Public Health England

International EPI Cell Daily Evidence Digest – 14/04/2020

This briefing is produced by the PHE COVID-19 Literature Digest Team. 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 and consensus statements (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Please note that we are including preprints (highlighted in red), which are preliminary reports of work that have NOT been peer-reviewed.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
13.04.2020	Inflammatory Response Cells During Acute Respiratory Distress Syndrome in Patients With Coronavirus Disease 2019 (COVID-19)	Annals of Internal Medicine / Letter	• Describe the type of immune cells identified by imaging mass cytometry in lung tissue from 2 patients with COVID-19 and fatal ARDS.

09.04.2020	Early virus clearance and delayed antibody response in a case of COVID-19 with a history of co-infection with HIV-1 and HCV	Clinical Infectious Diseases / Accepted manuscript	• The authors report the first case of COVID-19 with HIV-1 and HCV co-infection, who showed a persistently negative SARS-CoV-2 RNA test, but delayed antibody response in the plasma. This case highlights the influence of HIV-1-induced immune dysfunction on the early SARS-CoV-2 clearance.
11.04.2020	CT features of SARS-CoV-2 pneumonia according to clinical presentation: a retrospective analysis of 120 consecutive patients from Wuhan city	Eur Radiol / Article	• The clinical and CT features at admission may enable clinicians to promptly evaluate the prognosis of patients with SARS-CoV-2 pneumonia. • Clinicians should be aware that clinically silent cases may present with CT features similar to those of symptomatic common patients.
01.04.2020	An overview of the rapid test situation for COVID-19 diagnosis in the EU/EEA	European Centre for Disease Control and Prevention / Technical report	• The priorities for rapid testing in EU countries that are now dealing with community transmission should follow EU and WHO guidance on testing strategies. These include: testing people who are at risk of developing severe disease, patients with acute respiratory illness who require hospitalisation and advanced care for COVID-19, symptomatic health workers and the first symptomatic individuals in a closed setting such as prison or nursing care facility. • Rapid tests are qualitative or semi-quantitative in vitro diagnostics (IVDs), used singly or in a small series, which involve non-automated procedures and have been designed to give a fast result. • These rapid tests are relatively simple to perform and interpret and therefore require limited test operator training. They may be intended either for use in hospital laboratories or near the point-of-care.
09.04.2020	Roll-out of SARS-CoV-2 testing for healthcare workers at a large NHS Foundation Trust in the United Kingdom, March 2020	Eurosurveillance / Rapid communication	• Healthcare workers (HCW) are potentially at increased risk of infection with COVID-19 and may transmit SARS-CoV-2 to vulnerable patients. • The authors present results from staff testing at Sheffield Teaching Hospitals NHS Foundation Trust, United Kingdom. Between 16 and 29 March 2020, 1,533 symptomatic HCW were tested, of whom 282 (18%) were positive for SARS-CoV-2. Testing HCW is a crucial strategy to optimise staffing levels during this outbreak.
13.04.2020	Diagnostic Testing for Severe Acute Respiratory Syndrome–Related Coronavirus-2: A Narrative Review	Annals of Internal Medicine / Reviews	• Authors review the current array of tests for SARS–CoV-2, highlight gaps in current diagnostic capacity, and propose potential solutions. • Excellent tools for diagnosis of symptomatic patients in well-equipped laboratories; important gaps remain in screening asymptomatic persons in incubation phase, as well as in the accurate determination of live viral shedding during convalescence to inform decisions to end isolation.
09.04.2020	False-negative of RT-PCR and prolonged nucleic acid conversion	Journal of medical virology / Letter	• The authors studied the characteristics of nucleic acid conversion for SARS-CoV-2 from 70 COVID-19 patients.

	in COVID-19: Rather than recurrence		• The study found that 15 (21.4%) patients experienced a "turn positive" of nucleic acid detection by RT-PCR test for SARS-CoV-2 after two consecutive negative results, which may be related to the false negative of RT-PCR test and prolonged nucleic acid conversion.
14.04.2020	Analysis of factors associated early diagnosis in coronavirus disease 2019 (COVID-19)	medRxiv (not peer-reviewed) / Article	• Single RT-PCR test has relatively high false negative rate. • When first RT-PCR test show negative result in suspected patients, chest CT scan, contact history, age and lymphocyte count should be used combinedly to assess the possibility of SARS-CoV-2 infection.
12.04.2020	Magnetic Bead-Quantum Dot (MB-Qdot) CRISPR Assay for Instrument-Free Viral DNA Detection	bioRxiv (not peer-reviewed) / New results	• The authors have developed a novel detection system which couples CRISPR-Cas recognition of target sequences, Cas mediated nucleic acid probe cleavage, and quantum dots as highly sensitive reporter molecules for instrument-free detection of viral nucleic acid targets. • The positive samples are readily confirmed by visual inspection, completely avoiding the need for complicated devices and instruments. • This work establishes the feasibility of a simple, instrument free assay for rapid nucleic acid screening in both hospitals and point of-care settings.

