack of Empiric Evidence in the COVID-19 Pandemic: A By-proxy Society Recommendation Consensus Approach	American journal of transplantation / Article
21.04.2020	Radiological Society of North America Expert Consensus Statement on Reporting ChestCT Findings Related to COVID-19. Endorsed by the Society of Thoracic Radiology, the American College of Radiology, and RSNA	Journal of thoracic imaging / Consensus statement
19.04.2020	COVID-19 and diabetes mellitus: what we know, how our patients should be treated now, and what should happen next	Metabolism: clinical and experimental / Journal pre-proof
23.04.2020	Priority plan for invasive cardiac electrophysiology procedures during the coronavirus disease 2019 (COVID-19) pandemic	Journal of cardiovascular electrophysiology / Brief report
21.04.2020	Restructuring Electrophysiology During the COVID-19 Pandemic: A Practical Guide from a New York City Hospital Network	Critical pathways in cardiology / Original study
23.04.2020	COVID-19 transforms health care through telemedicine: evidence from the field	Journal of the American Medical Informatics Association / Article
23.04.2020	The management of emergency spinal surgery during the COVID-19 pandemic in Italy	The bone & joint journal
23.04.2020	Esophageal oncologic surgery in SARS-CoV-2 (COVID-19) emergency	Diseases of the esophagus / Article
23.04.2020	Effective infection prevention and control strategies in a large accredited psychiatric facility in Singapore	Infection control and hospital epidemiology / Article
22.04.2020	Tracheostomy in the COVID-19 pandemic	European archives of oto-rhino-laryngology / Short communication

Overviews, comments and editorials

Publication Date	Title/URL	Journal/ Article type
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23.04.2020	Mitigating the effect of the COVID-19 pandemic on sickle cell disease services in African countries	The Lancet Haematology / Comment
23.04.2020	Ten Weeks to Crush the Curve	New England Journal of Medicine / Editorial
23.04.2020	Reflecting on World Asthma Day in the era of COVID-19	The Lancet Respiratory Medicine / Editorial
23.04.2020	Coronavirus (COVID-19): Using data to track the virus	Public Health Matters (Blog)
23.04.2020	Pitfalls of judgment during the COVID-19 pandemic	The Lancet Public Health / Comment
21.04.2020	Medicine in the time of corona: Fundamental molecular research is “essential”	Science Advances / Editorial
23.04.2020	Respiratory Protection for Healthcare Workers Caring for Patients with COVID-19 Infection	Infection control and hospital epidemiology / Commentary
23.04.2020	Coronavirus Disease Outbreak in Call Center, South Korea	Emerging infectious diseases / Synopsis
21.04.2020	Prehabilitation May Help Mitigate an Increase in COVID-19 Peri-Pandemic Surgical Morbidity and Mortality	American journal of physical medicine & rehabilitation / Brief report
20.04.2020	COVID-19 pathophysiology: A review	Clinical immunology / Article
23.04.2020	Drug Development and Medicinal Chemistry Efforts Toward SARS-Coronavirus and Covid-19 Therapeutics	ChemMedChem / Review
19.04.2020	COVID-19: A New Virus, but a Familiar Receptor and Cytokine Release Syndrome	Immunity / Article
22.04.2020	Neurological Insights of COVID-19 Pandemic	ACS chemical neuroscience / Viewpoint
23.04.2020	Imaging Publications in the COVID-19 Pandemic: Applying New Research Results to Clinical Practice	Radiology / Special report
23.04.2020	Meeting the challenge of the 2019 novel coronavirus disease in patients with cancer	Cancer / Commentary

Produced by the PHE COVID-19 Literature Digest Team

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