



International EPI Cell Daily Evidence Digest – 26/05/2020

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
- Serology and immunology
- 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Please note that we are including preprints (**highlighted in red**), which are preliminary reports of work that have NOT been peer-reviewed.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
18.05.2020	Point-of-Care Diagnostic Tests for Detecting SARS-CoV-2 Antibodies: A Systematic Review and Meta-Analysis of Real-World Data	J Clin Med / Systematic review	<ul style="list-style-type: none">• The present systematic review and meta-analysis was undertaken to explore the feasibility of rapid diagnostic tests in the management of the COVID-19 outbreak.

			<ul style="list-style-type: none"> Based on ten studies, the authors conclude that: (1) rapid diagnostic tests for COVID-19 are necessary, but should be adequately sensitive and specific; (2) few studies have been carried out to date; (3) the studies included are characterized by low numbers and low sample power, and (4) in light of these results, the use of available tests is currently questionable for clinical purposes and cannot substitute other more reliable molecular tests, such as assays based on RT-PCR.
23.05.2020	Laboratory findings of COVID-19: a systematic review and meta-analysis	Scand J Clin Lab Invest / Systematic review	<ul style="list-style-type: none"> Systematic review with a meta-analysis to assess laboratory findings in patients with COVID-19. Of the 4,663 patients included, the most prevalent laboratory finding was increased C-reactive protein, followed by decreased albumin, increased erythrocyte sedimentation rate, decreased eosinophils, increased interleukin-6, lymphopenia, and increased lactate dehydrogenase. A meta-analysis of seven studies with 1905 patients showed that increased CRP, lymphopenia, and increased LDH were significantly associated with severity.
21.05.2020	Spatial and temporal dynamics of SARS-CoV-2 in COVID-19 patients: A systematic review	medRxiv (non-peer reviewed) / Systematic review	<ul style="list-style-type: none"> Systematic review to gain overview from published studies of the duration of viral detection and viral load in COVID-19 patients, stratified by specimen type, clinical severity and age. Analysis: consistent viral detection from specimen from upper respiratory tract (URT), lower respiratory tract (LRT) and faeces, irrespective of severity of COVID-19. Suggests longer duration in LRT compared to URT. Indication of longer duration of viral detection in faeces and the URT for moderate-severe patients was shown. Viral load peaked in URT within first week of infection, whereas maximum viral load observed to occur later and within the second week of infection in LRT.

Serology and immunology

Publication Date	Title/URL	Journal/ Article type	Digest
22.05.2020	Safety, tolerability, and immunogenicity of a recombinant adenovirus type-5 vectored COVID-19 vaccine: a dose-escalation, open-label, non-randomised, first-in-human trial	The Lancet / Article	<ul style="list-style-type: none"> Assessed the safety, tolerability, and immunogenicity of a recombinant adenovirus type-5 (Ad5) vectored COVID-19 vaccine expressing the spike glycoprotein of a SARS-CoV-2 strain. The Ad5 vectored COVID-19 vaccine is tolerable and immunogenic at

			28 days post-vaccination. Humoral responses against SARS-CoV-2 peaked at day 28 post-vaccination in healthy adults, and rapid specific T-cell responses were noted from day 14 post-vaccination. Findings suggest that the Ad5 vectored COVID-19 vaccine warrants further investigation.
21.05.2020	Systemic and mucosal antibody secretion specific to SARS-CoV-2 during mild versus severe COVID-19	bioRxiv (non-peer reviewed) / article	<ul style="list-style-type: none"> • Determined SARS-CoV-2-specific immunoglobulin A (IgA) and immunoglobulin G (IgG) in sera and mucosal fluids of two cohorts: COVID-19 patients (n = 56; median age 61 years) with mild versus severe COVID-19, and SARS-CoV-2-exposed healthcare workers (n = 109; median age 36 years) with or without symptoms and tested negative or positive. • Data show systemic IgA and IgG production develops mainly in severe COVID-19, with very high IgA levels seen in patients with severe ARDS, whereas mild disease may be associated with transient serum titres of SARS-CoV-2-specific antibodies but stimulate mucosal SARS-CoV-2-specific IgA secretion. • Findings suggest four grades of antibody responses dependent on COVID-19 severity.
22.05.2020	Convergent Antibody Responses to SARS-CoV-2 Infection in Convalescent Individuals	bioRxiv (non-peer reviewed) / article	<ul style="list-style-type: none"> • 149 COVID-19 convalescent individuals: plasmas collected an average of 39 days after onset of symptoms had variable half-maximal neutralizing titres ranging from undetectable in 33% to below 1:1000 in 79%, while only 1% showed titres >1:5000. Antibody cloning revealed expanded clones of RBD-specific memory B cells expressing closely related antibodies in different individuals. • Despite low plasma titres, antibodies to three distinct epitopes on RBD neutralized at half-maximal inhibitory concentrations (IC50s) as low as single digit ng/mL. Thus, most convalescent plasmas obtained from individuals who recover from COVID-19 do not contain high levels of neutralizing activity. • Nevertheless, rare but recurring RBD-specific antibodies with potent antiviral activity were found in all individuals tested, suggesting a vaccine designed to elicit such antibodies could be broadly effective.
19.05.2020	Serologic responses to SARS-CoV-2 infection among hospital staff with mild disease in eastern France	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Hospital staff recovered from mild COVID-19 (not hospitalised) tested for anti-SARS-CoV-2 antibodies using two assays: a rapid immunodiagnostic test (99.4% specificity) and the S-Flow assay (~99% specificity). Neutralizing activity of sera tested with a pseudovirus-based assay. • Antibodies detected in virtually all staff sampled from 13 days after