Genomics

Publication Date	Title/URL	Journal/ Article type	Digest
12.04.2020	Isolation, sequence, infectivity and replication kinetics of SARS-CoV-2	bioRxiv (not peer-reviewed) / New results	• In this study, the authors report the isolation of SARS-CoV-2 from two COVID-19 patients in Toronto, Canada. • They determined the genomic sequences of the two isolates and identified single nucleotide changes in representative populations of our virus stocks. • They have tested a wide range of human immune cells for infectivity with SARS-CoV-2. • They confirm from their studies that human primary peripheral blood mononuclear cells (PBMCs) are not permissive to SARS-CoV-2. • As SARS-CoV-2 continues to spread globally, it is essential to monitor any small nucleotide polymorphisms in the virus and to continue to isolate circulating strains of the virus to determine cell susceptibility and pathogenicity using in vitro and in vivo infection models.
14.04.2020	Myocyte Specific Upregulation of ACE2 in Cardiovascular Disease:	medRxiv (not peer-reviewed) / Article	• SARS-CoV-2 infection of host cells occurs predominantly via binding of the viral surface spike protein to the human angiotensin-converting

	Implications for SARS-CoV-2 mediated myocarditis		enzyme 2 (ACE2) receptor. • Hypertension and pre-existing cardiovascular disease are risk factors for morbidity from COVID-19, and it remains uncertain whether the use of angiotensin converting enzyme inhibitors (ACEi) or angiotensin receptor blockers (ARB) impacts infection and disease. • The authors aim to shed light on this question by assessing ACE2 expression in normal and diseased human myocardial samples profiled by bulk and single nucleus RNA-seq.
14.04.2020	PathoLive - Real-time pathogen identification from metagenomic Illumina datasets	bioRxiv (not peer-reviewed) / New results	• The authors implemented PathoLive, a real-time diagnostics pipeline for the detection of pathogens from clinical samples hours before sequencing has finished. • Based on real-time alignment with HiLive2, mappings are scored with respect to common contaminations, low-entropy areas, and sequences of widespread, non-pathogenic organisms. • Their approach is valuable to obtain fast and accurate NGS-based pathogen identifications and correctly prioritize and visualize them based on their clinical significance. Availability: PathoLive is open source and available on GitLab (https://gitlab.com/rki_bioinformatics/PathoLive) and BioConda (conda install -c bioconda patholive).
12.04.2020	Insights on early mutational events in SARS-CoV-2 virus reveal founder effects across geographical regions	bioRxiv (not peer-reviewed) / New results	• This paper describes early mutational events across samples from publicly available SARS-CoV-2 sequences from the sequence read archive repository. • Mutations in the helicase and orf1a coding regions from SARS-CoV-2 were predominant, among others, suggesting that these proteins are prone to evolve by natural selection. • The authors urge that primer sets for diagnosis be carefully designed, since rapidly occurring variants would affect the performance of the reverse transcribed quantitative PCR (RT-qPCR) based viral testing.
13.04.2020	Bioinformatic characterization of angiotensin-converting enzyme 2, the entry receptor for SARS-CoV-2	bioRxiv (not peer-reviewed) / New results	• A novel tool for the prediction of transcription factor binding sites identified several putative sites for determined transcription factors within the ACE2 gene promoter. • These results also confirmed that age and gender play no significant role in the regulation of ACE2 mRNA expression in the lung.
10.04.2020	Structure of the RNA-dependent RNA polymerase from COVID-19 virus	Science / Article	• The authors report the cryo-EM structure of COVID-19 virus full-length nsp12 in complex with cofactors nsp7 and nsp8 at 2.9-A resolution. • In addition to the conserved architecture of the polymerase core of the viral polymerase family, nsp12 possesses a newly identified beta-hairpin domain at its N terminus.

			• A comparative analysis model shows how remdesivir binds to this polymerase - the structure provides a basis for the design of new antiviral therapeutics targeting viral RdRp
13.04.2020	Robust neutralization assay based on SARS-CoV-2 S-bearing vesicular stomatitis virus (VSV) pseudovirus and ACE2-overexpressed BHK21 cells	bioRxiv (not peer-reviewed) / New results	• A convenient and reliable in vitro neutralization assay is very important for the development of neutralizing antibodies, vaccines and other inhibitors. • In this study, G protein-deficient vesicular stomatitis virus (VSVdG) bearing full-length and truncated spike (S) protein of SARS-CoV-2 were evaluated. • This efficient and reliable pseudovirus assay model could facilitate the development of new drugs and vaccines.

Epidemiology and clinical - children and pregnancy

Publication Date	Title/URL	Journal/ Article type	Digest
10.04.2020	Coronavirus Disease 2019 in Children - United States, February 12-April 2, 2020	MMWR Morb Mortal Wkly Rep / Article	• Data from 149,760 laboratory-confirmed COVID-19 cases in the US occurring during Feb 12-Apr 2, 2020 were analysed. • Among 149,082 (99.6%) reported cases for which age was known, 2,572 (1.7%) were among children aged <18 years. • Among those with available information, 73% of paediatric patients had symptoms of fever, cough, or shortness of breath compared with 93% of adults aged 18-64 years during the same period; 5.7% of all paediatric patients, or 20% of those for whom hospitalization status was known, were hospitalized, lower than the percentages hospitalized among all adults aged 18-64 years (10%) or those with known hospitalization status (33%); three deaths were reported among the paediatric cases
09.04.2020	Delayed access or provision of care in Italy resulting from fear of COVID-19	The Lancet. Child & adolescent health / Correspondence	• Substantial decreases—ranging from 73% to 88%—in Italian paediatric emergency department visits compared with the same time period in 2019 and 2018 • Small series of 12 cases, half of the children were admitted to an ICU and four died. In all cases, parents reported avoiding accessing hospital because of fear of infection with SARS-CoV-2. • In five cases, the family had contacted health services before accessing care, but their health provider was unavailable because of the COVID-19 epidemic, or hospital access discouraged due to infection risks. All cases were either negative for SARS-CoV-2 or had a clinical presentation (e.g.,

