



International EPI Cell Daily Evidence Digest – 06/05/2020

This Daily Evidence Digest is produced by the PHE COVID-19 Literature Digest Team as a resource for professionals working in public health. We do not accept responsibility for the availability, reliability or content of the items included in this resource and do not necessarily endorse the views expressed within them. The papers are organised under the following themes:

- Diagnostics
- Genomics
- Epidemiology and clinical - children and pregnancy
- Epidemiology and clinical - risk factors
- Epidemiology and clinical - other
- Infection control
- Treatment
- Social sciences
- Miscellaneous
- Modelling
- Guidance, consensus statements and hospital resources (no digest)
- Overviews, comments and editorials (no digest)

Please note that we are including preprints (**highlighted in red**), which are preliminary reports of work that have NOT been peer-reviewed. They should not be relied on to guide clinical practice or health-related behaviour and should NOT be reported in news media as established information.

Diagnostics

Publication Date	Title/URL	Journal/Article type	Digest
05.05.2020	Can Chest CT Features Distinguish Patients With Negative From Those With Positive Initial RT-PCR Results for Coronavirus Disease (COVID-19)?	AJR Am J Roentgenol / Original research	<ul style="list-style-type: none">• Study to explore the value of CT in the diagnosis of COVID-19 in patients with negative initial results of RT-PCR testing.• In 21 patients with symptoms who were evaluated, the main CT features were ground-glass opacity (95%) and consolidation (72%) with a subpleural

			<p>distribution (100%). The other CT features included air bronchogram (57%), vascular enlargement (67%), interlobular septal thickening (62%), and pleural effusions (19%).</p> <ul style="list-style-type: none"> • Compared with that in the group with positive initial RT-PCR results, CT of the group with negative initial RT-PCR results was less likely to show pulmonary consolidation ($p < 0.05$).
05.05.2020	Is the HScore useful in COVID-19?	The Lancet / Correspondence	<ul style="list-style-type: none"> • Emerging clinical data in severe COVID-19 infection highlight HScore limitations. • Leukopenia increases the likelihood of sHLH in the HScore, whereas severe COVID-19 has leukocytosis with leukocyte subset lymphopenia. The HScore misses this important distinction. • Although hyperferritinaemia, a hallmark of sHLH, occurs in severe COVID-19, ferritin concentrations rarely reach the HScore threshold of 2000.0 ng/mL until late in disease, limiting early intervention.
30.04.2020	Application of Lung Ultrasound during the COVID-19 Pandemic: A Narrative Review	Anesth Analg / Narrative review	<ul style="list-style-type: none"> • Review of ultrasound findings reported from a number of studies and case reports which discusses the unifying findings from COVID-19 patients as well as from the avian (H7N9) and H1N1 influenza epidemics. • The authors discuss the potential role for portable point-of-care ultrasound (PPOCUS) as a safe and effective bedside option in the initial evaluation, management, and monitoring of disease progression in patients with confirmed or suspected COVID-19 infection.
04.05.2020	Multicenter Evaluation of the Cepheid Xpert Xpress SARS-CoV-2 Test	Journal of Clinical Microbiology / Article	<ul style="list-style-type: none"> • The authors evaluated the analytical and clinical performance characteristics of the Xpert® Xpress SARS-CoV-2 (Xpert) test, a rapid, automated molecular test for SARS-CoV-2. • The Xpert test provided sensitive and accurate detection of SARS-CoV-2 in a variety of upper and lower respiratory tract specimens. • The high sensitivity and fast time to results of approximately 45 minutes may impact patient management.
04.05.2020	Artificial intelligence to codify lung CT in Covid-19 patients	La Radiologia Medica / Short communication	<ul style="list-style-type: none"> • The authors discuss the benefits of using artificial intelligence software for diagnosing COVID-19. • They focus in particular on thoracic VCAR, which can generate a clear, fast and concise report that communicates vital medical information to referring physicians.
29.04.2020	Inflammatory markers in Covid-19 Patients: a systematic review and meta-analysis	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • In this meta-analysis, the authors evaluated the White blood cell and lymphocyte count, NLR and CRP titre in COVID-19 to use these findings to improve diagnosis. • Twelve studies were included in the analysis, all of which were conducted in China in the year 2020.

			<ul style="list-style-type: none"> • Results showed that inflammatory markers increase in patients with Covid-19
05.05.2020	Rapid development of COVID-19 rapid diagnostics for low resource settings: accelerating delivery through transparency, responsiveness, and open collaboration	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • The authors present an open and transparent consortium for the rapid development of COVID-19 rapid diagnostics tests. • They report diagnostic accuracy data on the Mologic manufactured IgG COVID-19 ELISA. <ul style="list-style-type: none"> • This is the first in a series of Mologic products for COVID-19, which will be deployed for COVID-19 diagnosis, contact tracing and sero-epidemiological studies to estimate disease burden and transmission with a focus on ensuring access, affordability, and availability to lowest resource settings
29.04.2020	Antibody Profiling and Prevalence in the US population during the SARS-CoV2 Pandemic	MedRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • A protein microarray technology was used to detect the plurality of antibody response to four novel antigens namely S1 glycoprotein, Receptor binding domain (RBD), S2 glycoprotein and Nucleoprotein of SARS-CoV2 using serum samples. • The three main subclasses of antibodies IgM, IgA and IgG were analysed to see the variations in immune responses in the affected population and compared to their microbial RT-PCR based NP swab results. The clinical sensitivity and specificity were determined to be 98.1% and 98.6%. • Multiplex testing enables higher sensitivity and specificity which is essential while establishing exposure on a population scale.

