



International EPI Cell Daily Evidence Digest – 30/03/2020

This briefing is produced by the PHE COVID-19 Literature Digest Team. The papers are organised under the following themes:

- Diagnostics and genomics
- Epidemiology and clinical
- Infection control
- Treatment
- Social sciences
- Miscellaneous
- Modelling

Please note that we are including preprints, which are preliminary reports of work that have NOT been peer-reviewed.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 and genomics

Publication Date	Title/URL	Journal / Article type	Digest
26.03.2020	Human leukocyte antigen susceptibility map for SARS-CoV-2	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none">• Investigate how genetic variability across the three major histocompatibility complex (MHC) class I genes (human leukocyte antigen [HLA] A, B, and C) may affect susceptibility to and severity of SARS-CoV-2, the virus responsible for COVID-19.
28.03.2020	Non-neural expression of SARS-CoV-2 entry genes in the olfactory epithelium suggests mechanisms underlying anosmia in COVID-19 patients	bioRxiv (not peer-reviewed) / New results	<ul style="list-style-type: none">• These findings suggest possible mechanisms through which CoV-2 infection could lead to anosmia or other forms of olfactory dysfunction.
28.03.2020	Papa Giovanni XXIII Bergamo Hospital at the time of the COVID-	Int J Lab Hematol / Editorial	<ul style="list-style-type: none">• The rapid increase of positive cases in Italy has caused, on one hand, widespread panic among the people and on the other hand, the need for profound structural and logistical

	19 outbreak: letter from the warfront		reorganizations of the Papa Giovanni XXIII Hospital. <ul style="list-style-type: none"> • In this context, the authors describe the role of the laboratory.
30.03.2020	SARS-CoV-2 asymptomatic and symptomatic patients and risk for transfusion transmission	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> • Oral swabs, sputum and blood samples from 18 patients with SARS-CoV-2 infection were examined using real-time reverse transcription polymerase chain reaction (RT-PCR) testing. • Whereas oral swabs or sputum from the lower respiratory tract were tested RT-PCR positive in all patients, RNAemia was neither detected in 3 patients without symptoms nor in 14 patients with flu-like symptoms, fever or pneumonia.
28.03.2020	SARS-CoV-2 and ORF3a: Non-Synonymous Mutations and Polyproline Regions	bioRxiv (not peer-reviewed) / New results	<ul style="list-style-type: none"> • The accumulation of non-synonymous mutations and detected polyproline regions in ORF3a of SARS-CoV-2 could be driving the evasion of the host immune response thus favouring viral spread. • Rapid mutations accumulating in ORF3a should be closely monitored throughout the COVID-19 pandemic.
27.03.2020	Development and Evaluation of an AI System for COVID-19 Diagnosis	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> • The authors propose an artificial intelligence (AI) system for fast COVID-19 diagnosis with an accuracy comparable to experienced radiologists. • A large dataset was constructed by collecting 970 CT volumes of 496 patients with confirmed COVID-19 and 260 negative cases from three hospitals in Wuhan, China, and 1,125 negative cases from two publicly available chest CT datasets. • In a reader study involving five radiologists, only one radiologist is slightly more accurate than the AI system. • The AI system is two orders of magnitude faster than radiologists and the code is available at https://github.com/ChenWWWeixiang/diagnosis_covid19.
29.03.2020	The Nucleocapsid Protein of SARS-CoV-2 Abolished Pluripotency in Human Induced Pluripotent Stem Cells	bioRxiv (not peer-reviewed) / New results	<ul style="list-style-type: none"> • The data in this paper, suggested that nCoV-2 disrupted the pluripotent properties of iPSC and turned them into fibroblasts, which provided a new insight to the pathogenic mechanism of SARS-CoV-2.
27.03.2020	Serology characteristics of SARS-CoV-2 infection since the exposure and post symptoms onset	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> •The serology characteristics and complement diagnosis value of antibody test to RNA test needs to be demonstrated. A patient cohort study (n=80) was conducted at the first affiliated hospital of Zhejiang University, China. •The seroconversion rate for Ab, IgM and IgG in COVID-19 patients was 98.8% (79/80), 93.8% (75/80) and 93.8% (75/80), respectively. The first detectible serology marker is total antibody and followed by IgM and IgG, with a median seroconversion time of 15, 18 and 20 day post exposure (d.p.e) or 9, 10 and 12 days post onset, separately. •Typical acute antibody response is induced during the SARS-CoV-2 infection. The serology testing provides important complementation to RNA test for pathogenic specific diagnosis and helpful information to evaluate the adapted immunity status of patient.
28.03.2020	Re-analysis of SARS-CoV-2 infected host cell proteomics time-course data by impact pathway analysis	bioRxiv (not peer-reviewed) / New results	<ul style="list-style-type: none"> • The up-regulation of the inflammatory-related proteins observed could be linked to the propagation of inflammatory reaction and lung injury that is observed in advanced stages of COVID-19 patients.