			diabetes) that did not justify a diagnostic test according to the national criteria. • Parents should be made fully aware that the risks of delayed access to hospital care for emergency conditions can be much higher than those posed by COVID-19.
13.04.2020	Universal Screening for SARS-CoV-2 in Women Admitted for Delivery	New England Journal of Medicine / Correspondence	• Between Mar 22 and Apr 4, 2020, 215 pregnant women delivered infants at New York–Presbyterian Allen Hospital and Columbia University Irving Medical Centre. All were screened on admission for symptoms of Covid-19. • 29 of the 33 patients who were positive for SARS-CoV-2 at admission (87.9%) had no symptoms of Covid-19 at presentation
09.04.2020	Delivery in pregnant women infected with SARS-CoV-2: A fast review	International journal of gynaecology and obstetrics / Review	• The aim of this fast review is to bring together available information on mode of delivery, vertical/peripartum transmission, and neonatal outcome in pregnant women infected with SARS-CoV-2. • Two databases were searched, and 13 studies included. Two new-borns testing positive for SARS-CoV-2 by real-time RT-PCR assay were reported. In three neonates, SARS-CoV-2 IgG and IgM levels were elevated but the RT-PCR test was negative. • The rate of vertical or peripartum transmission of SARS-CoV-2 is low, if any, for caesarean delivery; no data are available for vaginal delivery. Low frequency of spontaneous preterm birth and general favourable immediate neonatal outcome are reassuring.

Epidemiology and clinical - risk factors

Publication Date	Title/URL	Journal/ Article type	Digest
09.04.2020	Attention should be paid to venous thromboembolism prophylaxis in the management of COVID-19	The Lancet. Haematology / Comment	• Among patients with COVID-19, especially those who are severely and critically ill, a variety of potential risk factors for venous thromboembolism exist, including infection, immobilisation, respiratory failure, mechanical ventilation, and central venous catheter use. • Authors use a nationwide dataset from China to provide a delineation of venous thromboembolism risk in patients with COVID-19 - retrospective analysis of deidentified data, 1099 patients. • Among the patients at high risk of venous thromboembolism in this cohort, 44 (11%) of 407 also had a high risk of bleeding. For these patients, the dose and duration of anticoagulants should be adjusted,

			and mechanical compressions such as elastic compression stockings or intermittent pneumatic compression are warranted. • Assessing venous thromboembolism and bleeding risks regularly is essential. Additionally, authors found that patients with COVID-19 with a high risk of venous thromboembolism had poorer outcomes than patients with a low risk, suggesting that these patients might require increased attention in case of rapid deterioration.
09.04.2020	COVID-19 in long-term liver transplant patients: preliminary experience from an Italian transplant centre in Lombardy	Lancet Gastroenterology & Hepatology / Correspondence	• Case study from Lombardy-based transplant centre: all three COVID-19-related deaths were long-term patients on minimal immunosuppressive regimens, compared to three recently transplanted, fully immunosuppressed patients. • Suggest that great attention should be paid to long-term liver transplant recipients with metabolic comorbidities. With American Association for the Study of Liver Diseases in suggesting that immunosuppression should not be reduced or stopped in asymptomatic liver transplant recipients.
11.04.2020	Clinical characteristics and outcomes of older patients with coronavirus disease 2019 (COVID-19) in Wuhan, China (2019): a single-centered, retrospective study	J Gerontol A Biol Sci Med Sci / Article	• In the recent outbreak of COVID-19, a hospital in Wuhan found that in 203 patients diagnosed with COVID-19, patients aged 65 and older had greater initial comorbidities, more severe symptoms, and were more likely to experience multi-organ involvement and death, as compared with younger patients
09.04.2020	High prevalence of obesity in severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) requiring invasive mechanical ventilation	Obesity / Brief Report	• In this retrospective cohort study the authors analysed the relationship between clinical characteristics, including body mass index (BMI), and the requirement for invasive mechanical ventilation (IMV) in 124 consecutive patients admitted in intensive care for SARS-CoV-2, in a single French centre. • The present study showed a high frequency of obesity among patients admitted in intensive care for SARS-CoV-2. Disease severity increased with BMI. Obesity is a risk factor for SARS-CoV-2 severity requiring increased attention to preventive measures in susceptible individuals.
09.04.2020	Factors associated with prolonged viral RNA shedding in patients with COVID-19	Clinical Infectious Diseases / Accepted manuscript	• In this retrospective study, risk factors associated with SARS-CoV-2 RNA shedding were evaluated in a cohort of 113 symptomatic patients from two hospitals outside Wuhan. • Male sex, delayed admission to hospital after illness onset, and invasive mechanical ventilation were associated with prolonged SARS-CoV-2 RNA shedding. Hospital admission and general treatments should be started

			as soon as possible in symptomatic COVID-19 patients, especially male patients.
10.04.2020	COVID-19 with Different Severity: A Multi-center Study of Clinical Features	Am J Respir Crit Care Med / Article	• The clinical characteristics, laboratory examinations, CT images and treatment of 476 COVID-19 patients from three different cities in China were compared. • Multiple organ dysfunction and impaired immune function were the typical characteristics of severe and critical patients. • There was a significant difference in angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers usage among patients with different severities; and involvement of multiple lung lobes and pleural effusion were associated with the severity of COVID-19; advanced age (>/=75 years) was also a risk factor for mortality