Genomics

Publication Date	Title/URL	Journal/Article type	Digest
04.05.2020	Rapid reconstruction of SARS-CoV-2 using a synthetic genomics platform	Nature / Unedited manuscript	<ul style="list-style-type: none"> • The authors show the full functionality of a yeast-based synthetic genomics platform to genetically reconstruct diverse RNA viruses, including members of the Coronaviridae, Flaviviridae and Paramyxoviridae families. • They have been able to engineer and resurrect chemically-synthesized clones of the recent epidemic SARS-CoV-2(4) in only a week after receipt of the synthetic DNA fragments.
04.05.2020	Site-specific glycan analysis of the SARS-CoV-2 spike	Science / Report	<ul style="list-style-type: none"> • This analysis enables mapping of the glycan-processing states across the trimeric 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.

30.04.2020	The SARS-CoV-2 Exerts a Distinctive Strategy for Interacting with the ACE2 Human Receptor	Viruses / Article	<ul style="list-style-type: none"> • To gain insight into the high infection rate of the SARS-CoV-2 virus, the authors compare the interaction between the human ACE2 receptor and the SARS-CoV-2 spike protein with that of other pathogenic coronaviruses using molecular dynamics simulations. • The SARS-CoV-2-ACE2 complex contains a higher number of contacts, a larger interface area, and decreased interface residue fluctuations.
30.04.2020	Codon Usage and Phenotypic Divergences of SARS-CoV-2 Genes	Viruses / Article	<ul style="list-style-type: none"> • Study comparing the codon usage of SARS-CoV-2 with that of other viruses belonging to the subfamily of Orthocoronavirinae. • They show that the two integral membrane proteins (matrix and envelope) tend to evolve slowly by accumulating nucleotide mutations on their corresponding genes. • Conversely, genes encoding nucleocapsid (N), viral replicase and spike proteins (S), although they are regarded as are important targets for the development of vaccines and antiviral drugs, tend to evolve faster in comparison to the two genes mentioned above.
03.05.2020	Large scale genomic analysis of 3067 SARS-CoV-2 genomes reveals a clonal geodistribution and a rich genetic variations of hotspots mutations	bioRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • Authors analysed 3,067 SARS-CoV-2 genomes isolated from 59 countries, using comparative genomics analysis to trace profiles of whole-genome mutations and compare frequency of each mutation in the studied population. Accumulation of mutations during epidemic period with their geographic locations was also monitored. • Results showed 716 site mutations, of which 457 (64%) had a non-synonymous effect. Frequencies of mutated alleles revealed the presence of 39 recurrent non-synonymous mutations, including 10 hotspot mutations with a prevalence higher than 0.10 in this population and distributed in six genes of SARS-CoV-2.
27.04.2020	Genome-wide variations of SARS-CoV-2 infer evolution relationship and transmission route	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • Authors retrieved genomic sequences of 373 SARS-CoV-2 strains from multiple databases and performed genome-wide variation analysis. • By comparing the detection capabilities of primers in different countries, the SARS-CoV-2 nucleotide variation may only affect molecular detection of very few strains. The differences in the transmissibility, pathogenicity and clinical manifestations of different types of strains require further investigations.
02.05.2020	Structural and Functional Implications of Non-synonymous Mutations in the Spike protein of 2,954 SARS-CoV-2 Genomes	bioRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • Detailed analysis of gene encoding the spike (S) protein in strains across globe shows non-synonymous mutations on 54 amino acid residues. Authors pinpoint 4 novel mutations in the region that interacts with the human ACE2 receptor (RBD). • Further in silico molecular docking analyses suggest that these RBD

			mutations could alter the binding affinity of S-protein with ACE2 that may lead to changes in SARS-CoV-2 infectivity.
02.05.2020	Rapid adaptation of SARS-CoV-2 in BALB/c mice: Novel mouse model for vaccine efficacy	bioRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • Reports the rapid adaption of SARS-CoV-2 in BALB/c mice, based on which a convenient, economical and effective animal model was developed. • Evaluated in vivo protective efficacy of an RBD-based SARS-CoV-2 subunit vaccine; elicited highly potent neutralizing antibodies, conferred full protection against SARS-CoV-2 MACSp6 challenge.
05.05.2020	Cross-talk between the airway epithelium and activated immune cells defines severity in COVID-19	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • The authors reveal the different types and states of airway epithelial cells that are vulnerable for SARS-CoV-2 infection. • They observed a two- to threefold increase of cells expressing the SARS-CoV-2 entry receptor ACE2 within the airway epithelial cell compartment. • In critical patients, increased expression of CCL2, CCL3, CCL5, CXCL9, CXCL10, IL8, IL1B and TNF in macrophages was identified as a likely cause of a hyperinflammatory lung pathology. • The study suggests an immunomodulatory therapy along the CCL2, CCL3/CCR1 axis as a promising option to prevent and treat critical course of COVID-19
30.04.2020	Single-cell Transcriptome Analysis Indicates New Potential Regulation Mechanism of ACE2 and NPs signaling among heart failure patients infected with SARS-CoV-2	MedRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • In this study, the authors retrospectively analysed single-centre case series of 91 patients with COVID-19 in China; 46 (50.5%) patients exhibited cardiac dysfunction as indicated by elevated Natriuretic Peptides B (BNP) levels. • The results indicate that ACE2 is predominantly enriched in cardiomyocytes (CMs), endothelial cells, fibroblasts and smooth muscle cells in normal heart.