			<p>onset of COVID-19 symptoms. Neutralizing activity of the antibodies increased overtime.</p> <ul style="list-style-type: none"> • Finding supports use of serologic testing for diagnosis of individuals who have recovered from SARS-CoV-2 infection. Future studies will help assess the persistence of the humoral response and its associated neutralization capacity in recovered patients.
22.05.2020	High seroreactivity against SARS-CoV-2 Spike epitopes in a pre SARS-CoV-2 cohort: implications for antibody testing and vaccine design	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • This study found a high level of anti-Spike SARS-CoV-2 seroreactivity in populations with no history of exposure to SARS-CoV-2. This is of clinical relevance and could underpin better understanding of COVID-19 pathophysiology in different populations.

Genomics

Publication Date	Title/URL	Journal/ Article type	Digest
22.05.2020	Structural basis for RNA replication by the SARS-CoV-2 polymerase	Cell / Article	<ul style="list-style-type: none"> • Examined the molecular basis of SARS-CoV-2 RNA replication by determining the cryo-EM structures of the stalled pre-/post-translocated polymerase complexes. • The structures show notable structural rearrangements occurring to nsp12 and its cofactors nsp7/nsp8 to accommodate the nucleic acid compared to the apo complex, while there are highly conserved residues in nsp12 positioning the template and primer for an in-line attack on the incoming nucleotide. • They also investigate the inhibition mechanisms of the triphosphate metabolite of remdesivir through structural and kinetic analyses.
22.05.2020	SARS-CoV-2 mutations and where to find them: An in silico perspective of structural changes and antigenicity of the Spike protein	bioRxiv (non-peer reviewed) / article	<ul style="list-style-type: none"> • Analysed 2363 sequences of the Spike protein from SARS-CoV-2 isolates and identified variability in 44 amino acid residues and their worldwide distribution in all continents. • Used the three-dimensional structure of the homo-trimer model for epitope predictions of B-cell, T-Cytotoxic and T-Helper cells. A total of 45 epitopes with amino acids variation were identified. Finally, they show the distribution of mutations within the epitopes.
21.05.2020	A previously uncharacterized gene in SARS-CoV-2 illuminates the functional dynamics and evolutionary origins of the COVID-19 pandemic	bioRxiv (non-peer reviewed) / article	<ul style="list-style-type: none"> • Identified a new gene, ORF3c. 21 representative sarbecovirus genomes show ORF3c is also present in some pangolin-CoVs but not more closely related bat-CoVs; 3,978 SARS-CoV-2 genomes reveal ORF3c gained a new stop codon (G25563U) that rose drastically in frequency during the current COVID-19 pandemic; and 401 deeply

			<p>sequenced samples of SARS-CoV-2 demonstrate the recurrence of this mutation in multiple hosts.</p> <ul style="list-style-type: none"> • Newly gained ORF3c stop codon hitchhiked early with haplotype 241U/3037U/14408U/23403G (Spike-D614G), which appears to drive the European pandemic spread. • OLGs deserve considerably more attention, as their rapid evolution may be more important than is currently appreciated in the emergence of zoonotic viruses.
22.05.2020	Potently neutralizing human antibodies that block SARS-CoV-2 receptor binding and protect animals	bioRxiv (non-peer reviewed) / article	<ul style="list-style-type: none"> • Panel of monoclonal antibodies (mAbs) targeting spike (S) glycoprotein isolated from B cells of infected subjects; several mAbs exhibited potent neutralizing activity with IC50 values as low as 0.9 or 15 ng/mL in pseudovirus or wild-type (wt) SARS-CoV-2 neutralization tests, respectively. • Findings include: most potent mAbs fully block the receptor-binding domain of S (SRBD) from interacting with human ACE2. Competition-binding, structural, and functional studies allowed clustering of the mAbs into defined classes recognizing distinct epitopes within major antigenic sites on the SRBD. • Results identify protective epitopes on the SRBD and provide a structure-based framework for rational vaccine design and the selection of robust immunotherapeutic cocktails.