Epidemiology and clinical – other

Publication Date	Title/URL	Journal/ Article type	Digest
12.04.2020	Blood and blood product use during COVID-19 Infection	Am J Hematol / Correspondence	• Out of 572 patients with Covid-19 infection, only 9 required blood transfusions in a 1700 bed acute care hospital in Singapore. • This case series presents the clinical profiles of the 9 patients who required transfusion.
11.04.2020	Cluster of coronavirus disease 2019 (Covid-19) in the French Alps, 2020	Clin Infect Dis / Article	• An index case stayed 4 days in the chalet with 10 English tourists and a family of 5 French residents; SARS-CoV-2 was detected in 5 individuals in France, 6 in England (including the index case), and 1 in Spain (overall attack rate in the chalet: 75%) • The occurrence in this cluster of one asymptomatic case with similar viral load as a symptomatic patient, suggests transmission potential of asymptomatic individuals - the fact that an infected child did not transmit the disease despite close interactions within schools suggests potential different transmission dynamics in children.
12.04.2020	Morphological anomalies of circulating blood cells in COVID-19	Am J Hematol / Article	• In patients with COIVD-19, in the early aggravation phase before treatment, observation of peripheral blood film shows the presence of pronounced morphological anomalies of the granulocyte series. • One week after the start of treatment, such anomalies subside, and an increasing proportion of reactive lymphocytes dominates
12.04.2020	Association of chemosensory dysfunction and Covid-19 in	Int Forum Allergy Rhinol / Article	• Smell and taste impairment were independently and strongly associated with Covid-19-positivity

	patients presenting with influenza-like symptoms		• Chemosensory dysfunction was strongly associated with Covid-19 infection and should be considered when screening symptoms.
10.04.2020	COVID-19 Autopsies, Oklahoma, USA	Am J Clin Pathol / Article	• This is the first report of complete autopsy findings in coronavirus disease 2019 COVID-19 in the English language literature. • A protocol detailing use of appropriate equipment is provided. • Autopsy findings such as diffuse alveolar damage and airway inflammation reflect true virus-related pathology; other findings represent superimposed or unrelated processes.

Infection control

Publication Date	Title/URL	Journal/ Article type	Digest
08.04.2020	Guidance for discharge and ending isolation in the context of widespread community transmission of COVID-19 – first update	European Centre for Disease Prevention and Control / Technical Report	• COVID-19 patients may be discharged based on: a) clinical resolution of symptoms, and b) evidence for viral RNA clearance from the upper respiratory tract, where testing capacity permits. In order to protect the healthcare system capacity, in the context of widespread community transmission and limited testing capacity, clinical criteria will gain priority. • Provides guidance on discharge and ending isolation in the context of widespread community transmission. • Although the oral-faecal route does not appear to be a driver of transmission, its significance remains to be determined. Discharged patients should be advised to strictly follow personal hygiene precautions in order to protect household contacts. This applies to all convalescing patients, but particularly to convalescent children.
08.04.2020	Rapid risk assessment: Coronavirus disease 2019 (COVID-19) pandemic: increased transmission in the EU/EEA and the UK – eighth update	European Centre for Disease Control and Prevention / Technical report	• Based on the available evidence, it is currently too early to start lifting all community and physical distancing measures in the EU/EEA and the UK. Before considering the lifting of any measures, Member States should ensure enhanced population and hospital-based testing and surveillance systems are in place to inform and monitor escalation/de-escalation strategies and assess the epidemiological consequences. • Solidarity and coordination between Member States will remain essential in the de-escalation phase in order to increase the effect of measures taken and minimise the risk of infection 'spill-over' between countries if they de-escalate at different rates and in different ways.

31.03.2020	Infection prevention and control and preparedness for COVID-19 in healthcare settings	European Centre for Disease Control and Prevention / Technical report	• This update focuses on measures to be applied in settings with increasing community transmission, a growing demand for care of COVID-19 patients and ensuing staff issues in the event of shortages of personal protective equipment (PPE) for healthcare facilities in EU/EEA countries and the United Kingdom. • This guidance provides recommendations for reducing risk of COVID-19 transmission in healthcare settings (including long-term care facilities) and laboratories in the EU/EEA. • It covers triage, initial contact and assessment in primary and emergency care, personal protective equipment, management of suspected cases, patient transport, hospitals (case management, PPE provision and use, staff monitoring, equipment cleansing, discharge, waste management, and laboratory testing), and managing COVID-19 in long-term care facilities. • This document also highlights best practices for PPE usage and options for hospitals and long-term care facilities with limited access to PPE materials. It looks at priorities for use of respirators (FFP2/3), use of surgical masks, use of alcohol-based hand rub, and other PPE and hand hygiene products.
31.03.2020	Contact tracing: Public health management of persons, including healthcare workers, having had contact with COVID-19 cases in the European Union – first update	European Centre for Disease Control and Prevention / Technical report	• This document aims to help EU/EEA public health authorities in the tracing and management of persons, including healthcare workers, who had contact with COVID-19 cases. • A contact of a COVID-19 case is any person who had contact with a COVID-19 case within a timeframe ranging from 48 hours before the onset of symptoms of the case to 14 days after the onset of symptoms. • The report contains an algorithm for the management of contacts of probable or confirmed COVID-19 cases, and outlines what to do after a case has been identified. • There is also a table highlighting key actions for the management of contacts by individuals and public health authorities.
08.04.2020	Sterilization of disposable face masks by means of standardized dry and steam sterilization processes; an alternative in the fight against mask shortages due to COVID-19	The Journal of hospital infection / Letter (Pre-proof)	• Study to investigate possibility of reprocessing disposable FFP2 face masks in order to verify their re-usability with a method that could be applied in practice using already available equipment. • Single use FFP2 masks were sterilized with a 15-minute procedure at 121 ^{o}C, using a dry sterilization process as well as with a regular steam process with the masks in sterilization/laminate bags. • Tested for permeability properties for bacteria, pressure/flow and particle tests, filtration capacity.