	and network analysis. A potential link with inflammatory response		
29.03.2020	Knowledge synthesis from 100 million biomedical documents augments the deep expression profiling of coronavirus receptors	bioRxiv (not peer-reviewed) / New results	<ul style="list-style-type: none"> • The authors present the nferX platform for dynamic inference from over 45 quadrillion possible conceptual associations extracted from unstructured biomedical text, and their triangulation with Single Cell RNA-sequencing based insights from over 25 tissues (https://academia.nferx.com/). • Using this platform, they identify intersections between the pathologic manifestations of COVID-19 and the comprehensive expression profile of the SARS-CoV-2 receptor ACE2.
28.03.2020	SARS-CoV-2 proteome microarray for mapping COVID-19 antibody interactions at amino acid resolution	bioRxiv (not peer-reviewed) / New results	<ul style="list-style-type: none"> • Understanding the humoral antibody response to SARS-CoV-2 proteins may help identify biomarkers that can be used to detect and treat COVID-19 infection. • No immuno-proteomics platform exists that can perform such proteome-wide analysis. • The authors created a SARS-CoV-2 proteome microarray to analyse antibody interactions at amino acid resolution by spotting peptides 15 amino acids long with 5-amino acid offsets representing full-length SARS-CoV-2 proteins.
27.03.2020	Immune Cell Profiling of COVID-19 Patients in the Recovery Stage by Single-Cell Sequencing	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> • Applied single-cell technology to comprehensively characterize transcriptional changes of peripheral blood mononuclear cells in ten patients recovered from COVID-19. Compared with healthy control, COVID-19 induced a unique signature of immune cells in humans, especially in the early recovery stage (ERS). • Concluded that the study provides the first evidence of inflammatory immune signature in early recovery stage, suggesting that the COVID-19 patients are still vulnerable after hospital discharge. The identification of novel BCR signalling may lead to the development of vaccine and antibodies for the treatment of COVID-19.
27.03.2020	Frequency and Distribution of Chest Radiographic Findings in COVID-19 Positive Patients	Radiology / Research article	<ul style="list-style-type: none"> • PURPOSE: To describe the time course and severity of the CXR findings of COVID-19 and correlate these with real time reverse transcription polymerase chain reaction (RT-PCR) testing for SARS-Cov-2 nucleic acid. • CONCLUSION: Chest x-ray findings in COVID-19 patients frequently showed bilateral lower zone consolidation which peaked at 10-12 days from symptom onset.
29.03.2020	Comparative performance of four nucleic acid amplification tests for SARS-CoV-2 virus	bioRxiv (not peer-reviewed) / New results	<ul style="list-style-type: none"> • The authors evaluated the performance of four nucleic acid amplification tests (NAATs), which were marked by the Conformité Européenne and widely used in China during the pandemic. • Results showed that the analytical sensitivity of the four assays was significantly lower than that claimed by the NAAT manufacturers.
28.03.2020	Quantitative Detection and Viral Load Analysis of SARS-CoV-2 in Infected Patients	Clinical Infectious Diseases / Research article	<ul style="list-style-type: none"> • The widely used reverse transcription PCR (RT-PCR) method has limitations for clinical diagnosis and treatment. • CONCLUSIONS: Quantitative monitoring of viral load in lower respiratory tract samples helps to evaluate disease progression, especially in cases of low viral load.

28.03.2020	Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019	Clinical Infectious Diseases / Research article	<ul style="list-style-type: none"> • The antibody response in infected patients remains largely unknown, and the clinical values of antibody testing have not been fully demonstrated. • CONCLUSIONS: The antibody detection offers vital clinical information during the course of SARS-CoV-2 infection. The findings provide strong empirical support for the routine application of serological testing in the diagnosis and management of COVID-19 patients.
27.03.2020	Serological diagnostic kit of SARS-CoV-2 antibodies using CHO-expressed full-length SARS-CoV-2 S1 proteins	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> • Report the development and validation of a COVID-19/SARS-CoV-2 S1 serology ELISA kit for the detection of total anti-virus antibody (IgG+IgM) titres in sera from either the general population or patients suspected to be infected.
29.03.2020	Site-specific N-glycosylation Characterization of Recombinant SARS-CoV-2 Spike Proteins using High-Resolution Mass Spectrometry	bioRxiv (not peer-reviewed) / New results	<ul style="list-style-type: none"> • The authors characterized the site-specific N-glycosylation of SARS-CoV-2 S protein using stepped collision energy (SCE) mass spectrometry (MS). • This N-glycosylation profiling and determination of differences between distinct expression systems could shed light on the infection mechanism and promote development of vaccines and targeted drugs.
28.03.2020	Site-specific analysis of the SARS-CoV-2 glycan shield	bioRxiv (not peer-reviewed) / New results	<ul style="list-style-type: none"> • Using a site-specific mass spectrometric approach, the authors reveal the glycan structures on a recombinant SARS-CoV-2 S immunogen. • This analysis enables mapping of the glycan-processing states across the viral spike. • The authors show how SARS-CoV-2 S glycans differ from typical host glycan processing, which may have implications in viral pathobiology and vaccine design.
28.03.2020	Computational simulations reveal the binding dynamics between human ACE2 and the receptor binding domain of SARS-CoV-2 spike protein	bioRxiv (not peer-reviewed) / New results	<ul style="list-style-type: none"> • Using homology modelling and molecular dynamics (MD) simulation methods, the authors report here the detailed structure of the ACE2 in complex with the receptor binding domain (RBD) of the SARS-CoV-2 spike protein.
27.03.2020	Haplotype networks of SARS-CoV-2 infections in the Diamond Princess cruise ship outbreak	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> • The Diamond Princess (DP) cruise ship was put under quarantine offshore Yokohama, Japan, after a passenger who disembarked in Hong Kong was confirmed as a COVID-19 case. The authors performed whole genome sequencing of SARS-CoV-2 directly from PCR-positive clinical specimens and conducted a haplotype network analysis of the outbreak. • All tested isolates exhibited a transversion at G11083T, suggesting that SARS-CoV-2 dissemination on the DP originated from a single introduction event before the quarantine started.
28.03.2020	SARS-CoV-2 exhibits intra-host genomic plasticity and low-frequency polymorphic quasispecies	bioRxiv (not peer-reviewed) / New results	<ul style="list-style-type: none"> • The results highlight the intra-host genomic diversity and plasticity of SARS-CoV-2, pointing out genomic regions that are prone to alterations. • The isolated single nucleotide variations (SNVs) and genomic rearrangements, reflect the intra-patient capacity of the polymorphic quasispecies, which may arise rapidly during the outbreak, allowing immunological escape of the virus, offering resistance to anti-viral drugs and affecting the sensitivity of the molecular diagnostics assays.

