Public Health England

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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:

- Serology and immunology
- Genomics
- Epidemiology and clinical - children and pregnancy
- Epidemiology and clinical - risk factors
- Epidemiology and clinical - other
- Treatment
- Social sciences
- Modelling
- Guidance, consensus statements and hospital resources (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Please note that we are including preprints (highlighted in red), which are preliminary reports of work that have NOT been peer-reviewed.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.

Serology and immunology

Publication Date	Title/URL	Journal/Article type	Digest
15.05.2020	Yeast-Expressed SARS-CoV Recombinant Receptor-Binding Domain (RBD219-N1) Formulated with Alum Induces Protective Immunity and Reduces Immune Enhancement	bioRxiv (non-peer reviewed) / Article	• The authors report the development of a severe acute respiratory syndrome (SARS) subunit recombinant protein vaccine candidate based on a high-yielding, yeast-engineered, receptor-binding domain (RBD219-N1) of the SARS beta-coronavirus (SARS-CoV) spike (S) protein. • Here, they report that mice immunized with RBD219-N1/Alhydrogel® were fully protected from lethal SARS-CoV challenge (0% mortality), compared to ~ 30% mortality in mice when immunized with the SARS S protein formulated with Alhydrogel®, and 100% mortality in negative

			controls. • As a result, this vaccine formulation is under consideration for further development against SARS-CoV and other emerging and re-emerging beta-CoVs such as SARS-CoV-2.
19.05.2020	Human IgG cell neutralizing monoclonal antibodies block SARS-CoV-2 infection	bioRxiv (non-peer reviewed) / Article	• The authors purified more than one thousand memory B cells specific to SARS-CoV-2 recombinant S1 or RBD antigens from 11 convalescent COVID-19 patients, and a total of 729 naturally paired heavy and light chain fragments were obtained by single B cell cloning technology. • 12 antibodies could block pseudoviral entry into HEK293T cells overexpressing ACE2, with the best ones showing IC50 around 2-3 nM. • These 12 antibodies were tested in authentic virus infection assay, and 414-1 was able to effectively block live viral entry with IC50 at 1.75 nM and in combination with 105-38 could achieve IC50 as low as 0.45 nM. They also found 3 antibodies cross reacting with the SARS-CoV spike protein, and one of them, 515-5, could block SARS-CoV pseudovirus infection.
21.05.2020	Immunization with the receptor-binding domain of SARS-CoV-2 elicits antibodies cross-neutralizing SARS-CoV-2 and SARS-CoV without antibody-dependent enhancement	bioRxiv (non-peer reviewed) / Article	• Study reporting the immunogenicity and vaccine potential of SARS-CoV-2 RBD (SARS2-RBD)-based recombinant proteins. • Immunization with SARS2-RBD recombinant proteins potently induced a multi-functional antibody response in mice. The resulting antisera could efficiently block the interaction between SARS2-RBD and ACE2, inhibit S-mediated cell-cell fusion, and neutralize both SARS-CoV-2 pseudovirus entry and authentic SARS-CoV-2 infection. • In addition, the anti-RBD sera also exhibited cross binding, ACE2-blockade, and neutralization effects towards SARS-CoV. • The findings provide a solid foundation for developing RBD-based subunit vaccines for SARS-CoV2.
17.05.2020	Immunogenic profile of SARS-CoV-2 spike in individuals recovered from COVID-19	medRxiv (non-peer reviewed) / Article	• The authors undertook an in-depth characterisation of humoral and cellular immunity against SARS-CoV-2 spike in humans following mild to moderate SARS-CoV-2 infection. • Findings show serological antibody responses against spike are routinely elicited by infection and correlate with plasma neutralising activity and capacity to block ACE2/RBD interaction. Expanded populations of spike-specific memory B cells and circulating T follicular helper cells (cTFH) were detected within convalescent donors, while responses to the receptor binding domain (RBD) constitute a minor fraction. • Using regression analysis, high plasma neutralisation activity was

			associated with increased spike-specific antibody, but notably also with the relative distribution of spike-specific cTFH subsets.
18.05.2020	The Dynamic Changes of Antibodies against SARS-CoV-2 during the Infection and Recovery of COVID-19	medRxiv (non-peer reviewed) / Article	• By comprehensively analysing the laboratory findings of 1,850 patients, the authors describe the dynamic changes of the total antibody, spike protein (S)-, receptor-binding domain (RBD)-, and nucleoprotein (N)-specific IgM and IgG levels during SARS-CoV-2 infection and recovery. • Results indicate that the S-, RBD-, and N- specific IgG generation of severe/critical COVID-19 patients is one week later than mild/moderate cases, while the levels of these antibodies are 1.5-fold higher in severe/critical patients during hospitalization ($P<0.01$). The decrease of these IgG levels indicates the poor outcome of severe/critical patients. The RBD- and S-specific IgG levels are 2-fold higher in virus-free patients ($P<0.05$). • The patients who got re-infected had a low level of protective antibody on discharge.