			• The effectiveness of these processes are sufficient to inactivate the coronavirus based on knowledge of inactivation of such viruses.
09.04.2020	Face masks for the public during the covid-19 crisis	BMJ (Clinical research ed.) / Analysis	• The precautionary principle states we should sometimes act without definitive evidence, just in case. • Whether masks will reduce transmission of covid-19 in the general public is contested. • Even limited protection could prevent some transmission of covid-19 and save lives, and because covid-19 is such a serious threat, wearing masks in public should be advised.
12.04.2020	Sustainable social distancing through facemask use and testing during the Covid-19 pandemic	medRxiv (not peer-reviewed) / Article	• The authors investigate how individual protective behaviours, different levels of testing, and isolation influence the transmission and control of the COVID-19 pandemic. • Based on an SEIR-type model incorporating asymptomatic but infectious individuals (40%), they show that the pandemic may be readily controllable through a combination of testing, treatment if necessary, and self-isolation after testing positive (TTI) of symptomatic individuals together with social protection (e.g., facemask use, handwashing). • Even with 20% effective social protection, TTI of 1 in 4 symptomatic individuals can substantially 'flatten the curve' cutting the peak daily incidence in half.
10.04.2020	Association of Public Health Interventions With the Epidemiology of the COVID-19 Outbreak in Wuhan, China	JAMA / Original Investigation	• In this cohort study, rates of laboratory-confirmed COVID-19 infections (defined as the number of cases per day per million people), across age, sex, and geographic locations were calculated across 5 periods: Dec 8 to Jan 9 (no intervention), Jan 10 to 22 (massive human movement due to the Chinese New Year holiday), Jan 23 to Feb 1 (cordons sanitaire, traffic restriction and home quarantine), Feb 2 to 16 (centralized quarantine and treatment), and Feb 17 to Mar 8 (universal symptom survey). Effective reproduction number of SARS-CoV-2 (an indicator of secondary transmission) was also calculated over the periods. • The effective reproduction number fluctuated above 3.0 before January 26, decreased to below 1.0 after February 6, and decreased further to less than 0.3 after March 1. • A series of multifaceted public health interventions was temporally associated with improved control of the COVID-19 outbreak in Wuhan, China. These findings may inform public health policy in other countries and regions.
10.04.2020	Public Health Interventions for COVID-19: Emerging Evidence	JAMA / Editorial	• For the time being, nonpharmaceutical interventions (NPIs) are the only tool in the armamentarium for controlling COVID-19, and this report

	and Implications for an Evolving Public Health Crisis		in JAMA serves to quantify important metrics suggesting their potential effectiveness. • Until the extent and persistence of SARS-CoV-2 immunity is understood, acute need to better understand the roles that quarantine, cordons sanitaire, and the suspension of within- and between-city travel restrictions have in the control of COVID-19.
14.04.2020	Transmission routes of Covid-19 virus in the Diamond Princess Cruise ship	medRxiv (not peer-reviewed) / Article	• The authors infer that the ship central air conditioning system did not play a role, i.e. the long-range airborne route was absent in the outbreak. • Most transmission appears to have occurred through close contact and fomites.
12.04.2020	Precautions in ophthalmic practice in a hospital with the risk of COVID-19: experience from China	Acta Ophthalmol / Letter	• Personal protection of ophthalmologists: since the safe distance of droplets transmission is ≥1.5 m, it is suggested that ophthalmologists take different levels of protection according to clinical practices.
11.04.2020	Letter: Strategies for Prevention and Control of 2019 Novel Coronavirus Infection Among Medical Staff	Neurosurgery / Letter	• The experiences of a hospital in Wuhan where 14 staff members were infected with SARS-Cov-2, and recovered, are summarized, to help medical staff prepare in advance for a similar situation. • This includes the characteristics of SARS-Cov-2 infection, principles of prevention and control of infection, management of infected patients, and epidemic prevention in the outpatient department, ward, operating room, and medical staff.
09.04.2020	Acute stroke management pathway during Coronavirus-19 pandemic	Neurological sciences / Article	• This article describes the steps taken to ensure no COVID-19 infection was brought onto the stroke unit, which involved substantial changes to the hospital's acute stroke management pathway. • In addition to creating a dedicated hot-spot as a pre-triage just outside the Emergency Department, together with the Neuroradiology Unit, the Stroke Unit obtained a mobile CT unit that could be used by COVID-positive or COVID-suspected patients. Dedicated areas were activated for infected patients. • The authors share their experiences as they have observed a decreased number of patients with minor strokes, longer onset-to-door and door-to-treatment times for major strokes, and a reduced number of transfers from spokes. High attention should be kept on stroke as an emergency condition.