26.03.2020	Coast-to-coast spread of SARS-CoV-2 in the United States revealed by genomic epidemiology	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> •To uncover the sources of SARS-CoV-2 introductions and patterns of spread within the U.S., the authors sequenced nine viral genomes from early reported COVID-19 patients in Connecticut. •The phylogenetic analysis places the majority of these genomes with viruses sequenced from Washington state. By coupling the genomic data with domestic and international travel patterns, the authors show that early SARS-CoV-2 transmission in Connecticut was likely driven by domestic introductions. Moreover, the risk of domestic importation to Connecticut exceeded that of international importation by mid-March regardless of the estimated impacts of federal travel restrictions. •This study provides evidence for widespread, sustained transmission of SARS-CoV-2 within the U.S. and highlights the critical need for local surveillance.
29.03.2020	Codon usage and evolutionary rates of the 2019-nCoV genes	bioRxiv (not peer-reviewed) / New results	<ul style="list-style-type: none"> • The authors compare the codon usage of 2019-nCoV with that of other 30 viruses belonging to the subfamily of orthocoronavirinae. • The results suggest that the higher evolutionary rate observed for these two genes could represent a major barrier in the development of antiviral therapeutics 2019-nCoV.

Epidemiology and clinical

Publication Date	Title/URL	Journal / Article type	Digest
27.03.2020	Epidemiology of Covid-19 in a Long-Term Care Facility in King County, Washington	NEJM / Article	<ul style="list-style-type: none"> •After identification on Feb 28, 2020, of a confirmed case of Covid-19 in a skilled nursing facility in King County, Washington, Public Health–Seattle and King County, aided by the CDC launched a case investigation, contact tracing, quarantine of exposed persons, isolation of confirmed and suspected cases, and on-site enhancement of infection prevention and control. •As of March 18, a total of 167 confirmed cases of Covid-19 affecting 101 residents, 50 health care personnel, and 16 visitors were found to be epidemiologically linked to the facility. Most cases among residents included respiratory illness consistent with Covid-19; however, in 7 residents no symptoms were documented. Hospitalization rates for facility residents, visitors, and staff were 54.5%, 50.0%, and 6.0%, respectively. The case fatality rate for residents was 33.7% (34 of 101). As of March 18, a total of 30 long-term care facilities with at least one confirmed case of Covid-19 had been identified in King County. •Proactive steps by long-term care facilities to identify and exclude potentially infected staff and visitors, actively monitor for potentially infected patients, and implement appropriate infection prevention and control measures are needed to prevent the introduction of Covid-19.

27.03.2020	Predicting COVID-19 malignant progression with AI techniques	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> • A total of 133 consecutively mild COVID-19 patients at admission who were hospitalized in Wuhan Pulmonary Hospital from January 3 to February 13, 2020, were selected in this retrospective IRB-approved study. • The proposed model can be effectively used for finding out the mild patients who are easy to deteriorate into severe/critical cases, so that such patients get timely treatments while alleviating the limitations of medical resources.
28.03.2020	Clinical analysis of pregnant women with 2019 novel coronavirus pneumonia	Journal of Medical Virology / Research article	<ul style="list-style-type: none"> • It is probable that pregnant women diagnosed with COVID-19 have no fever before delivery. Their primary initial manifestations were merely low-grade postpartum fever or mild respiratory symptoms. • Therefore, the protective measures are necessary on admission; the instant CT scan and real-time reverse-transcriptase polymerase-chain-reaction (RT-PCR) assay should be helpful in early diagnosis and avoid cross-infection on the occasion that patients have fever and other respiratory signs.
27.03.2020	Are certain drugs associated with enhanced mortality in COVID-19?	QJM / Short article	<ul style="list-style-type: none"> • The authors posit that drugs commonly used in the treatment of hypertension, diabetes and cardiovascular disease, prevalent comorbidities in COVID-19, may actually increase the risk of severe pneumonia, ARDS and mortality in the setting of COVID-19. • The drugs of primary concern include angiotensin receptor blockers (ARBs) used for blood pressure lowering and statins used for cholesterol lowering.
27.03.2020	History of Coronary Heart Disease Increases the Mortality Rate of Coronavirus Disease 2019 (COVID-19) Patients: A Nested Case-Control Study Based on Publicly Reported Confirmed Cases in Mainland China	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> • Evaluated the risk of common pre-existing comorbidities, including hypertension, coronary heart diseases (CHD), respiratory diseases and diabetes on COVID-19 mortality, and provide clinical suggestions accordingly. • Concluded that a history of comorbidity significantly increases the death risk of COVID-19: one additional pre-existing comorbidity will lead to an estimated 29% higher risk of death ($p=0.01$). Patients with CHD had a 92% higher risk of mortality, compared to patients without CHD, along with an estimated 13 days of median survival time. Extra care and early medical intervention maybe needed for patients with pre-existing CHD.
27.03.2020	Non-steroidal anti-inflammatory drugs and covid-19	BMJ / Editorial	<ul style="list-style-type: none"> • Editorial examining the evidence of a link between NSAIDs and both respiratory and cardiovascular adverse effects in several settings. • So far we have no evidence relating specifically to people with covid-19. Pending further research, a pragmatic and cautionary approach would be for the public to avoid these plausible harms: regular NSAID use should probably not be recommended as the first line option for managing the symptoms of covid-19.
27.03.2020	Prevalence, Severity and Mortality associated with COPD and Smoking in patients with COVID-19: A Rapid Systematic Review and Meta-Analysis	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> • The authors investigate the potential severity and mortality risks caused by COVID-19 in patients with chronic obstructive pulmonary disease (COPD) and also in patients with a history smoking. • They carried out a systematic review and meta-analysis, and a total of 15 studies met the inclusion criteria, which included a total of 2473 confirmed COVID-19 patients. • They concluded that although COPD prevalence in COVID-19 cases was low in current