Epidemiology and clinical - children and pregnancy

Publication Date	Title/URL	Journal/Article type	Digest
05.05.2020	ACE2, COVID-19, and ACE Inhibitor and ARB Use during the Pandemic: The Pediatric Perspective	Hypertension / Review	<ul style="list-style-type: none"> • Review highlighting the relationship of COVID-19 with hypertension, use of angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers, and lifetime risk of cardiovascular disease from the paediatric perspective.
04.05.2020	Potential influence of COVID-19/ACE2 on the female reproductive system	Molecular Human Reproduction / Accepted manuscript	<ul style="list-style-type: none"> • The available evidence suggests that ACE2 is widely expressed in the ovary, uterus, vagina and placenta. • The authors believe that apart from droplets and contact transmission, the possibility of mother-to-child and sexual transmission also exists. • Ang II, ACE2 and Ang-(1-7) regulate follicle development and ovulation,

			modulate luteal angiogenesis and degeneration, and also influence the regular changes in endometrial tissue and embryo development.
04.05.2020	Severe Pediatric COVID-19 Presenting With Respiratory Failure and Severe Thrombocytopenia	Pediatrics / Case report	<ul style="list-style-type: none"> • Case report of a 12-year-old girl with no past medical history who presented with fever, cough and vomiting. Laboratory evaluation revealed severe thrombocytopenia and elevated markers of inflammation. The patient progressed to respiratory failure and testing for the SARS-CoV-2 returned positive. • She was treated with intravenous immunoglobulin (IVIG) and steroids with prompt improvement in platelets. • After azithromycin and hydroxychloroquine were given without improvement, the patient received tocilizumab and remdesivir with significant clinical benefit soon afterwards.

Epidemiology and clinical - risk factors

Publication Date	Title/URL	Journal/Article type	Digest
05.05.2020	BAME COVID-19 DEATHS – What do we know? Rapid Data & Evidence Review	CEBM Research / Rapid review	<ul style="list-style-type: none"> • Evidence indicates markedly higher mortality risk from COVID-19 among Black, Asian and Minority Ethnic (BAME) groups, but deaths are not consistent across BAME groups. • Similarly, adverse outcomes are seen for BAME patients in intensive care units and amongst medical staff and Health and Care Workers. • The exact reasons for this increased risk and vulnerability from COVID-19 in BAME populations are not known.
05.05.2020	Epidemiology of and Risk Factors for Coronavirus Infection in Health Care Workers: A Living Rapid Review	Ann Intern Med / Living review	<ul style="list-style-type: none"> • Living review to examine the burden of SARS-CoV-2, SARS-CoV-1, and MERS-CoV on HCWs, looking at 64 studies. • Health care workers accounted for a significant proportion of coronavirus infections and may experience particularly high infection incidence after unprotected exposures. Illness severity was lower than in non-HCWs. Depression, anxiety, and psychological distress were common in HCWs during the coronavirus disease 2019 outbreak. • The strongest evidence on risk factors was on PPE use and decreased infection risk. No study evaluated PPE reuse. Certain exposures were associated with increased infection risk. Infection control training was associated with decreased risk.

27.04.2020	Seroprevalence of antibodies against SARS-CoV-2 among health care workers in a large Spanish reference hospital	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • Random sample of 578 Health care workers (HCW): 39 previously diagnosed with COVID-19, 14 had a positive rRT-PCR at recruitment, 54 were seropositive for IgM and/or IgG and/or IgA against SARS-CoV-2. • Seropositive higher in participants who reported any COVID-19 symptom. • IgM levels positively correlated with age, higher in participants 10 days+ since onset of symptoms and IgA levels were higher in symptomatic than asymptomatic subjects. • The seroprevalence of antibodies against SARS-CoV-2 among HCW was lower than expected.
29.05.2020	Risk of symptomatic Covid-19 among frontline healthcare workers	MedRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • The authors performed a prospective cohort study among 2,135,190 individuals using the COVID Symptom Tracker smartphone application since March 24, 2020 (United Kingdom) and March 29, 2020 (United States). • Among 2,035,395 community individuals and 99,795 frontline HCWs, they documented 5,545 incident reports of a positive Covid-19 test over 34,435,273 person-days. • Frontline HCWs had a significantly increased risk of symptomatic Covid-19 infection, which was highest among HCWs with inadequate access to PPE who cared for Covid-19 patients; however, adequate supplies of PPE did not completely mitigate high-risk exposure
01.05.2020	Association of Blood Glucose Control and Outcomes in Patients with COVID-19 and Pre-existing Type 2 Diabetes	Cell Metabolism / Clinical and translational report	<ul style="list-style-type: none"> • A cohort of 7,337 COVID-19 patients with or without diabetes was retrospectively studied. • Diabetes status increased the need for medical interventions during COVID-19, and the mortality risk. • Well-controlled blood glucose correlated with improved outcomes in infected patients.
30.04.2020	A clinical and biological framework on the role of visceral fat tissue and leptin in SARS-CoV-2 infection related respiratory failure	MedRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • A cross sectional study found the mean BMI was 31 kg/m² (range 24.8-48.4) for 31 SARS-CoV-2 ventilated patients and 26 kg/m² (range 22.4-33.5) for the 8 controls. • SARS-CoV-2 infected patients with a similar BMI as control patients appear to have significantly higher levels of serum leptin. • With these findings the authors designed a clinical and biological framework to explain clinical observations of deterioration in patients with obesity.
05.05.2020	Association of Use of Angiotensin-Converting Enzyme Inhibitors and Angiotensin II Receptor Blockers With Testing Positive for Coronavirus Disease 2019 (COVID-19)	JAMA Cardiol / Original investigation	<ul style="list-style-type: none"> • Overlap propensity score weighting showed no significant association of ACEI and/or ARB use with COVID-19 test positivity. • These clinical data support current professional society guidelines to not discontinue ACEIs or ARBs in the setting of the COVID-19 pandemic.