Treatment

Publication Date	Title/URL	Journal/ Article type	Digest
09.04.2020	COVID-19: Respiratory support outside the intensive care unit	The Lancet. Respiratory medicine / Comment	• Current debate about optimal mode of respiratory support for individuals with severe COVID-19 before invasive mechanical ventilation (IMV). Some advocate high flow nasal cannulae (HFNC) over non-invasive ventilation (NIV) or vice versa. Importance of ascertaining whether selected patients can be safely managed outside of the ICU, given considerable resource limitations. • Evidence from China suggests large minority of patients with severe respiratory failure can avoid intubation via use of NIV - a well-established therapy with which general respiratory physicians and nurses are familiar, and which is readily applicable in the non-critical care setting. Caveats would include careful patient selection so as not to delay IMV where appropriate, modified settings specific to the pathophysiology of COVID-19, and mitigation against infection transmission by aerosol.
09.04.2020	COVID-19 and risks to the supply and quality of tests, drugs, and vaccines	The Lancet. Global health / Comment	• 53 signatories from 20 countries • Without preparation for the quality assurance of diagnostic tests, drugs, and vaccines, the world risks a parallel pandemic of substandard and falsified products. Interventions are needed globally to ensure access to safe, quality assured, and effective medical products • Need to plan strategically to ensure global manufacture, access, protection, and monitoring of supply chains in the face of unescapable shortages, cost increases, and national hoarding. Recommendations include coordinated information-sharing among global medicines regulators on authorisations for clinical trials, comprehensive and rapid reporting of shortages of active ingredients and finished products by industry and regulators, robust evaluation of diagnostics tests (premarket and postmarket) to ensure accuracy.
13.04.2020	Pharmacologic Treatments for Coronavirus Disease 2019 (COVID-19): A Review	JAMA / Article	• The speed and volume of clinical trials launched to investigate potential therapies for COVID-19 highlight both the need and capability to produce high-quality evidence even in the middle of a pandemic. No therapies have been shown effective to date. • More than 300 active clinical treatment trials are underway. This narrative review summarizes current evidence regarding major proposed treatments, repurposed or experimental, for COVID-19 and provides a summary of current clinical experience and treatment guidance for this novel epidemic coronavirus.

14.04.2020	Lopinavir/ritonavir: A rapid review of effectiveness in COVID-19	Centre for Evidence-Based Medicine, University of Oxford	• Concluded at present there is insufficient evidence to recommend the use of Lopinavir/ritonavir (LPVr) for COVID-19 outside of research studies. Rapid review identified limited number of studies, all subject to methodological flaws.
11.04.2020	Regulators split on antimalarials for COVID-19	Lancet / World Report	• US and French authorities have authorised use of chloroquine and hydroxychloroquine; opposed by EU regulator and WHO. • Both drugs unproven and untested for COVID-19; rare but potentially deadly side-effects. Decision bypassed the usual drug approval process including double-blind, placebo-controlled clinical trial • US genetic cardiologist suggests at least 1% of patients at increased risk for a hydroxychloroquine or chloroquine QT reaction capable of triggering drug-induced sudden cardiac death; physicians need to carefully evaluate vulnerable patients.
09.04.2020	Trials of anti-tumour necrosis factor therapy for COVID-19 are urgently needed	Lancet / Comment	• Anti-tumour necrosis factor (TNF) antibodies have been used for more than 20 years in severe cases of autoimmune inflammatory disease such as rheumatoid arthritis, inflammatory bowel disease (IBD), or ankylosing spondylitis. • Authors propose there is sufficient evidence to support clinical trials of anti-TNF therapy in patients with COVID-19. IBD patients with COVID-19 on anti-TNF therapy do not fare worse than those treated with other drugs, but there are insufficient data to make conclusions about a better outcome. • If preliminary evidence of benefit and safety of anti-TNF therapy in hospitalised patients: therapy should be initiated as early as is practicable on hospital admission to prevent progression to needing intensive care support; consideration should be given to out of hospital treatment for patients with COVID-19 at high risk, e.g. older people / pre-existing conditions, and who can be monitored appropriately.
10.04.2020	Compassionate Use of Remdesivir for Patients with Severe Covid-19	The New England journal of medicine / Article	• Remdesivir, a nucleotide analogue prodrug that inhibits viral RNA polymerases, has shown in vitro activity against SARS-CoV-2. • In this cohort of patients hospitalized for severe Covid-19 who were treated with compassionate-use remdesivir, clinical improvement was observed in 36 of 53 patients (68%). Measurement of efficacy will require ongoing randomized, placebo-controlled trials of remdesivir therapy. (This paper has received a lot of criticism online)
01.06.2020	Vademecum for the treatment of people with COVID-19.	Infez Med / Article	• This paper aims to explore the current evidence about the drugs likely to be efficacious in the treatment of COVID-19. •A new grading scale has been proposed to help patients' stratification