			reports, COVID-19 infection was associated with substantial severity and mortality rates in COPD. Compared to former and never smokers, current smokers were at greater risk of severe complications and higher mortality rate. Effective preventive measures are required to reduce COVID-19 risk in COPD patients and current smokers.
27.03.2020	Anti-hypertensive Angiotensin II receptor blockers associated to mitigation of disease severity in elderly COVID-19 patients	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> • This study was designed to investigate any difference in disease severity between COVID-19 patients (n=511) with hypertension comorbidity. The included COVID-19 patients used ACEI, ARB, calcium channel blockers (CCB), beta blockers (BB), or thiazide to treat pre-existing hypertension prior to the hospital were compared to patients who did not take any of those drugs. • Concluded that elderly (age>65) COVID-19 patients with hypertension comorbidity who are taking ARB anti-hypertension drugs may be less likely to develop severe lung disease compared to patients who take no anti-hypertension drugs.
26.03.2020	Modes of contact and risk of transmission in COVID-19 among close contacts	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> • Modes of contact and risk of transmission among close contacts have not been well estimated. The authors included 4950 close contacts from Guangzhou, and extracted data including modes of contact, laboratory testing, clinical characteristics of confirmed cases and source cases. • Concluded that the proportion of asymptomatic and mild infections account for almost half of the confirmed cases among close contacts. The household contacts were the main transmission mode, and clinically more severe cases were more likely to pass the infection to their close contacts. Generally, the secondary cases were clinically milder than those of source cases.
27.03.2020	Perioperative Presentation of COVID-19 Disease in a Liver Transplant Recipient	Hepatology / Case report	<ul style="list-style-type: none"> • The authors report the case of a patient with hepatocellular carcinoma (HCC) who underwent liver transplantation and experienced COVID-19 infection during the perioperative period.
27.03.2020	COVID-19 infection in children	The Lancet Respiratory Medicine / Spotlight	<ul style="list-style-type: none"> • The authors highlight the challenges faced by children and health-care professionals involved in their care, and propose key strategies to address these challenges. • Severe COVID-19 in children is rare. To date, the largest review of children with COVID-19 included 2143 children in China. Only 112 (5.6%) of 2143 children had severe disease (defined as hypoxia) and 13 (0.6%) children developed respiratory or multiorgan failure or acute respiratory distress syndrome (ARDS). At the time of writing, there have been two reported deaths in children testing positive for COVID-19 in China, and no deaths in Italy.
27.03.2020	Sound Science before Quick Judgement Regarding RAS Blockade in COVID-19	Clin J Am Soc Nephrol / Opinion	<ul style="list-style-type: none"> • After reviewing the available data, the authors conclude that the link between hypertension and/or the use of RAS inhibitors (ACEIs or ARBs) in patients with SARS-CoV-2 infection and COVID-19 outcomes has not been firmly established. • There is no definitive evidence linking RAS inhibition with increased ACE2 expression and subsequent enhanced SARS-CoV-2 infection. • Furthermore, there is preclinical data suggesting a potential benefit with RAS inhibition in SARS-CoV-1.

			<ul style="list-style-type: none"> • Their recommendation is for patients to continue the use of prescribed RAS inhibitors unless there exists an evidence-based indication to discontinue these important life-saving medications.
27.03.2020	Factors associated with prolonged viral shedding and impact of Lopinavir/Ritonavir treatment in patients with SARS-CoV-2 infection	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> • This paper investigated risk factors associated with prolonged SARS-CoV-2 shedding and the potential impact of Lopinavir/Ritonavir (LPV/r) treatment remain scarce. • Concluded that older age and lack of LPV/r treatment were independently associated with prolonged SARS-CoV-2 RNA shedding in patients with COVID-19. Earlier administration of LPV/r treatment could shorten viral shedding.
27.03.2020	A New Predictor of Disease Severity in Patients with COVID-19 in Wuhan, China	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> • This study sought to elucidate a novel predictor of disease severity in patients with COVID-19 caused by SARS-CoV-2. A total of 377 patients diagnosed with COVID-19 were enrolled in this study, including 117 with severe pneumonia and 260 with non-severe pneumonia. • Concluded that a product of N/L*CRP*D-dimer may be an important predictor of disease severity in patients with COVID-19.
27.03.2020	Clinical and immunologic features in severe and moderate Coronavirus Disease 2019	Journal of Clinical Investigation / Research article	<ul style="list-style-type: none"> • AIM: to delineate and compare the immunologic features of severe and moderate COVID-19. • CONCLUSION: The SARS-CoV-2 infection may affect primarily T lymphocytes particularly CD4+T and CD8+ T cells, resulting in decrease in numbers as well as IFN-γ production. These potential immunological markers may be of importance due to their correlation with disease severity in COVID-19.
27.03.2020	Analysis of adaptive immune cell populations and phenotypes in the patients infected by SARS-CoV-2	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> • Collected the blood samples from 18 healthy donors (HD) and 38 COVID-19 patients to analyse changes in the adaptive immune cell populations and phenotypes. • In comparison to HD, the lymphocyte percentage was slightly decreased, the percentages of CD4 and CD8 T cells in lymphocytes are similar, whereas B cell percentage increased in COVID-19 patients. T cells, especially CD8 T cells, showed an enhanced expression of late activation marker CD25 and exhaustion marker PD-1.
26.03.2020	Viral Kinetics and Antibody Responses in Patients with COVID-19	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> • The viral dynamics, host serologic responses, and their associations with clinical manifestations in COVID-19 patients, have not been well described. The authors conducted a prospective cohort and enrolled 67 COVID-19 patients admitted between Jan 26 and Feb 5, 2020. • They concluded that nasopharyngeal, sputum and stools rather than blood and urine, were the major shedding routes for SARS-CoV-2, and meanwhile sputum had a prolonged viral shedding. Symptom cough seems to be aligned with viral shedding in clinical respiratory and faecal specimens. Stronger antibody response was associated with delayed viral clearance and disease severity.
27.03.2020	A comparison study of SARS-CoV-2 IgG antibody between male and female COVID-19 patients: a	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> • Compared the difference of SARS-CoV-2 IgG antibody between male and female COVID-19 patients (n=331). • In severe status, the average IgG antibody level in female patients tended to be higher than that of in male patients.