28.04.2020	The Chronic Kidney Disease and Acute Kidney Injury Involvement in COVID-19 Pandemic: A Systematic Review and Meta-analysis	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • Thirty-six trials were included in systematic review with a total of 6395 COVID-19 patients. • Comorbidity of chronic kidney disease (CKD) (OR = 3.28), complication of acute kidney injury (AKI) (OR = 11.02), serum creatinine (SMD = 0.68), abnormal serum creatinine (OR = 4.86), blood urea nitrogen (SMD = 1.95), abnormal blood urea nitrogen (OR = 6.53), received continuous renal replacement therapy (CRRT) (OR = 23.63) significantly increased in severe group. • Complication of AKI (OR = 13.92) and blood urea nitrogen (SMD = 1.18) were remarkably elevated in critical group than that in severe group
05.05.2020	Clinical characteristics and outcomes of cancer patients with COVID-19	J Med Virol / Research article	<ul style="list-style-type: none"> • Retrospective study of 52 patients aiming to analyse clinical characteristics and outcomes of cancer patients with COVID-19. • The infection rate of SARS-COV-2 in cancer patients was higher than the general population and cancer patients showed deteriorating conditions and poor outcomes.
04.05.2020	Genetic alteration, RNA expression, and DNA methylation profiling of coronavirus disease 2019 (COVID-19) receptor ACE2 in malignancies: a pan-cancer analysis	Journal of Hematology and Oncology / Letter to the editor	<ul style="list-style-type: none"> • Cancer has been identified as an individual risk factor for COVID-19. • This study for the first time curated both genetic and epigenetic variations of ACE2 in human malignancies.
30.04.2020	Associations between psychiatric disorders, COVID-19 testing probability and COVID-19 testing results: Findings from a population-based study	MedRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • The authors used data on COVID-19 testing in the UK Biobank (UKB) cohort to compare the prevalence of COVID-19 testing and test outcomes among individuals with psychiatric disorders to those without such diagnoses. • Individuals with psychiatric disorders were overrepresented among the 1 474 UKB participants with test data. • UKB participants with psychiatric disorders have been tested for COVID-19 more frequently than individuals without a psychiatric history.
29.04.2020	Clinical characteristics of 106 patients with neurological diseases and co-morbid coronavirus disease 2019: a retrospective study	MedRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • Describes the clinical characteristics of 106 patients with COVID-19 with co-morbid neurological symptoms in Wuhan, China. • Patients with co-morbid neurological diseases had an advanced age, a high rate of severe illness, and a high mortality rate.
05.05.2020	Smoking links to the severity of Covid-19: An update of a meta-analysis	J Med Virol / Letter	<ul style="list-style-type: none"> • Letter updating results previously published in "The impact of COPD and smoking history on the severity of Covid-19: A systemic review and meta-analysis", published in Journal of Medical Virology on 15 April, 2020 (https://dx.doi.org/10.1002/jmv.25889). • The results revealed the pooled OR of COPD and the development of severe Covid-19 was 4.38 (Fixed effect model, 95% CI: 2.34-8.20), while the OR of ongoing smoking was 1.98 (Fixed effect model, 95% CI: 1.29-3.05).

Epidemiology and clinical – other

Publication Date	Title/URL	Journal/Article type	Digest
05.05.2020	SARS-CoV-2 and influenza virus co-infection	The Lancet / Correspondence	<ul style="list-style-type: none"> The authors present four cases of SARS-CoV-2 and influenza co-infection, diagnosed simultaneously. This is the second known instance of co-infection.
30.04.2020	COVID-19 length of hospital stay: a systematic review and data synthesis	MedRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> The authors performed a systematic review to gather data on length of stay (LoS) of patients with COVID-19 in hospital and in ICU. They identified 52 studies, the majority from China (46/52); median hospital LoS ranged from 4 to 53 days within China, and 4 to 21 days outside of China, across 45 studies. Patients with COVID-19 in China appeared to remain in hospital for longer than elsewhere.
04.05.2020	Evidence Supporting Transmission of Severe Acute Respiratory Syndrome Coronavirus 2 While Presymptomatic or Asymptomatic	Emerging Infectious Diseases / Online report	<ul style="list-style-type: none"> The incidence of asymptomatic compared with symptomatic SARS-CoV-2 infection needs to be determined. The extent of pre-symptomatic or asymptomatic SARS-CoV-2 infection may be clarified by studies using serial virologic data, serologic data, or a combination of both in observational cohorts or surveillance systems. If a substantial proportion of infections are asymptomatic, enhanced testing strategies may be needed to detect these persons.
01.05.2020	Characteristics of lymphocyte subsets and their predicting values for the severity of COVID-19 patients	MedRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> This study retrospectively analysed the clinical and laboratory data of 16 COVID-19 patients and found that the absolute counts of three T-cells (CD3+, CD4+, and CD8+) were significantly lower in the moderate and severe patients than those in mild patients and were significantly lower in severe patients than in moderate patients on admission.
05.05.2020	Prediction of severe illness due to COVID-19 based on an analysis of initial Fibrinogen to Albumin Ratio and Platelet count	Platelets / Research study	<ul style="list-style-type: none"> Retrospective analysis of 113 patients with SARS-CoV-2 infection aiming to describe the parameters of coagulation function and reveal the risk factors of developing severe disease. Data showed that Fibrinogen, FAR, and D-dimer were higher in the severe patients, while PLTcount, Alb were much lower. This study revealed that FAR and PLT count were independent risk factors for severe illness and the severity of COVID-19 might be excluded when FAR<0.0883 and PLT count>135*10⁹/L.
04.05.2020	Using IL-2R/lymphocyte for predicting the clinical progression of patients with COVID-19	Clinical and Experimental Immunology / Original article	<ul style="list-style-type: none"> Lymphopenia and increased levels of cytokines were closely associated with the disease severity. IL-2R/lymphocyte was a prominent biomarker for early identification of severe COVID-19 and predicting the clinical progression of the disease.