			according to the severity of the respiratory conditions and a collaborating group with immunologists and rheumatologists has been built with the aim of providing some guidance about the use of tocilizumab
09.04.2020	The use of Janus kinase inhibitors in the time of SARS-CoV-2	Journal of the American Academy of Dermatology / Letter	• This letter discusses the risk of Janus kinase inhibitor (JAKi) treatment. The authors analyse and collate adverse events data from clinical trials, with a focus on infections and pulmonary toxicities.
12.04.2020	Threatening drug-drug interaction in a kidney transplant patient with Coronavirus Disease 2019 (COVID-19)	Transpl Infect Dis / Case study	• The authors present the case of a 36-year-old kidney transplanted woman affected by Senior-Loken syndrome diagnosed with COVID-19 pneumonia after a contact with her positive mother. • Hydroxychloroquine and lopinavir/ritonavir were started, and the antiviral drug was replaced with darunavir/cobicistat after two days of diarrhoea. • The need for guidelines in transplant recipients with COVID-19 infection with particular regard to the management of therapy is stressed.
13.04.2020	Classical drug digitoxin inhibits influenza cytokine storm, with implications for COVID-19 therapy	bioRxiv (not peer-reviewed) / New results	• The authors show that the cardiac glycoside digitoxin suppresses the response induced by influenza virus strain A/Wuhan/H3N2/359/95 in the cotton rat lung. • The cytokines TNFa, GRO/KC, MIP2, MCP1, TGFb, and IFNg. are significantly reduced. • Since the hyper-proinflammatory overproduction of cytokines is a host response, they suggest that digitoxin may have therapeutic potential for not only influenza and but also for coronavirus infections.
12.04.2020	The SARS-CoV-2 receptor-binding domain elicits a potent neutralizing response without antibody-dependent enhancement	bioRxiv (not peer-reviewed) / New results	• The authors show that immunization with the SARS-CoV-2 RBD elicits a robust neutralizing antibody response in rodents, comparable to 100 µg/ml of ACE2-Ig, a potent SARS-CoV-2 entry inhibitor. • Anti-sera from immunized animals did not mediate antibody-dependent enhancement (ADE) of S-protein-mediated entry under conditions in which Zika virus ADE was readily observed. • These data suggest that an RBD-based vaccine for SARS-CoV-2 could be safe and effective.
09.04.2020	Drug repositioning an alternative for the treatment of coronavirus COVID-19	International journal of antimicrobial agents / Journal Pre-proof	• This article brings together a selection of studies involving drugs from different pharmaceutical classes with activity against SARS-CoV-2 and SARS-Cov, with potential use in the treatment of COVID-19 disease.
09.04.2020	In silico studies on therapeutic agents for COVID-19: Drug repurposing approach	Life sciences / Journal Pre-proof	• Drug repurposing has become an emerging tactic to fight COVID-19. • Known antiviral agents used to study docking interaction with COVID-19 enzymes. • HIV protease inhibitors showed close interaction with COVID-19.

			• Methisazone, CGP42112A and ABT450 may become useful treatment against COVID-19.

Social sciences

Publication Date	Title/URL	Journal/ Article type	Digest
10.04.2020	The Mental Health Consequences of COVID-19 and Physical Distancing: The Need for Prevention and Early Intervention	JAMA Internal Medicine / Viewpoint	• In the context of the COVID-19 pandemic, it appears likely that there will be substantial increases in anxiety and depression, substance use, loneliness, and domestic violence; and with schools closed, there is a very real possibility of an epidemic of child abuse.
13.04.2020	Mental Health and the Covid-19 Pandemic	New England Journal of Medicine / Perspective	• Most Covid-19 cases will be identified and treated in health care settings by workers with little to no mental health training, so imperative that assessment and intervention for psychosocial concerns be administered in those settings.
11.04.2020	The gendered dimensions of COVID-19	The Lancet / Editorial	• Global Health 50/50 tracks sex-disaggregated infection and mortality COVID-19 data from the 39 most-affected countries: http://globalhealth5050.org/covid19/. • Authors echo call from The European Association of Science Editors and other organisation for all involved in collecting COVID-19 data to follow guidelines (e.g., CONSORT, STROBE) and include age and sex in demographic data. • Encourage a gender focus in all research efforts. Obscuring sex and gender differences in treatment and vaccine development could result in harm. Incomplete reporting compromises meta-analyses. Addressing the health needs of men and women equally will help societies recover and resist future human tragedies.
09.04.2020	Health-Related-Quality of Life in Common Variable Immunodeficiency Italian patients switched to remote assistance during the COVID-19 pandemic	The journal of allergy and clinical immunology. In practice / Journal Pre-proof	• Aim of the study was to identify factors impacting the Health-Related-Quality of Life among Italian patients affected by Primary Antibody Deficiencies switched to remote assistance at the time of the COVID-19 pandemic. Surveys were used to measure QoL and GHQ-12 data scores. • 158 patients participated. The quality of life worse in the group of patients who become at risk of anxiety/depression at the study time. Health-Related-Quality of Life was similar in patients forced to shift from hospital-based to home-based immunoglobulin treatment and in patients who continued their usual home-based replacement. The risk of anxiety/depression is associated to SARS-CoV-2 pandemic and to

			patients' fragility, and not to related clinical conditions associated with Common Variable Immune Deficiencies. The anxiety to run out of medications is a major new issue.
09.04.2020	Awareness, Attitudes, and Actions Related to COVID-19 Among Adults With Chronic Conditions at the Onset of the U.S. Outbreak: A Cross-sectional Survey	Annals of internal medicine / Original research	• Determined COVID-19 awareness, knowledge, attitudes, and related behaviours among U.S. adults who are more vulnerable to complications of infection because of age and comorbid conditions. • Concluded that many adults with comorbid conditions lacked critical knowledge about COVID-19 and, despite concern, were not changing routines or plans. Noted disparities suggest that greater public health efforts may be needed to mobilize the most vulnerable communities.
09.04.2020	Coronavirus Epidemic and Geriatric Mental Healthcare in China: How a Coordinated Response by Professional Organizations Helped Older Adults During an Unprecedented Crisis	International psychogeriatrics / Article	• Details how professional organisations collaborated to develop a national level response. Includes lessons learned for the future.