Epidemiology and clinical – children and pregnancy

Publication Date	Title/URL	Journal/ Article type	Digest
23.05.2020	Clinical Characteristics of COVID-19 Infection in Newborns and Pediatrics: A Systematic Review	Arch Acad Emerg Med / Systematic review	<ul style="list-style-type: none"> • A total of 2228 children, new-borns and infants were studied. Clinical manifestation in children may be mild (72%), moderate (22%) or severe (6%), and the most common symptoms include dry cough (91%) and fever (96%). • According to the included articles, two children had died, one of which was a 14-year-old boy and his exposure history and underlying disease were unclear, and the other was a male new-born with gestational age of 35 weeks and 5 days, birth weight of 2200, Apgar score of 8, 8 (1 min and 5 min) and his first symptom was increased heart rate. No differences were found between male and female children regarding infection with COVID-19.

			<ul style="list-style-type: none"> • Most paediatrics were infected with COVID-19 due to family cluster or history of close contact. Infected children have relatively milder clinical symptoms compared to infected adults.
22.05.2020	The EPICENTRE (ESPNIC Covid pEdiatric Neonatal Registry) initiative: background and protocol for the international SARS-CoV-2 infections registry	Eur J Pediatr / Article	<ul style="list-style-type: none"> • The European Society for Paediatric and Neonatal Intensive Care (ESPNIC) launched the EPICENTRE (ESPNIC Covid pEdiatric Neonatal Registry) international, multicentre, and multidisciplinary initiative to study the epidemiology, clinical course, and outcomes of paediatric and neonatal SARS-CoV-2 infections. • EPICENTRE is open to centres all over the world, and this will allow to provide a pragmatic picture of the epidemic, with a particular attention to paediatric and neonatal critical care issues. • EPICENTRE will allow researchers to clarify the epidemiology, clinical presentation, and outcomes of paediatric and neonatal SARS-CoV-2 infection, refining its clinical management and hopefully providing new insights for clinicians.
22.05.2020	A Case Report of Neonatal Acute Respiratory Failure Due to SARS-CoV-2	J Pediatric Infect Dis Soc / Case study	<ul style="list-style-type: none"> • Report of a case of COVID-19 in a 10-day old infant with no underlying health conditions who presented with acute respiratory failure, with discussion of clinical presentation, treatment course, clinical outcomes, and testing of alternative sample types for presence of SARS-CoV-2.
20.05.2020	Susceptibility to and transmission of COVID-19 amongst children and adolescents compared with adults: a systematic review and meta-analysis	medRxiv (non-peer reviewed) / Systematic review	<ul style="list-style-type: none"> • Rapid systematic review of contact-tracing studies and population-screening studies to address the question of susceptibility to and transmission of SARS-CoV-2 by children and adolescents compared with adults. • Preliminary evidence that children and young people have lower susceptibility to SARS-CoV-2, with a 56% lower odds of being an infected contact. Weak evidence that children and young people play a lesser role in transmission of SARS-CoV-2 at a population level. Study provides no information on infectivity of children.

Epidemiology and clinical - risk factors

Publication Date	Title/URL	Journal/ Article type	Digest
22.05.2020	Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical	Bmj / Cohort study	<ul style="list-style-type: none"> • Prospective observational cohort study to characterise the clinical features of patients admitted to hospital with covid-19 in the UK during the growth phase of the first wave of this outbreak who were

	Characterisation Protocol: prospective observational cohort study		<p>enrolled in the ISARIC WHO Clinical Characterisation Protocol UK (CCP-UK) study, and to explore risk factors associated with mortality in hospital.</p> <ul style="list-style-type: none"> • In study participants, mortality was high, independent risk factors were increasing age, male sex, and chronic comorbidity, including obesity.
22.05.2020	Occupation and risk of COVID-19: prospective cohort study of 120,621 UK Biobank participants	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • UK Biobank data linked to COVID-19 test results: 120,621 UK Biobank participants employed or self-employed at baseline (2006-2010); 65 years or younger in March 2020. • Relative to non-essential workers, healthcare workers (RR 7.59, 95% CI: 5.43 to 10.62) and social and education workers (RR 2.17, 95% CI: 1.37 to 3.46) had higher risk of testing positive in hospital. • Medical support staff (RR 8.57, 95% CI: 4.35 to 16.87) and social care workers (RR 2.99, 95% CI: 1.71 to 5.24) had highest risk within healthcare and social and education categories.
22.05.2020	Predictors of mortality in hospitalized COVID-19 patients: A systematic review and meta-analysis	J Med Virol / Systematic review	<ul style="list-style-type: none"> • 14 studies documenting the outcomes of 4659 patients were included in this systematic review looking for associations between mortality and patient characteristics, comorbidities, and laboratory abnormalities. • The presence of comorbidities such as hypertension, coronary heart disease and diabetes were associated with significantly higher risk of death amongst COVID-19 patients. • Those who died, compared to those who survived, differed on multiple biomarker levels on admission including elevated levels of cardiac troponin; C-reactive protein; interleukin-6; D-dimer; creatinine and alanine transaminase; as well as decreased levels of albumin.
19.05.2020	COVID-19 related neuroimaging findings: A signal of thromboembolic complications and a strong prognostic marker of poor patient outcome	J Neurol Sci / Article	<ul style="list-style-type: none"> • Retrospective cohort study of 3218 COVID-19 confirmed patients. • Acute stroke was the most common finding on neuro-imaging, seen in 92.5% of patients with positive neuro-imaging studies, and present in 1.1% of hospitalized COVID-19 patients. • Patients with acute large ischemic and haemorrhagic stroke had much higher mortality risk adjusted for age, BMI and hypertension compared to those COVID-19 patients without neuroimaging.
22.05.2020	Ventilation Techniques and Risk for Transmission of Coronavirus Disease, Including COVID-19	Ann Intern Med / Article	<ul style="list-style-type: none"> • WHO-funded review of multiple streams of evidence regarding the benefits and harms of ventilation techniques for coronavirus infections, including that causing COVID-19. (PROSPERO registration: CRD42020178187). • Indirect and low-certainty evidence suggests that use of non-invasive