	possible reason underlying different outcome between gender		<ul style="list-style-type: none"> • Concluded that the inconsistent of SARS-CoV-2 IgG antibody generation in male and female patients may account for the different outcome of COVID-19 between gender
27.03.2020	Familial cluster of COVID-19 infection from an asymptomatic	Critical Care / Research letter	<ul style="list-style-type: none"> • Report of a familial cluster case of five patients infected with COVID-19 from an asymptomatic confirmed case in Beijing.
28.03.2020	[Clinical and coagulation characteristics of 7 patients with critical COVID-2019 pneumonia and acro-ischemia]	Zhonghua Xue Ye Xue Za Zhi / Chinese article	<ul style="list-style-type: none"> • Objective: To investigate the clinical and coagulation characteristics of the critical Coronavirus disease 2019 (COVID-19) patients with acro-ischemia in the intensive care unit (ICU). • Conclusions: The existence of hypercoagulation status in critical COVID-2019 patients should be monitored closely, and anticoagulation therapy can be considered in selected patients. More clinical data is needed to investigate the role of anticoagulation in COVID-2019 treatment.
27.03.2020	Gastrointestinal tract symptoms in coronavirus disease 2019: Analysis of clinical symptoms in adult patients	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> • Investigated the clinical presentation of coronavirus disease 2019 (COVID-19), particularly the incidence of gastrointestinal tract symptoms. • Concluded that gastrointestinal tract symptoms are common in COVID-19 and most occur during the middle stage of the disease and lasts for a short period of time. Clinicians need to pay greater attention to gastrointestinal tract symptoms of COVID-19.
27.03.2020	The first report of the prevalence of COVID-19 in Chronic myelogenous leukemia patients in the core epidemic area of China: multicentre, cross-sectional survey	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> • While the 392 chronic myelogenous leukaemia (CML) respondents required regular referrals to hospitals, they did not have much contact with COVID-19 patients during the outbreak. • Patients who failed to achieved an optimal response to CML therapy appear more likely to have a symptomatic infection with SARS-CoV-2. • Older patients with comorbidities are at increased risk of death.
27.03.2020	A War on Two Fronts: Cancer Care in the Time of COVID-19	Annals of Internal medicine / Ideas and Opinions	<ul style="list-style-type: none"> • Oncology specialists as well as other providers regularly involved in the diagnosis, active treatment, and longitudinal follow-up of patients with cancer must consider how to 1) balance a delay in cancer diagnosis or treatment against the risk for a potential COVID-19 exposure, 2) mitigate the risks for significant care disruptions associated with social distancing behaviours, and 3) manage the appropriate allocation of limited health care resources in this unprecedented time of health care crisis.
27.03.2020	The Italian COVID-19 outbreak: experiences and recommendations from clinical practice	Anaesthesia / Article	<ul style="list-style-type: none"> • The authors report the impact of the COVID-19 outbreak on regional and national healthcare infrastructure, and also report on recommendations based on clinical experiences of managing patients throughout Italy. • They describe key elements of clinical management, including safe oxygen therapy, airway management, personal protective equipment and non-technical aspects of caring for patients diagnosed with COVID-19.
27.03.2020	Impact of changing case definitions for COVID-19 on the epidemic curve and transmission parameters in mainland China	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> • The authors examined changes in the case definition for COVID-19 in mainland China during the first epidemic wave. • Concluded that the case definition was initially narrow, but was gradually broadened to allow detection of more cases as knowledge increased, particularly milder cases and those

			without epidemiological links to Wuhan or other known cases. This should be taken into account when making inferences on epidemic growth rates and doubling times, and therefore on the reproductive number, to avoid bias.
27.03.2020	Practical considerations in the anaesthetic management of patients during a COVID-19 epidemic	Anaesthesia / Letter	<ul style="list-style-type: none"> • The authors concur with existing guidance for the anaesthetic management of patients during a COVID-19 outbreak, and highlight additional anaesthetic considerations in this COVID-19 pandemic. • The discussion is limited to patients not known to be COVID infected.
28.03.2020	COVID-19 outbreak and inflammatory bowel disease management: a questionnaire survey from realistic practice	J Crohns Colitis / Article	<ul style="list-style-type: none"> • A team located in a tertiary hospital in Beijing and providing follow up service for more than 150 patients with IBD, report on new methods of communication for follow up such as mobile communication applications, distance text consultation, hotline and telehealth, in response to the special conditions over the last 2 months.
27.03.2020	Consensus guidelines for managing the airway in patients with COVID-19	Anaesthesia / Guidance	<ul style="list-style-type: none"> • Consensus statement to advise on airway management for patients with COVID-19, drawing on published literature and immediately available information from clinicians and experts. • Recommendations on the prevention of contamination of healthcare workers, the choice of staff involved in airway management, the training required and the selection of equipment are discussed. • The fundamental principles of airway management in these settings are described for: emergency tracheal intubation; predicted or unexpected difficult tracheal intubation; cardiac arrest; anaesthetic care; and tracheal extubation.
27.03.2020	Use of in situ simulation to evaluate the operational readiness of a high consequence infectious disease intensive care unit	Anaesthesia / Research article	<ul style="list-style-type: none"> • The authors ran high-fidelity, in situ simulation of high-risk procedures on patients with COVID-19 in a negative-pressure side room on our intensive care unit. • The simulations revealed several important latent risks and allowed the authors to put corrective measures in place prior to the admission of patients with COVID-19. • They recommend that staff working in clinical areas expected to receive patients with COVID-19 conduct in situ simulation in order to detect their own unique risks and aid in the creation of local guidelines of management of patients with COVID-19.