04.05.2020	SARS-CoV-2 can induce brain and spine demyelinating lesions	Acta Neurochirurgica / Case report	<ul style="list-style-type: none"> • SARS-CoV-2 can attack the central nervous system (CNS) in the early stages of infection. • Prompt invasive treatment should be adopted to avoid hypoxic neurotoxicity and prevent CNS injuries.
04.05.2020	Neurological manifestations of patients with COVID-19: potential routes of SARS-CoV-2 neuroinvasion from the periphery to the brain	Frontiers of Medicine / Review	<ul style="list-style-type: none"> • In some immune-compromised individuals, the virus may invade the brain through multiple routes, such as the vasculature and peripheral nerves. • In addition to drug treatments, such as pharmaceuticals and traditional Chinese medicine, non-pharmaceutical precautions, including facemasks and hand hygiene, are critically important.
04.05.2020	High risk of thrombosis in patients with severe SARS-CoV-2 infection: a multicenter prospective cohort study	Intensive Care Medicine / Article	<ul style="list-style-type: none"> • Despite anticoagulation, a high number of patients with acute respiratory distress syndrome (ARDS) secondary to COVID-19 developed life-threatening thrombotic complications. • Higher anticoagulation targets than in usual critically ill patients should therefore probably be suggested.
05.05.2020	Incidence of venous thromboembolism in hospitalized patients with COVID-19	J Thromb Haemost / Original article	<ul style="list-style-type: none"> • Single-centre cohort study of 198 hospitalized patients with COVID-19. • The observed risk for VTE in COVID-19 is high, particularly in ICU patients, which should lead to a high level of clinical suspicion and low threshold for diagnostic imaging for DVT or PE.
03.04.2020	Gastrointestinal Manifestations of SARS-CoV-2 Infection and Virus Load in Fecal Samples from the Hong Kong Cohort and Systematic Review and Meta-analysis	Gastroenterology / Case report and systematic review	<ul style="list-style-type: none"> • Among 59 patients studied, 15 patients (25.4%) had gastrointestinal symptoms and 9 patients (15.3%) had stool that tested positive for virus RNA. • In a meta-analysis of 60 studies, comprising 4243 patients, the pooled prevalence of all gastrointestinal symptoms was 17.6%; 11.8% of patients with non-severe COVID-19 had gastrointestinal symptoms and 17.1% of patients with severe COVID-19 had gastrointestinal symptoms.
05.05.2020	Hepatic involvement in COVID-19 patients: pathology, pathogenesis and clinical implications [Review]	J Med Virol / Review	<ul style="list-style-type: none"> • Review of hepatic injury occurring in COVID-19. • Mild increase in sinusoidal lymphocytic infiltration and multifocal hepatic necrosis are the main pathologic changes. Direct viral induced cellular injuries and potential hepatotoxicity from therapeutic drugs are two likely underlying mechanisms. • In addition, pre-existing chronic liver disease exacerbated during COVID-19, and COVID-19-related hyper-inflammatory reactions may contribute to liver injury as well.
26.04.2020	Liver Chemistries in COVID-19 Patients with Survival or Death: A Meta-Analysis	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • Meta-analysis of 18 studies - search on liver damage in COVID-19 patients with death or survival - which included a total of 2,862 patients. • Authors describe three patterns of liver impairment: hepatocellular injury, cholestasis, and hepatocellular dysfunction. Deaths linked to different liver chemistries from those are discharged alive.

04.05.2020	Early recovery following new onset anosmia during the COVID-19 pandemic - an observational cohort study	Journal of otolaryngology - Head and Neck Surgery / Original research article	<ul style="list-style-type: none"> • This paper presents the results of an online Survey of patients reporting self-diagnosed new onset smell and taste disturbance during the COVID-19 pandemic, with 1 week follow-up. • While early recovery rates are encouraging, long term rates will need to be further investigated and there may be an increase in patients with persistent post-viral loss as a result of the pandemic.
05.05.2020	The Prevalence of Olfactory and Gustatory Dysfunction in COVID-19 Patients: A Systematic Review and Meta-analysis	Otolaryngol Head Neck Surg / Systematic review	<ul style="list-style-type: none"> • SR and meta-analysis to determine the pooled global prevalence of olfactory and gustatory dysfunction in patients with COVID-19. • Olfactory and gustatory dysfunction are common and may represent early symptoms in the clinical course of infection. Increased awareness of this fact may encourage earlier diagnosis and treatment, as well as heighten vigilance for viral transmission.