			ventilation, similar to invasive mechanical ventilation, probably reduces mortality but may increase the risk for transmission of COVID-19 to health care workers.
22.05.2020	Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study	Bmj / Cohort study	<ul style="list-style-type: none"> • Prospective cohort study of 5279 patients with laboratory confirmed SARS-Cov-2 infection. • Age and comorbidities were found to be strong predictors of hospital admission and to a lesser extent of critical illness and mortality in people with covid-19; however, impairment of oxygen on admission and markers of inflammation were most strongly associated with critical illness and mortality. Outcomes seem to be improving over time, potentially suggesting improvements in care.
13.05.2020	Combination of four clinical indicators predicts the severe/critical symptom of patients infected COVID-19	J Clin Virol / Research article	<ul style="list-style-type: none"> • Using data from 336 cases of patients infected COVID-19 along with 220 clinical and laboratory observations/records, 36 clinical indicators significantly associated with severe/critical symptom were identified. • The clinical indicators are mainly thyroxine, immune related cells and products. Support Vector Machine (SVM) and optimized combination of age, GSH, CD3 ratio and total protein has a good performance in discriminating the mild and severe/critical cases.
21.05.2020	Prognostic factors in patients with diabetes hospitalized for COVID-19: Findings from the CORONADO study and other recent reports	Diabetes Metab / Article	<ul style="list-style-type: none"> • Brief review with a focus on diabetes, discussing the main findings of CORONADO, a prospective observational study in France to determine the risk factors of progression to a more serious life-threatening COVID-19 infection, as well as related observations from other countries, mainly China and the US. • Hyperglycaemia at the time of hospital admission is associated with poor outcomes, but it may simply be considered a marker of severity of the infection. Thus, the impact of glucose control during hospitalization on outcomes related to COVID-19, which was not investigated in the CORONADO study, is certainly deserving of specific investigation.
25.05.2020	Impact of ethnicity on outcome of severe COVID-19 infection. Data from an ethnically diverse UK tertiary centre	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Looked at the impact of ethnicity in 1200 consecutive patients admitted between 1st March 2020 and 12th May 2020 to King's College Hospital NHS Trust in London (UK). • Key findings are firstly that BAME patients are significantly younger and have different co-morbidity profiles than White individuals. Secondly, there is no significant independent effect of ethnicity on severe outcomes (death or ITU admission) within 14-days of symptom onset, after adjustment for age, sex and comorbidities.

22.05.2020	Comorbidities, clinical signs and symptoms, laboratory findings, imaging features, treatment strategies, and outcomes in adult and pediatric patients with COVID-19: A systematic review and meta-analysis	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • 148 studies met the inclusion criteria for the systematic review and meta-analysis with 12149 patients (5739 female) and a median age was 47.0. • 617 patients died from COVID-19 and its complications, while 297 patients were reported as asymptomatic. • Older age (SMD: 1.25 [0.78- 1.72]; p < 0.001), being male (RR = 1.32 [1.13-1.54], p = 0.005) and pre-existing comorbidity (RR = 1.69 [1.48- 1.94]; p < 0.001) were identified as risk factors of in-hospital mortality. The heterogeneity between studies varied substantially (I²; range: 1.5- 98.2%).
22.05.2020	Low blood sodium increases risk and severity of COVID-19: a systematic review, meta-analysis and retrospective cohort study	medRxiv (non-peer reviewed) / Systematic review	<ul style="list-style-type: none"> • COVID-19 infects human lung tissue cells through angiotensin-converting enzyme-2 (ACE2); the body sodium is an important factor for regulating expression of ACE2. • Mean serum sodium concentration: in patients with COVID-19 was 138.6 mmol/L, much lower than median level in population (142.0); in severe/critical patients (137.0), significantly lower than mild and moderate patients (140.8 and 138.7, respectively). • Systematic review, meta-analysis and retrospective cohort study found that low blood sodium population may significantly increase the risk and severity of SARS-CoV-2 infection.
23.05.2020	Morbid Obesity as an Independent Risk Factor for COVID-19 Mortality in Hospitalized Patients Younger than 50	Obesity (Silver Spring) / Article	<ul style="list-style-type: none"> • Retrospective analysis of obesity as an independent risk factor for mortality in hospitalized patients younger than fifty. • Overall, 3,406 patients were included. 572 (17.0%) of the patients were younger than 50. In the younger age group, 60 (10.5%) patients died. In the older age group, 1,076 (38.0%) patients died. • For the younger population, BMI above 40 kg/m² was independently associated with mortality. For the older population, BMI above 40 kg/m² was also independently associated with mortality to a lesser extent.
25.05.2020	ASSESSMENT OF WORKERS PERSONAL VULNERABILITY TO COVID-19 USING COVID-AGE	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Developed a risk model that provides estimates of personal vulnerability to Covid-19 according to sex, age, ethnicity, and various comorbidities.