Infection control

Publication Date	Title/URL	Journal / Article type	Digest
28.03.2020	Sourcing Personal Protective Equipment During the COVID-19 Pandemic	JAMA / Editorial	<ul style="list-style-type: none"> • Preventing spread of infection to and from health care workers (HCWs) and patients relies on effective use of personal protective equipment (PPE)—gloves, face masks, air-purifying respirators, goggles, face shields, respirators, and gowns. A critical shortage of all of these is projected to develop or has already developed in areas of high demand. PPE, formerly ubiquitous and disposable in the hospital environment, is now a scarce and precious

			commodity in many locations when it is needed most to care for highly infectious patients. An increase in PPE supply in response to this new demand will require a large increase in PPE manufacturing, a process that will take time many health care systems do not have, given the rapid increase in ill COVID-19 patients.
27.03.2020	Simulation as a tool for assessing and evolving your current personal protective equipment: lessons learned during the coronavirus disease (COVID-19) pandemic	Canadian Journal of Anesthesia / Letter	<ul style="list-style-type: none"> The authors describe how their hospital used low-fidelity airway simulation to assess and evolve the personal protective equipment (PPE) used for airway management of patients with COVID-19.
27.03.2020	Application of personal-oriented digital technology in preventing transmission of COVID-19, China	Irish Journal of Medical Science / Lecture	<ul style="list-style-type: none"> The authors report several personal-oriented and mobile phone-based information technologies which were recently developed and widely used during the outbreak of COVID-19 in China. These technologies help reduce the transmission of COVID-19 and maintain normal social order.
27.03.2020	Screening and managing of suspected or confirmed novel coronavirus (COVID-19) patients: experiences from a tertiary hospital outside Hubei province	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> A 1,200 bed tertiary care teaching hospital in Chengdu, Sichuan, China. Participants: 802 adults presenting to hospital with concerns of having COVID-19, 1,246 inpatients and 2,531 hospital visitors. Interventions: Screening and management of patients using a hospital-specific protocol, which included fever triage, monitoring visitors and patients, emergency response, personnel training for healthcare team members, health education for patients and family, medical materials management, disinfection and wastes disposal protocols. Whilst screening out-patients presenting to a fever clinic remains important, monitoring visitors must not be overlooked.
30.03.2020	In-flight Transmission Cluster of COVID-19: A Retrospective Case Series	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> After a flight, laboratory-confirmed COVID-19 was reported in 12 patients. Data were collected from 25th January to 28th February 2020. There is potential for COVID-19 transmission by airplane, but the symptoms are mild.
27.03.2020	Estimating Preventable COVID19 Infections Related to Elective Outpatient Surgery in Washington State: A Quantitative Model	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> Cancelling elective outpatient surgeries during the COVID19 pandemic could prevent a large number of patient and healthcare worker infections.

Treatment

Publication Date	Title/URL	Journal / Article type	Digest
27.03.2020	Treatment of 5 Critically Ill Patients With COVID-19 With Convalescent Plasma	JAMA / Article	<ul style="list-style-type: none"> The authors investigated if the administration of convalescent plasma transfusion would be beneficial in the treatment of critically ill patients with coronavirus disease 2019 (COVID-19). In this uncontrolled case series of 5 critically ill patients with COVID-19 and acute