Miscellaneous

Publication Date	Title/URL	Journal/ Article type	Digest
12.04.2020	Comparison of SARS-CoV-2 infections among 3 species of non-human primates	bioRxiv (not peer-reviewed) / New results	• In this study, two families of non-human primates, old world monkeys (12 Macaca mulatta, 6 Macaca fascicularis) and new world monkeys (6 Callithrix jacchus), were experimentally inoculated with SARS-CoV-2. • All of M. mulatta and M. fascicularis showed chest radiographic abnormality. • Viral genomes were detected in nasal swabs, throat swabs, anal swabs and blood from all 3 species of monkeys. • Viral shedding from upper respiratory reached the peak between day 6 and day 8 post inoculation. • The authors have established a NHP model for COVID-19, which could be used to evaluate drugs and vaccines, and investigate viral pathogenesis.

Modelling

Publication Date	Title/URL	Journal/ Article type	Digest
09.04.2020	Only strict quarantine measures can curb the coronavirus disease (COVID-19) outbreak in Italy, 2020	Euro Surveill / Article	• Several Italian towns are under lockdown to contain the COVID-19 outbreak. The level of transmission reduction required for physical distancing interventions to mitigate the epidemic is a crucial question. • The authors show that very high adherence to community quarantine (total stay-home policy) and a small household size is necessary for curbing the outbreak in a locked-down town. The larger the household size and amount of time in the public, the longer the lockdown period needed.
12.04.2020	A data-driven model for predicting the course of COVID-19 epidemic with applications for China, Korea, Italy, Germany, Spain, UK and USA	medRxiv (not peer-reviewed) / Article	• The accuracy of the prediction of the peaks of the epidemic is validated using data in different regions in China showing the effects of different levels of quarantine. • The validated tool can be applied to other countries where Covid-19 has spread, and generally to future epidemics. • US is found to have the largest net infection rate, and is predicted to have the largest total infected cases (708K) and will take two weeks longer than Wuhan to reach its turning point, and one week longer than Italy and Germany.
14.04.2020	Standardization and Age-Distribution of COVID-19: Implications for Variability in Case Fatality and Outbreak Identification	medRxiv (not peer-reviewed) / Article	• Direct and indirect standardization are simple tools that provide key insights into between-country variation in the apparent size and severity of COVID-19 epidemics.
12.04.2020	A modified SEIR model to predict the COVID-19 outbreak in Spain and Italy: simulating control scenarios and multi-scale epidemics	medRxiv (not peer-reviewed) / Article	• The authors fit data to quarantined populations in order to account for the uncertainties in case reporting and study the scenario projections for the 17 individual regions (CCAA). • Results indicate that with data for March 23, the epidemics follow an evolution similar to the isolation of 1,5 percent of the population and if there were no effects of intervention actions it might reach a maximum of over 1.4M infected around April 27. • The effect on the epidemics of the ongoing partial confinement measures is yet unknown (an update of results with data until March 31st is included), but increasing the isolation around ten times more could drastically reduce the peak to over 100k cases by early April, while each day of delay in taking this hard containment scenario represents a 90 percent increase of the infected population at the peak.

Guidance and consensus statements

Publication Date	Title/URL	Journal/ Article type
09.04.2020	Strategies for the surveillance of COVID-19	European Centres for Disease Prevention and Control / Technical report
11.04.2020	Practical Guidance for Managing EMG Requests and Testing during the COVID-19 Pandemic	Muscle Nerve / Article
11.04.2020	Summarizing societal guidelines regarding bronchoscopy during the COVID-19 pandemic	Respirology / Commentary
09.04.2020	Corticosteroid Guidance for Pregnancy during COVID-19 Pandemic	American journal of perinatology
11.04.2020	COVID-19 and endocrine diseases. A statement from the European Society of Endocrinology	Endocrine / Viewpoint
11.04.2020	Urgent Considerations for the Neuro-oncologic Treatment of Patients with Gliomas During the COVID-19 Pandemic	Neuro Oncol / Article

Overviews, comments and editorials

Publication Date	Title/URL	Journal/ Article type
11.04.2020	Palliative care and the COVID-19 pandemic	The Lancet / Editorial
09.04.2020	Abortion during the Covid-19 Pandemic - Ensuring Access to an Essential Health Service	The New England journal of medicine / Perspective
09.04.2020	Disease Control, Civil Liberties, and Mass Testing - Calibrating Restrictions during the Covid-19 Pandemic	The New England journal of medicine / Perspective
09.04.2020	Challenges in lung cancer therapy during the COVID-19 pandemic	The Lancet Respiratory medicine / Comment
09.04.2020	COVID-19: immunopathology and its implications for therapy	Nature reviews. Immunology / Comment
13.04.2020	Oncology Practice During the COVID-19 Pandemic	JAMA / Viewpoint
09.04.2020	Cardiac and arrhythmic complications in patients with COVID-19	Journal of cardiovascular electrophysiology / Review

09.04.2020	Body Temperature Measurement to Prevent Pandemic COVID-19 in Hospitals in Taiwan: Repeated Measurement is Necessary	The Journal of hospital infection / Letter
09.04.2020	A framework for identifying regional outbreak and spread of COVID-19 from one-minute population-wide surveys	Nature medicine / Correspondence
09.04.2020	COVID-19 and the gastrointestinal tract: more than meets the eye	Gut / Commentary

Produced by the PHE COVID-19 Literature Digest Team

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