Epidemiology and clinical – other

Publication Date	Title/URL	Journal/ Article type	Digest
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21.05.2020	COVID-19: Results of a national survey of United Kingdom healthcare professionals' perceptions of current management strategy - a cross-sectional questionnaire study	Int J Surg / Research article	<ul style="list-style-type: none"> • Questionnaire survey of NHS Healthcare professionals in the UK regarding their perceptions of preparedness in their workplace and general views of current pandemic management strategy. • 1007 responses were obtained with majority of the responses from England (n=850, 84.40 %). There were 670 (66.53%) responses from doctors and 204 (20.26%) from nurses. • Only one third of the respondents agreed that they felt supported at their trust and half of the respondents reported that adequate training was provided to the frontline staff. Two-thirds of the respondents were of the view that there was not enough Personal Protective Equipment available while 80% thought that this pandemic has improved their hand washing practice. • Most of the respondents were in the favour of an earlier lockdown (90%) and testing all the NHS frontline staff (94%).
22.05.2020	COVID-19 in Great Britain: epidemiological and clinical characteristics of the first few hundred (FF100) cases: a descriptive case series and case control analysis	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • This study presents the first epidemiological and clinical summary of COVID-19 cases in Great Britain. The FFX study design enabled systematic data collection. • The study was able to characterize the risk factors for infection with population prevalence estimates setting these relative risks into a public health context. • It also provides important evidence for generating case definitions to support public health risk assessment, clinical triage and diagnostic algorithms.
22.05.2020	Pathophysiology of SARS-CoV-2: targeting of endothelial cells renders a complex disease with thrombotic microangiopathy and aberrant immune response. The Mount Sinai COVID-19 autopsy experience	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Autopsies of 67 Mount Sinai Hospital COVID-19 patients. Lab results show elevated inflammatory markers, abnormal coagulation values, elevated cytokines IL-6, IL-8 and TNFα. • COVID-19 causes endothelial dysfunction, a hypercoagulable state, and an imbalance of both innate and adaptive immune responses. • Novel findings: an endothelial phenotype of ACE2 in selected organs, which correlates with clotting abnormalities and thrombotic microangiopathy, addressing the prominent coagulopathy and neuropsychiatric symptoms; macrophage activation syndrome, with haemophagocytosis and a hemophagocytic lymphohistiocytosis-like disorder, underlying the microangiopathy and excessive cytokine release.
24.05.2020	Neuropathology of COVID-19: a spectrum of vascular and acute disseminated encephalomyelitis (ADEM)-like pathology	Acta Neuropathol / Case study	<ul style="list-style-type: none"> • Report of the neuropathological findings of a patient who died from complications of COVID-19. • The autopsy revealed a range of neuropathological lesions, with

			<p>features resembling both vascular and demyelinating aetiologies. Haemorrhagic white matter lesions were present throughout the cerebral hemispheres with surrounding axonal injury and macrophages. The subcortical white matter had scattered clusters of macrophages, a range of associated axonal injury, and a perivascular acute disseminated encephalomyelitis (ADEM)-like appearance.</p> <ul style="list-style-type: none"> • Additional white matter lesions included focal microscopic areas of necrosis with central loss of white matter and marked axonal injury. Rare neocortical organizing microscopic infarcts were also identified.
23.05.2020	The role of self-reported smell and taste disorders in suspected COVID-19	Eur Arch Otorhinolaryngol / Systematic review	<ul style="list-style-type: none"> • Systematic review aiming to provide insight to the pandemic and evaluate anosmia as a potential screening symptom that might contribute to the decision to test suspected cases or guide quarantine instructions. • A significant prevalence of anosmia is reported in COVID-19 patients. Controlled studies indicate that anosmia is more common in COVID-19 patients than in patients suffering from other viral infections or controls. • Most of the studies reported either smell loss or smell plus taste loss. Less severe COVID-19 disease is related to a greater prevalence of anosmia. A quick recovery of the smell loss may be expected in most COVID-19 cases.
22.05.2020	Relationship between odor intensity estimates and COVID-19 prevalence prediction in a Swedish population	Chem Senses / Article	<ul style="list-style-type: none"> • Online measures of how intense common household odours are perceived and symptoms of COVID-19 were collected from 2440 Swedes. Average odour intensity ratings were then compared to predicted COVID-19 population prevalence over time in the Swedish population and were found to closely track each other. • The findings suggest that measures of odour intensity, if obtained in a large and representative sample, can be used as an indicator of COVID-19 disease in the general population.
24.05.2020	More than smell. COVID-19 is associated with severe impairment of smell, taste, and chemesthesis	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Report the development, implementation and initial results of a multi-lingual, international questionnaire to assess self-reported quantity and quality of perception in three distinct chemosensory modalities (smell, taste, and chemesthesis) before and during COVID-19. In the first 11 days after questionnaire launch, 4039 participants (2913 women, 1118 men, 8 other, ages 19-79) reported a COVID-19 diagnosis either via laboratory tests or clinical assessment. • The results show that COVID-19-associated chemosensory impairment is not limited to smell, but also affects taste and