			<p>respiratory distress syndrome (ARDS), administration of convalescent plasma containing neutralizing antibody was followed by an improvement in clinical status.</p> <ul style="list-style-type: none"> •These preliminary findings raise the possibility that convalescent plasma transfusion may be helpful in the treatment of critically ill patients with COVID-19 and ARDS, but this approach requires evaluation in randomized clinical trials.
27.03.2020	Convalescent Plasma to Treat COVID-19: Possibilities and Challenges	JAMA / Editorial	<ul style="list-style-type: none"> •Comment on the study by Shen et al. which reported findings from a preliminary study of 5 severely ill patients with COVID-19 who were treated using plasma from recovered individuals •Even though the cases in the report by Shen et al are compelling and well-studied, this investigation has important limitations that are characteristic of other “anecdotal” case series. The intervention, administration of convalescent plasma, was not evaluated in a randomized clinical trial, and the outcomes in the treatment group were not compared with outcomes in a control group of patients who did not receive the intervention. Therefore, it is not possible to determine the true clinical effect of this intervention or whether patients might have recovered without this therapy.
27.03.2020	Favipiravir versus Arbidol for COVID-19: A Randomized Clinical Trial	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> •Compared to arbidol, in moderate COVID-19 patients untreated with antiviral previously, favipiravir showed superior efficacy in terms of clinical recovery rate of day 7 and reduced incidence of fever, cough with manageable antiviral-associated adverse effects. •Concluded that Favipiravir can be considered as a preferred treatment approach to moderate COVID-19 pneumonia.
28.03.2020	Structure-Based Design, Synthesis and Biological Evaluation of Peptidomimetic Aldehydes as a Novel Series of Antiviral Drug Candidates Targeting the SARS-CoV-2 Main Protease	bioRxiv (not peer-reviewed) / New results	<ul style="list-style-type: none"> • The main protease (Mpro) of SARS-CoV-2 is a key CoV enzyme that plays a pivotal role in mediating viral replication and transcription, which makes it an attractive drug target. • In an effort to rapidly discover lead compounds targeting Mpro, two compounds (11a and 11b) were designed and synthesized, both of which exhibited excellent inhibitory activity with an IC50 value of 0.05 μM and 0.04 μM respectively.
27.03.2020	A SARS-CoV-2-Human Protein-Protein Interaction Map Reveals Drug Targets and Potential Drug-Repurposing	bioRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> •The scientific community has little knowledge of the molecular details of SARS-CoV-2 infection. To illuminate this, the authors cloned, tagged and expressed 26 of the 29 viral proteins in human cells and identified the human proteins physically associated with each using affinity purification mass spectrometry, which identified 332 high confidence SARS-CoV-2-human protein-protein interactions (PPIs). •Among these, they identified 67 druggable human proteins or host factors targeted by 69 existing FDA-approved drugs, drugs in clinical trials and/or preclinical compounds, that they are currently evaluating for efficacy in live SARS-CoV-2 infection assays.
27.03.2020	Modelling SARS-CoV-2 Dynamics: Implications for Therapy	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> • The results of this study indicated that therapies that block de novo infections or virus production are most likely to be effective if initiated before the peak viral load (which occurs around three days after symptom onset on average), but therapies that promote cytotoxicity are likely to have only limited effects.

27.03.2020	Caution on Kidney Dysfunctions of COVID-19 Patients	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> • To prevent fatality in kidney conditions, the authors suggested a high degree of caution in monitoring the kidney functions of severe COVID-19 patients regardless of the past disease history. • Upon day-by-day monitoring, clinicians should consider any potential interventions to protect kidney functions at the early stage of the disease and renal replacement therapies in severely ill patients, particularly for those with strong inflammatory reactions or a cytokine storm.
28.03.2020	Possible method for the production of a Covid-19 vaccine	Vet Record / Letter	<ul style="list-style-type: none"> • P multocida used in the production of a live intranasal haemorrhagic septicaemia vaccine was used to transform and express classical swine fever viral antigens. The resultant product was applicable as an intranasal aerosol, subcutaneous injection or as an injectable killed vaccine. • The production of a Covid-19 vaccine by this method – based on the SARS-CoV-2 virus – is a possibility if the extraction of antibodies (from serum, respiratory tract mucus and so on) from people that have recovered from the virus is performed effectively. • The human pathogen that can cause pneumonia, Haemophilus influenzae, is in the family Pasteurellaceae, and commensal species of Haemophilus are found in the human respiratory tract. Employment of these, and other species of bacteria, in place of Pasteurella, can be considered.
27.03.2020	Core Outcome Set for Traditional Chinese and Western Medicine Clinical Trials of COVID-19	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> • A core outcome set (COS) for COVID-19 may improve consistency of outcome reporting in clinical trials, which may help identify valued interventions after comparing different trials when the researchers report the same outcomes.
27.03.2020	Preventing respiratory illness in older adults aged 60 years and above living in long-term care: A rapid overview of reviews	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> • The overall objective of this rapid overview of reviews was to identify evidence from systematic reviews (SRs) for infection control and prevention practices for adults aged 60 years and older in long-term care settings. • The current evidence suggests that with antiviral chemoprophylaxis with adamantane is effective in managing respiratory illness in residents of long-term care facilities. The rest of the strategies can be used in long-term care facilities, yet have limited evidence supporting their use from systematic reviews.
28.03.2020	Therapeutic opportunities to manage COVID-19/SARS-CoV-2 infection: Present and future	Indian J Ophthalmol / Review	<ul style="list-style-type: none"> • This review outlines the key aspects of the pathobiology associated with the morbidity and mortality in COVID-19 patients, which includes a viral response phase and an exaggerated host response phase. • The review also summarizes therapeutic agents that are currently being explored along with those with potential for consideration. • The various kinds of pharmaceutical prophylactic options that may be followed to prevent COVID-19 have also been discussed.
29.03.2020	Individualized System for Augmenting Ventilator Efficacy (iSAVE): A Rapidly deployable	bioRxiv (not peer-reviewed) / New results	<ul style="list-style-type: none"> • The authors have developed the Individualized System for Augmenting Ventilator Efficacy (iSAVE), a rapidly deployable platform to more safely use a single ventilator to simultaneously support multiple critically-ill patients.

	system to expand ventilator capacity		<ul style="list-style-type: none"> The iSAVE enables patient-specific volume and pressure control and incorporates safety features to mitigate cross-contamination between patients and flow changes due to patient interdependencies within the respiratory circuit.
28.03.2020	Structural Basis for Potent Neutralization of Betacoronaviruses by Single-domain Camelid Antibodies	bioRxiv (not peer-reviewed) / New results	<ul style="list-style-type: none"> The data provide a molecular basis for the neutralization of pathogenic betacoronaviruses by single-domain antibodies (VHHs) and suggest that these molecules may serve as useful therapeutics during coronavirus outbreaks.
27.03.2020	Early antiviral treatment contributes to alleviate the severity and improve the prognosis of patients with novel coronavirus disease (COVID-19)	Journal of Internal Medicine / research article	<ul style="list-style-type: none"> Retrospective survey investigating the clinical, imaging, and laboratory characteristics of confirmed 280 cases of novel coronavirus disease (COVID-19). CONCLUSIONS: The elderly and patients with underlying diseases are more likely to experience a severe progression of COVID-19. It is recommended that timely antiviral treatment should be initiated to slow the disease progression and improve the prognosis.
28.03.2020	Design of potent membrane fusion inhibitors against SARS-CoV-2, an emerging coronavirus with high fusogenic activity	bioRxiv (not peer-reviewed) / New results	<ul style="list-style-type: none"> The presented results provide important information for understanding the entry pathway of SARS-CoV-2 and the design of antivirals that target the membrane fusion step.