Infection control

Publication Date	Title/URL	Journal/Article type	Digest
05.05.2020	Contact tracing for COVID-19: current evidence, options for scale-up and an assessment of resources needed	European Centre For Disease Control and Prevention / Technical report	<ul style="list-style-type: none"> • It is possible to scale up contact tracing by adapting traditional contact tracing approaches to available local resources and by using a number of resource-saving measures. • This document outlines a number of resource measures including the use of well-trained non-public-health staff and volunteers; repurposing existing resources such as call centres; reducing the intensity of contact follow-up and using new technologies such as contact management software and mobile apps.
04.05.2020	Effect of non-pharmaceutical interventions to contain COVID-19 in China	Nature / Unedited manuscript	<ul style="list-style-type: none"> • The early detection and isolation of cases was estimated to have prevented more infections than travel restrictions and contact reductions, but combined non-pharmaceutical interventions (NPIs) achieved the strongest and most rapid effect.
04.05.2020	Ethics of instantaneous contract tracing using mobile phone apps in the control of the COVID-19 pandemic	Journal of Medical Ethics / Current controversy	<ul style="list-style-type: none"> • The proposed use of mobile phone data for 'intelligent physical distancing' in such contexts raises a number of important ethical questions. • The authors outline some ethical considerations that need to be addressed in any deployment of this kind of approach as part of a multidimensional public health response.
05.05.2020	Can N95 Respirators Be Reused after Disinfection? How Many Times?	ACS Nano / Article	<ul style="list-style-type: none"> • Study investigating multiple commonly used disinfection schemes on media with particle filtration efficiency of 95%. • They found that heat (≤ 85 °C) under various humidities ($\leq 100\%$ relative

			<p>humidity, RH) was the most promising, non-destructive method for the preservation of filtration properties in melt blown fabrics as well as N95-grade respirators.</p> <ul style="list-style-type: none"> • Ultraviolet (UV) irradiation was a secondary choice, which was able to withstand 10 cycles of treatment and showed small degradation by 20 cycles.
05.05.2020	Airway management for COVID-19: a move towards universal videolaryngoscopy?	The Lancet Respiratory Medicine / Spotlight	<ul style="list-style-type: none"> • The authors believe that all patients with COVID-19, and ideally every patient during the pandemic, should be intubated using video laryngoscopy.
30.04.2020	COVID-19 Surface Persistence: A Recent Data Summary and Its Importance for Medical and Dental Settings	Int J Environ Res Public Health / Review	<ul style="list-style-type: none"> • Review of the literature concerning the persistence of the different coronaviruses in the environment as well as in medical and dental settings.
26.04.2020	Stability and infectivity of coronaviruses in inanimate environments	World J Clin Cases / Systematic review	<ul style="list-style-type: none"> • Review summarizing data on the persistence of different coronaviruses on inanimate surfaces from all retrieved reports with experimental evidence on the duration persistence of coronaviruses on any type of surface included. • SARS-CoV-2 can be sustained in air in closed unventilated buses for at least 30 min without losing infectivity. • Absorbent materials like cotton are safer than unabsorbent materials for protection from virus infection. The risk of transmission via touching contaminated paper is low.

Treatment

Publication Date	Title/URL	Journal/Article type	Digest
05.05.2020	Tocilizumab for the Treatment of Severe COVID-19	J Med Virol / Retrospective study	<ul style="list-style-type: none"> • Retrospective review of 25 patients with laboratory-confirmed severe COVID-19 who received tocilizumab and completed 14 days of follow up. • All patients received at least two concomitant investigational antiviral agents. • The majority (92%) of patients experienced at least one adverse event. However, it is not possible to ascertain which adverse events were directly related to tocilizumab therapy.
01.05.2020	Profiling COVID-19 pneumonia progressing into the cytokine storm syndrome: results from a single Italian Centre study on tocilizumab versus standard of care	MedRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • Between February 29 to April 6, 2020, 111 consecutive hospitalized patients with COVID-19 pneumonia, including 42 severe cases treated with tocilizumab (TOCI) , and 69 standard of care patients (SOC). • In the TOCI group, all received anti-viral therapy and 40% also received glucocorticoids; 62% of cases were ventilated and there were 3 deaths with 7/26 cases remaining on ventilators, without improvement, and 17/26