			chemesthesis. The multimodal impact of COVID-19 and lack of perceived nasal obstruction suggest that SARS-CoV-2 infection may disrupt sensory-neural mechanisms.
20.05.2020	Asymptomatic infection and atypical manifestations of COVID-19: comparison of viral shedding duration	J Infect / Letter	<ul style="list-style-type: none"> • More than 25% (out of 199) patients with COVID-19 were asymptomatic. • Among patients with COVID-19, 26.1% presented anosmia, and 22.6% complained of ageusia with median duration of 7 days. • Mean duration of SARS-CoV-2 viral shedding was 24.5 days. • Irrespective of clinical manifestations, all patients with COVID-19 showed prolonged viral shedding.
20.05.2020	A Rapid Review of the Asymptomatic Proportion of PCR-Confirmed SARS-CoV-2 Infections in Community Settings	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Rapid review and meta-analysis of current evidence on asymptomatic proportion of COVID-19 infections based on 6 studies in community settings: pooled estimate for asymptomatic proportion of infections was 11% (95% CI 4%-18%). • Estimates of baseline viral load appeared similar for asymptomatic and symptomatic cases based on available data in three studies, though detailed reporting limited. • Asymptomatic proportion of infections is relatively low when estimated from methodologically-appropriate studies. Further investigation into degree and duration of infectiousness for asymptomatic infections is warranted.
19.05.2020	Comparing hospitalised, community and staff COVID-19 infection rates during the early phase of the evolving COVID-19 epidemic	J Infect / Letter	<ul style="list-style-type: none"> • East Midlands study of infection rates using swab samples obtained from symptomatic hospitalised and community-based patients, and hospital staff. • The team derive some useful epidemiological parameters to understand better the characteristics of the evolving COVID-19 epidemic during its early exponential growth phase in a local population. These methods are easily applied by other teams where such SARS-CoV-2 testing data from the initial phase of the epidemic is available.
23.05.2020	SARS-CoV-2 lethality decreased over time in two Italian Provinces	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Retrospective cohort study of 1946 subjects diagnosed in Ferrara and Pescara provinces, Italy. Compared case-fatality rate of subjects diagnosed during April and March, 2020. • From March to April, the CFR significantly decreased in total sample (10.8% versus 6.0%; $p < 0.001$), and in any subgroup of patients. • Large reductions of lethality among elderly (from 30.0% to 13.4%), subjects with hypertension (23.0% to 12.1%), diabetes (30.3% to 8.4%), CVD (31.5% to 12.1%), COPD (29.7% to 11.4%), and renal disease

			(32.3% to 11.5%). <ul style="list-style-type: none"> In April, the adjusted hazard ratio of death was 0.42 (95% Confidence Interval: 0.29-0.60). Mean age of those who died substantially increased from March (77.9y) to April (86.9y).
25.05.2020	The spectrum of COVID-19-associated dermatologic manifestations: an international registry of 716 patients from 31 countries	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> In this international registry-based case series of 716 patients representing 31 countries, the most common dermatologic morphologies encountered in the 171 COVID-19 confirmed case included morbilliform, pernio-like, urticarial, macular erythema, vesicular, papulosquamous, and retiform purpura. Retiform purpura was seen exclusively in critically ill, hospitalized patients.
19.05.2020	SARS-CoV-2 RNA concentrations in primary municipal sewage sludge as a leading indicator of COVID-19 outbreak dynamics	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> Report time course of SARS-CoV-2 RNA concentrations in primary sewage sludge during Spring COVID-19 outbreak in a North Eastern U.S. metropolitan area. Detected in all environmental samples. When adjusted for time lag, virus RNA concentrations were highly correlated with COVID-19 epidemiological curve ($R^2=0.99$) and local hospital admissions ($R^2=0.99$). SARS-CoV-2 RNA concentrations were a seven-day leading indicator ahead of compiled COVID-19 testing data and led local hospital admissions data by three days. Decisions to implement or relax public health measures and restrictions require timely information on outbreak dynamics in a community.