Social sciences

Publication Date	Title/URL	Journal / Article type	Digest
27.03.2020	Posttraumatic stress symptoms and attitude toward crisis mental health services among clinically stable patients with COVID-19 in China	Psychological Medicine / Research article	<ul style="list-style-type: none"> The authors report the findings of an online survey to examine the pattern of posttraumatic stress symptoms in clinically stable COVID-19 patients. They also explored patients' attitude toward crisis mental health services during the COVID-19 outbreak.
30.03.2020	The psychological distress and coping styles in the early stages of the 2019 coronavirus disease (COVID-19) epidemic in the general mainland Chinese population: a web-based survey	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> In the early stages of COVID-19, general population with epidemic contact characteristics, excessive concern with media reports, and those with more severe impacts perceived have higher levels of psychological distress. Interventions should be implemented early, especially for those population with a high level of psychological distress and/or with a negative coping style.

Miscellaneous

Publication Date	Title/URL	Journal / Article type	Digest
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28.03.2020	Can companion animals become infected with Covid-19?	Vet Record / Letter	<ul style="list-style-type: none"> • Describes two cases of pet dogs in Hong Kong that have tested positive for Covid-19 using PCR testing. • As in the previous SARS-CoV outbreak in Hong Kong in 2003, where a number of pets were infected but never became sick, there is no evidence that dogs or cats could become sick or infect people.
27.03.2020	Undocumented U.S. Immigrants and Covid-19	The Lancet / Perspective	<ul style="list-style-type: none"> • Under the Trump administration, immigrants have faced relentless attacks — tightening of the public charge rule, threats to the Deferred Action for Childhood Arrivals program, raids by Immigration and Customs Enforcement (ICE), asylum restrictions, and separation of families at the border — so immigrants are justifiably scared. Expecting them to trust the government now, during the Covid-19 crisis, is naive at best. • As community organizations, activists, and health care providers scramble to reach out to immigrants and encourage them to seek care for Covid-19 if necessary, they are using mitigation strategies that will not compensate for years of harm.

Modelling

Publication Date	Title/URL	Journal / Article type	Digest
29.03.2020	Assessing the Global Tendency of COVID-19 Outbreak	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> • If the current policy environment is maintained, the cumulative number of patients worldwide will be 1,225,059 (95% CI: 486,934 -4,533,392).
27.03.2020	Global transmission network of SARS-CoV-2: from outbreak to pandemic	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> • The authors employed molecular surveillance data of SARS-CoV-2 epidemics for inference and comprehensive analysis of its global transmission network before the pandemic declaration. The goal was to characterize the spatial-temporal transmission pathways that led to the establishment of the pandemic. • The inferred network structural properties, transmission clusters and pathways and virus introduction routes emphasize the extent of the global epidemiological linkage and demonstrate the importance of internationally coordinated public health measures.
27.03.2020	Systematic review and critical appraisal of prediction models for diagnosis and prognosis of COVID-19 infection	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> • Reviewed and critically appraised the published and preprint reports of models that aim to predict either (i) presence of existing COVID-19 infection, or (ii) future complications in individuals already diagnosed with COVID-19. • Concluded that COVID-19 related prediction models for diagnosis and prognosis are quickly entering the academic literature through publications and preprint reports, aiming to support medical decision making in a time where this is needed urgently. Many models were poorly reported and all appraised as high risk of bias. The authors call for immediate sharing of the individual participant data from COVID-19 studies worldwide to support collaborative efforts in building more rigorously developed and validated COVID-19 related prediction models.

30.03.2020	Short-term forecasts and long-term mitigation evaluations for the COVID-19 epidemic in Hubei Province, China	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> • Since recent studies show that COVID-19 epidemiological parameters do not follow exponential distributions leading to Markov processes, future works need to focus on non-Markovian models to better capture the COVID-19 spreading trajectories. • Shortening the infectious period via early case identification and isolation can slow the epidemic spreading significantly.
27.03.2020	World governments should protect their population from COVID-19 pandemic using Italy and Lombardy as precursor	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> • Italy emerged early on as the country with the largest outbreak outside Asia. The outbreak in Northern Italy demonstrates that it is fundamental to contain the virus' spread at a very early stage of diffusion. At later stages, no containment measure, even if strict, can prevent the saturation of the hospitals and of the intensive care units in any country. • Here the authors show that it is possible to predict when the intensive care units will saturate, within a few days from the first cases of COVID-19 intensive care patients. Using early counts of intensive care patients, the authors predict the saturation for Lombardy, Italy. Governments should use the Italian precursor to control the outbreak of COVID-19 and prevent the saturation of their intensive care units to protect their population.
26.03.2020	A model to estimate bed demand for COVID-19 related hospitalization	medRxiv (not peer-reviewed) / Article	<ul style="list-style-type: none"> • The authors developed a model to facilitate hospital planning with estimates of the number of Intensive Care (IC) beds, Acute Care (AC) beds, and ventilators necessary to accommodate patients who require hospitalization for COVID-19 and how these compare to the available resources. They deployed this model as an interactive online tool.

Produced by the PHE COVID-19 Literature Digest Team

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