			<p>developed bacterial superinfection; there were one fatality and 1 serious bacterial superinfection in the 15 non-invasive ventilation patients; of the 69 cases in SOC, there was no fatalities and no bacterial complications.</p> <ul style="list-style-type: none"> • Higher inflammatory markers, more superimposed infections and worse outcomes characterized ventilated TOCI cases compared to ward based TOCI therapy.
18.03.2020	Experimental Treatment with Favipiravir for COVID-19: An Open-Label Control Study	Engineering (Beijing, China) / Research article	<ul style="list-style-type: none"> • Open-label nonrandomized control study examining the effects of Favipiravir (FPV) versus Lopinavir (LPV)/ritonavir (RTV) for the treatment of COVID-19. • A shorter viral clearance time was found for the FPV arm versus the control arm. The FPV arm also showed significant improvement in chest imaging compared with the control arm, with an improvement rate of 91.43% versus 62.22% (P = 0.004). After adjustment for potential confounders, the FPV arm also showed a significantly higher improvement rate in chest imaging. • Multivariable Cox regression showed that FPV was independently associated with faster viral clearance. In addition, fewer adverse reactions were found in the FPV arm than in the control arm.
04.05.2020	A human monoclonal antibody blocking SARS-CoV-2 infection	Nature Communications / Article	<ul style="list-style-type: none"> • The authors report a human monoclonal antibody that neutralizes SARS-CoV-2 (and SARS-CoV) in cell culture. • This cross-neutralizing antibody targets a communal epitope on these viruses and may offer potential for prevention and treatment of COVID-19.
27.04.2020	Review and methodological analysis of trials currently testing treatment and prevention options for the novel coronavirus disease (COVID-19) globally	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • Review summarises and methodologically appraised the ongoing 371 therapeutic and preventive trials for COVID-19: 309 trials evaluating therapeutic management options, 23 studies assessing preventive strategies and 3 studies examining both. • Interventional treatment studies were mostly randomised (n=150, 76%) and open-label (n=73, 37%) with a median number of planned inclusions of 90 (IQR 40-200). Major categories of interventions that are currently being investigated are discussed.
05.05.2020	An Evidence Based Perspective on mRNA-SARS-CoV-2 Vaccine Development	Med Sci Monit / Review article	<ul style="list-style-type: none"> • Review describing the background to the rationale for the development of mRNA-based SARS-CoV-2 vaccines and the current status of the mRNA-1273 vaccine.
05.05.2020	Lupus Anticoagulant and Abnormal Coagulation Tests in Patients with Covid-19	New England Journal of Medicine / Correspondence	<ul style="list-style-type: none"> • Prolonged activated partial-thromboplastin time (aPTT) have been reported in patients with Covid-19. • This finding could be seen as a reason to avoid the use of anticoagulation at both therapeutic and prophylactic doses.

04.05.2020	Considerations for Post-acute Rehabilitation for Survivors of COVID-19	JMIR Public Health and Surveillance / Accepted manuscript	<ul style="list-style-type: none"> • Three areas relevant to rehabilitation after COVID-19 were identified. • Guidelines for rehabilitation (physiotherapy, occupational therapy, speech-language pathology) following COVID-19 have been made, with respect to recovery of the respiratory system as well as mobility and function.
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Social sciences

Publication Date	Title/URL	Journal/Article type	Digest
05.05.2020	Occurrence, prevention, and management of the psychological effects of emerging virus outbreaks on healthcare workers: rapid review and meta-analysis	BMJ / Research	<ul style="list-style-type: none"> • Effective interventions are available to help mitigate the psychological distress experienced by staff caring for patients in an emerging disease outbreak. • These interventions were similar despite the wide range of settings and types of outbreaks covered in this review, and thus could be applicable to the current covid-19 outbreak.
04.05.2020	Mental health, risk factors, and social media use during the COVID-19 epidemic and cordon sanitaire among the community and health professionals in Wuhan, China	JMIR Public Health Surveillance / Preprint	<ul style="list-style-type: none"> • The authors examined risk factors, including the use of social media use, for probable anxiety and depression in the community and health professionals in the epicentre, Wuhan, China. • The internet could be harnessed for telemedicine and restoring daily routines, yet caution is warranted on excessive time spent on COVID-19 news on social media given the ‘infodemic’ and emotional contagion through online social networks.
28.04.2020	Mental Health of Clinical Staff Working in High-Risk Epidemic and Pandemic Health Emergencies: A Rapid Review of the Evidence and Meta-Analysis	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • Rapid review to estimate the additional mental health burden of working directly with infected patients during epidemic and pandemic health emergencies. • Risk factors: being a nurse, seeing colleagues infected, experiencing quarantine, non-voluntary role assignment, and experiencing stigma. • Protective factors included team and institutional support, use and faith in infection prevention measures, sense of professional duty and altruistic acceptance of risk. • Formal psychological support services valued by frontline staff; however those with highest burden of mental health difficulties least likely to request or receive support.
04.05.2020	Implementing a Protocol to Assess Real-Time Mental Health Challenges of COVID-19 in Individuals with Serious Mental Illnesses	JMIR Research Protocols / Preprint	<ul style="list-style-type: none"> • The aim of this study is to examine the mental health impact of COVID-19 and social distancing behaviours among persons with serious mental illness and the behaviours taken to prevent COVID-19 infection. • Participants will include individuals with serious mental illness (e.g.,

			schizophrenia, bipolar disorder) and non-psychiatric control participants who are currently or previously participated in several ongoing parent observational studies.
04.05.2020	An e-mental health intervention to support burdened people in times of the COVID-19 pandemic: CoPE It	Journal of Public Health / Article	<ul style="list-style-type: none"> • The e-mental health intervention 'CoPE It' offers manualized, evidence-based psychotherapeutic/psychological support to overcome psychological distress in times of COVID-19. • E-mental health approaches offer great possibilities to support burdened people during the SARS-CoV-2 pandemic effectively.
04.05.2020	Evidence from internet search data shows information-seeking responses to news of local COVID-19 cases	Proceedings of the National Academy of Sciences of the United States of America / Research article	<ul style="list-style-type: none"> • The authors found that people respond to the first report of COVID-19 in their area by immediately seeking information about COVID-19, as measured by searches for coronavirus, coronavirus symptoms, and hand sanitizer. • Searches for information regarding community-level policies (e.g., quarantine, school closures, testing) or personal health strategies (e.g., masks, grocery delivery, over-the-counter medications) do not appear to be immediately triggered by first reports.