Infection control

Publication Date	Title/URL	Journal/ Article type	Digest
21.05.2020	SARS-CoV-2 infection in London, England: Impact of lockdown on community point-prevalence, March-May 2020	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> COVID-19 point prevalence PCR community testing allows disease burden estimation. In London residents sample, point prevalence decreased from 2.2% (95%CI 1.4;3.5) in early April (reflecting infection around lockdown implementation) to 0.2% (95%CI 0.03-1.6) in early May (reflecting infection 3-5 weeks into lockdown). Extrapolation from reports of confirmed cases suggest that 5-7.6% of total infections were confirmed by testing during this period. Data complement seroprevalence surveys improving the understanding of transmission in London.

22.05.2020	What is the performance and impact of disposable and reusable respirators for healthcare workers in the context of COVID-19?	Oxford COVID-19 Evidence Service / COVID-19	<ul style="list-style-type: none"> • This review looked at the performance of respirators (in terms of the protection they provide) and their impact (on wearers and clinical activities). Included disposable filtering facepiece respirator masks such as FFP3, N95 and P2 and reusable types such as elastomeric facepiece respirators and powered air-purifying respirators. • Examined filtration standards for respirators and how they compare across different industries and 8 different international standards agencies.
25.05.2020	Risk of COVID-19 among frontline healthcare workers and the general community: a prospective cohort study	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Prospective cohort study of general community, including frontline HCWs, who reported information through COVID Symptom Study smartphone application from March 24 (U.K.) and March 29 (U.S.) through April 23, 2020. • Compared with the general community, frontline HCWs had an aHR of 11.6 (95% CI: 10.9 to 12.3) for reporting a positive test. • HCWs caring for COVID-19 patients had aHRs for a positive test of 4.83 (95% CI: 3.99 to 5.85) if they had adequate PPE, 5.06 (95% CI: 3.90 to 6.57) for reused PPE, and 5.91 (95% CI: 4.53 to 7.71) for inadequate PPE • Frontline HCWs had significantly increased risk of COVID-19 infection, highest among HCWs who reused PPE or had inadequate access to PPE. Adequate PPE supplies did not completely mitigate high-risk exposures.

Treatment

Publication Date	Title/URL	Journal/ Article type	Digest
22.05.2020	Thymosin alpha 1 (Tα1) reduces the mortality of severe COVID-19 by restoration of lymphocytopenia and reversion of exhausted T cells	Clin Infect Dis / Article	<ul style="list-style-type: none"> • Retrospective review of the clinical outcomes of 76 severe cases with COVID-19. • Tα1 supplement significantly reduced mortality of severe COVID-19 patients. • COVID-19 patients with counts of CD8+ T cells or CD4+ T cells in circulation lower than 400/μL or 650/μL, respectively, gain more benefits from Tα1. • Tα1 reverses T cell exhaustion and recovers immune reconstitution through promoting thymus output during SARS-CoV-2 infection.

20.05.2020	Arbidol/IFN-α2b Therapy for Patients With Corona Virus Disease 2019: A Retrospective Multicenter Cohort Study	Microbes Infect / Cohort study	<ul style="list-style-type: none"> • Multicentre retrospective cohort study of 141 adult patients with laboratory-confirmed COVID-19 infection. • Combined group patients were given Arbidol and IFN-α2b, monotherapy group patients inhaled IFN-α2b for 10-14 days. • The duration of viral RNA of respiratory tract in the monotherapy group was not longer than that in the combined therapy group. There was no significant differences between two groups. The absorption of pneumonia in the combined group was faster than that in the monotherapy group. • Arbidol/IFN - 2b therapy can be used as an effective method to improve the COVID-19 pneumonia of mild patients, although was not found to accelerate the viral clearance.
22.05.2020	Heparin resistance in COVID-19 patients in the intensive care unit	J Thromb Thrombolysis / Research article	<ul style="list-style-type: none"> • Cohort of 69 ICU patients investigated for evidence of heparin resistance in those that have received therapeutic anticoagulation. 15 of the patients received therapeutic anticoagulation with either unfractionated heparin (UFH) or low molecular weight heparin (LMWH), of which full information was available on 14 patients. • Heparin resistance to UFH was documented in 8/10 (80%) patients and sub-optimal peak anti-Xa following therapeutic LMWH in 5/5 (100%) patients where this was measured (some patients received both anticoagulants sequentially). Spiking plasma from 12 COVID-19 ICU patient samples demonstrated decreased in-vitro recovery of anti-Xa compared to normal pooled plasma.
21.05.2020	Metformin Treatment Was Associated with Decreased Mortality in COVID-19 Patients with Diabetes in a Retrospective Analysis	Am J Trop Med Hyg / Research article	<ul style="list-style-type: none"> • Study comparing the outcome of 104 metformin users and 179 nonusers in hospitalized COVID-19 patients with diabetes. There were no significant differences between the two groups in gender, age, underlying diseases, clinical severity, and oxygen-support category at admission. • The fasting blood glucose level of the metformin group was higher than that of the no-metformin group at admission and was under effective control in both groups after admission. Other laboratory parameters at admission and treatments after admission were not different between the two groups. • The length of hospital stay did not differ between the two groups (21.0 days for metformin versus 19.5 days for no metformin, P = 0.74). However, in-hospital mortality was significantly lower in the metformin group (3/104 (2.9%) versus 22/179 (12.3%), P = 0.01).