Genomics

Publication Date	Title/URL	Journal/Article type	Digest
03.05.2020	Large scale genomic analysis of 3067 SARS-CoV-2 genomes reveals a clonal geo-distribution and a rich genetic variations of hotspots mutations	bioRxiv (non-peer reviewed) / Article	• In this study, the authors collected and analysed 3,067 SARS-CoV-2 genomes isolated from 55 countries during the first three months after the onset of this virus. The accumulation of mutations during the epidemic period with geographic locations was monitored. • The results showed 782 variant sites, of which 512 (65.47%) had a non-synonymous effect. Frequencies of mutated alleles revealed the presence of 38 recurrent non-synonymous mutations, including ten hotspot mutations with a prevalence higher than 0.10 in this population and distributed in six SARS-CoV-2 genes. The distribution of these recurrent mutations on the world map revealed certain genotypes specific to the geographic location. • They make available an inclusive unified database (http://genoma.ma/covid-19/) that lists all of the genetic variants of the SARS-CoV-2 genomes found in this study with phylogeographic analysis around the world.

15.05.2020	Understanding olfactory dysfunction in COVID-19: Expression of ACE2, TMPRSS2 and Furin in the nose and olfactory bulb in human and mice	bioRxiv (non-peer reviewed) / Article	• Study addressing the unique pathophysiology of COVID-19-associated olfactory dysfunction. The expression of ACE2 (virus binding receptor) and TMPRSS2 and Furin (host cell proteases facilitating virus entry) was examined in the nasal mucosa, composed of respiratory mucosa (RM), olfactory mucosa (OM), and olfactory bulb (OB) of mouse and human tissues using immunohistochemistry and gene analyses. • ACE2 was widely expressed in all tissues, whereas TMPRSS2 and Furin were expressed only in certain types of cells and were absent in the ORNs. • These findings, together with clinical reports, suggest that COVID-19-related anosmia occurs mainly through sensorineural and central dysfunction and, to some extent, conductive olfactory dysfunction. The expression of ACE2, but not TMPRSS2 or Furin, in ORNs may explain the early recovery from anosmia.
21.05.2020	An insertion unique to SARS-CoV-2 exhibits superantigenic character strengthened by recent mutations	bioRxiv (non-peer reviewed) / Article	• Structure-based computational models were used to demonstrate that the SARS-CoV-2 spike (S) exhibits a high-affinity motif for binding TCR, interacting closely with both the α- and β-chains variable domains complementarity-determining regions. The binding epitope on S harbours a sequence motif unique to SARS-CoV-2 (not present in any other SARS coronavirus), which is highly similar in both sequence and structure to bacterial superantigens. • Further examination found that this interaction between the virus and human T cells is strengthened in the context of a recently reported rare mutation (D839Y/N/E) from a European strain of SARS-CoV-2. • These data suggest that the SARS-CoV-2 S may act as a superantigen to drive the development of MIS-C as well as cytokine storm in adult COVID-19 patients, with important implications for the development of therapeutic approaches.
21.05.2020	No evidence for increased transmissibility from recurrent mutations in SARS-CoV-2	bioRxiv (non-peer reviewed) / Article	• Due to its extremely recent association with humans, SARS-CoV-2 may not yet be fully adapted to its human host. This has led to speculations that some lineages of SARS-CoV-2 may be evolving towards higher transmissibility. • The authors report that no single recurrent mutation is convincingly associated with increased viral transmission. Instead, recurrent SARS-CoV-2 mutations currently in circulation appear to be either neutral or weakly deleterious. These mutations seem primarily induced by the human immune system via host RNA editing, rather than being signatures of adaption to the novel human host.

			• There is no evidence at this stage for the emergence of more transmissible lineages of SARS-CoV-2 due to recurrent mutations.

Epidemiology and clinical – children and pregnancy

Publication Date	Title/URL	Journal/Article type	Digest
21.05.2020	Detection of SARS-CoV-2 in human breastmilk	The Lancet / Correspondence	• Reports the clinical data and time course of infection of milk from two nursing mothers infected with SARS-CoV-2. • SARS-CoV-2 RNA was detected in milk samples from Mother 2 for 4 consecutive days. • Detection of viral RNA in milk from Mother 2 coincided with mild COVID-19 symptoms and a SARS-CoV-2 positive diagnostic test of the new-born (new-born 2).