Miscellaneous

Publication Date	Title/URL	Journal/Article type	Digest
27.04.2020	Global academic response to COVID-19: Cross-sectional study	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • Cross-sectional bibliometric review of COVID-19 literature - global academic response during early stages; explore responsiveness of investigators, editorial teams, and publishers. A parallel search of Middle East Respiratory Syndrome (MERS) literature was performed for comparison. • Most COVID-19 studies were clinical reports of which majority were case series and single cases. • Times from manuscript submission to acceptance and acceptance to publication were strikingly shorter for COVID-19. • Almost all COVID-19 and MERS studies were open-access.

Modelling

Publication Date	Title/URL	Journal/Article type	Digest
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05.05.2020	Segmentation and shielding of the most vulnerable members of the population as elements of an exit strategy from COVID	University of Edinburgh (not peer reviewed) / Preprint	<ul style="list-style-type: none"> • The authors demonstrate that the adoption of a segmenting and shielding strategy (S&S) could increase scope to partially exit COVID19 lockdown while limiting the risk of an overwhelming second wave of infection • They illustrate the S&S strategy using a mathematical model that segments the vulnerable population and their closest contacts, the “shielders”. • They explore the effects on the epidemic curve of a gradual ramping up of protection for the vulnerable population and a gradual ramping down of restrictions on the non-vulnerable population over a period of 12 weeks after lockdown
29.04.2020	How and when to end the COVID-19 lockdown: an optimisation approach	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • Authors applied an optimal control framework to an adapted Susceptible-Exposure-Infection-Recovery (SEIR) model framework to investigate efficacy of two potential lockdown release strategies, with UK population as test case. • Ending quarantine for entire population simultaneously is high-risk, gradual re-integration approach more reliable. Worst-case scenario of gradual release more manageable than worst-case scenario of an on-off strategy. • Optimal strategy: release approx. half population two-to-four weeks from end of an initial infection peak, wait three-to-four months to allow for a second peak before releasing everyone else.
27.04.2020	Better Strategies for Containing COVID-19 Epidemics --- A Study of 25 Countries via an Extended Varying Coefficient SEIR Model	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • Extended SEIR model that allows infections in both the exposed and infected states, the key epidemic parameters are estimated from each of 25 country's data • Quicker control measures significantly reduce the average reproduction numbers and shorten the time length to infection peaks. If the swift control measures of Korea and China were implemented, average reductions of 88% in the confirmed cases and 80% in deaths would have been attained for the other 23 countries from start to April 10. • Effects of earlier or delayed interventions in the US and the UK are experimented
05.05.2020	Individualized prediction nomograms for disease progression in mild COVID-19	J Med Virol / Article	<ul style="list-style-type: none"> • Description of the development of two models for predicting the requirement of oxygen support in mild COVID-19, comprising common symptoms (fever and sputum), underlying diseases (diabetes and coronary heart disease) and blood routine test.
28.04.2020	Risk prediction for poor outcome and death in hospital in-patients with COVID-19: derivation in Wuhan, China and external validation in London, UK	medRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • Study to derive and validate risk prediction models for poor outcome and death in adult inpatients with COVID-19. • Data from Wuhan, China used logistic regression with death and poor outcome (death or severe disease) as outcomes. Best performing models externally validated in data from London, UK. • Prediction model using demography and routinely-available laboratory

			tests performed very well in internal validation in lower-risk derivation population, less well in much higher-risk external validation population.
28.04.2020	Warmer weather and global trends in the coronavirus COVID-19	MedRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • The authors proposed a new concept of environmental infection rate (RE), based on floating time of respiratory droplets in the air and inactivation rate of virus • As the weather warms, its distribution area expands and extends to higher latitudes of northern hemisphere, reaching its maximum in April, and then shrinking northward. • The high modelled RE values up to July, however, suggested that warmer weather will not stop COVID-19 from spreading
29.04.2020	Does weather affect the growth rate of COVID-19, a study to comprehend transmission dynamics on human health	MedRxiv (not peer reviewed) / Article	<ul style="list-style-type: none"> • This study focuses on the relationship between environmental parameters and the growth rate of COVID-19. • The statistical analysis suggests that the temperature changes retarded the growth rate and found that -6.28°C and +14.51°C temperature is the favourable range for COVID-19 growth. • Temperature is the most influential parameter that reduces the growth at the rate of 13-16 cases/day with a 1°C rise in temperature

Guidance, consensus statements and hospital resources

Publication Date	Title/URL	Journal/Article type
05.05.2020	Molecular testing for acute respiratory tract infections: clinical and diagnostic recommendations from the IDSA's Diagnostics Committee	Clin Infect Dis / Guidance
03.05.2020	Emergency Medical Services resource capacity and competency amid COVID-19 in the United States: Preliminary findings from a national survey	Heliyon / Survey results
04.05.2020	Interim Guidance for Basic and Advanced Life Support in Children and Neonates With Suspected or Confirmed COVID-19	Pediatrics / Guidance

Produced by the PHE COVID-19 Literature Digest Team

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