20.05.2020	Convalescent plasma treatment of severe COVID-19: A matched control study	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Outcomes of 39 hospitalized patients with severe to life-threatening COVID-19 who received convalescent plasma transfusion compared to cohort of retrospectively matched controls: more likely to remain same or have improvements in their supplemental oxygen requirements by post-transfusion day 14, with an odds ratio of 0.86 (95% CI: 0.75~0.98; p=0.028); improved survival, compared to control patients (log-rank test: p=0.039). • Potentially efficacious treatment option for patients hospitalized with COVID-19; suggest non-intubated patients may benefit more than those requiring mechanical ventilation.
25.05.2020	Hydroxychloroquine and Tocilizumab Therapy in COVID-19 Patients - An Observational Study	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Among 2512 hospitalized patients with COVID-19 there have been 547 deaths (22%), 1539 (61%) discharges and 426 (17%) remain hospitalized. 1914 (76%) received at least one dose of hydroxychloroquine and 1473 (59%) received hydroxychloroquine with azithromycin. • This observational cohort study suggests hydroxychloroquine, either alone or in combination with azithromycin, was not associated with a survival benefit among hospitalized COVID-19 patients. • Tocilizumab demonstrated a trend association towards reduced mortality among ICU patients.

Social science

Publication Date	Title/URL	Journal/ Article type	Digest
21.05.2020	Video calls for reducing social isolation and loneliness in older people: a rapid review	Cochrane Database Syst Rev / Systematic review	<ul style="list-style-type: none"> • Based on this review there is currently very uncertain evidence on the effectiveness of video call interventions to reduce loneliness in older adults. • The review did not include any studies that reported evidence of the effectiveness of video call interventions to address social isolation in older adults. • The evidence regarding the effectiveness of video calls for outcomes of symptoms of depression was very uncertain.

Modelling

Publication Date	Title/URL	Journal/ Article type	Digest
20.05.2020	Age- and sex-specific total mortality impacts of the early weeks of the Covid-19 pandemic in England and Wales: Application of a Bayesian model ensemble to mortality statistics	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • 16 Bayesian models that probabilistically estimate the weekly number of deaths that would be expected had the Covid-19 pandemic not occurred. • Week of 21st March, same week national lockdown put in place, >92% probability that there were more deaths in men and women aged ≥ 45 years than would occur in the absence of the pandemic; the probability was 100% from the subsequent week. • Death toll of pandemic, in middle and older ages, is substantially larger than number of deaths reported as a result of confirmed infection; visible in vital statistics when national lockdown put in place. • When all-cause mortality considered, mortality impact of pandemic on men and women is more similar than when comparing deaths assigned to Covid-19 as underlying cause.
15.05.2020	Differential Effects of Intervention Timing on COVID-19 Spread in the United States	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • The authors use county-level observations of reported infections and deaths, in conjunction with human mobility data and a metapopulation transmission model, to quantify changes of disease transmission rates in US counties from March 15, 2020 to May 3, 2020. • They find significant reductions of the basic reproductive numbers in major metropolitan areas in association with social distancing and other control measures. Counterfactual simulations indicate that, had these same control measures been implemented just 1-2 weeks earlier, a substantial number of cases and deaths could have been averted. • They also examine the effects of delays in re-implementing social distancing following a relaxation of control measures. A longer response time results in a stronger rebound of infections and death.

Guidance, consensus statements

Publication Date	Title/URL	Journal/ Article type
20.05.2020	COVID-19 Aviation Health Safety Protocol: Guidance for the management of airline passengers in relation to the COVID-19 pandemic	European Centre For Disease Control and Prevention / Technical Guidance

21.05.2020	Thromboembolism and anticoagulant therapy during the COVID-19 pandemic: interim clinical guidance from the anticoagulation forum	J Thromb Thrombolysis / Guidance
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Overviews, comments and editorials

Publication Date	Title/URL	Journal/ Article type
23.05.2020	England and Wales see 20000 excess deaths in care homes	The Lancet / World Report
22.05.2020	BBMRI-ERIC's contributions to research and knowledge exchange on COVID-19	Eur J Hum Genet / Article
22.05.2020	Chloroquine or hydroxychloroquine for COVID-19: why might they be hazardous?	The Lancet / Comment
25.05.2020	Caution against corticosteroid-based COVID-19 treatment	The Lancet / Correspondence

Produced by the PHE COVID-19 Literature Digest Team

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