Epidemiology and clinical - risk factors

Publication Date	Title/URL	Journal/Article type	Digest
12.05.2020	COVID-19 and diabetes mellitus: A need for prudence in elderly patients from a pooled analysis	Diabetes & metabolic syndrome / Article	• Eleven studies included accounting for 2084 COVID-19 patients. The overall prevalence of diabetes in elderly COVID-19 cohort (mean age>50 yrs) was 13.2%. • Relatively younger COVID-19 cohort (mean age <50 yrs) had a pooled prevalence of 9.0%.
12.05.2020	Obesity as a predictor for a poor prognosis of COVID-19: A systematic review	Diabetes & metabolic syndrome / Article	• This review reports that obesity is an independent risk and prognostic factor for the disease severity and the requirement of advanced medical care in COVID-19. Obese patients with COVID-19 should be treated as a higher risk population.
20.05.2020	Clinical course and risk factors for mortality of COVID-19 patients with pre-existing cirrhosis: a multicentre cohort study	Gut / Letter	• Retrospective multicentre study of patients with COVID-19 and pre-existing cirrhosis. • The cause of death in most patients was respiratory failure rather than progression of liver disease (i.e., development of acute-on-chronic liver failure). • Lower lymphocyte and platelet counts, and higher direct bilirubin level might represent poor prognostic indicators in this patient population.

19.05.2020	Cancer immunotherapy does not increase the risk of death by COVID-19 in melanoma patients	medRxiv (non-peer reviewed) / Article	• Preliminary findings from a retrospective analysis of melanoma patients infected by SARS-Cov-2, included in the Spanish national registry, showed that the risk of death in patients undergoing treatment with anti PD-1 antibodies did not exceed the global risk of death in this population. • These results could be relevant in order to select melanoma therapy during the COVID-19 pandemic.
18.05.2020	Current tobacco smoking and risk from COVID-19: results from a population symptom app in over 2.4 million people	medRxiv (non-peer reviewed) / Article	• Study of 2,401,982 UK users of the COVID Symptom Study app to determine the association between current smoking and the development of classic symptoms of COVID-19. The number of concurrent COVID-19 symptoms was used as a proxy for severity. • Current smokers were more likely to develop symptoms suggesting a diagnosis of COVID-19; classic symptoms adjusted OR[95%CI] 1.14[1.10 to 1.18]; >5 symptoms 1.29[1.26 to 1.31]; >10 symptoms 1.50[1.42 to 1.58]. Smoking was associated with reduced ACE2 expression in adipose tissue (Beta(SE)= -0.395(0.149); p=7.01x10-3). • These data are consistent with smokers having an increased risk from COVID-19.
18.05.2020	Risk of Ischemic Stroke in Patients with Covid-19 versus Patients with Influenza	medRxiv (non-peer reviewed) / Article	• Retrospective cohort study to compare the rate of ischemic stroke between patients with Covid-19 and patients with influenza, which has been previously linked to stroke. • Among 2,132 patients with emergency department visits or hospitalizations with Covid-19, 31 patients had an acute ischemic stroke. The median age of patients with stroke was 69 years and 58% were men. • In the comparison cohort, of 1,516 patients with influenza, 0.2% had an acute ischemic stroke. • After adjustment for age, sex, and race, the likelihood of stroke was significantly higher with Covid-19 than with influenza infection (odds ratio, 7.5; 95% CI, 2.3-24.9).
18.05.2020	Risk factors associated with mortality of COVID-19 in 2692 counties of the United States	medRxiv (non-peer reviewed) / Article	• Study to find out the risk factors associated with mortality of COVID-19 using county-level mortality counts of 2692 infected counties on April 15, 2020 in the United States. • Several risk factors were significantly associated with the mortality of COVID-19: Hispanic (0.024, P=0.002), female (0.253, P=0.027), elder (0.218, P=0.017) and Native Hawaiian or other Pacific islander (2.032, P=0.027) individuals were more vulnerable to the mortality of COVID-19. More locations open to exercise (0.030, P=0.004), higher levels of air pollution (0.184, P=0.044), and segregation between non-White and White increased the mortality rate.

			• The mortality of COVID-19 depends on sex, ethnicity, and outdoor environment. The increasing awareness of these significant factors may lead to the reduction in the mortality rate of COVID-19.

Epidemiology and clinical – other

Publication Date	Title/URL	Journal/Article type	Digest
21.05.2020	Increase in Covid-19 Cases and Case Fatality and Case Recovery Rates in Europe: A Cross Temporal Meta-Analysis	Journal of medical virology / Review	• In this study, case increase, case fatality and case recovery rates of COVID-19 in 36 European countries were analysed with meta-analysis method using data released by the health organizations and WHO. • The standardized case increase rate of COVID-19 is 5% (95% CI [0.040, 0.063]) and the average case increase rate in European countries has started to decline by around 3% (95% CI [0.047, 0.083]) weekly. The countries with the highest rate of case increase are Belgium, Sweden, Russia, the Netherlands and the UK.
21.05.2020	Epidemiology of Covid-19 in a Long-Term Care Facility in King County, Washington	New England Journal of Medicine	• As of March 18, a total of 167 confirmed cases of Covid-19 affecting 101 residents, 50 health care personnel, and 16 visitors were found to be epidemiologically linked to a skilled nursing facility in King County. • Hospitalization rates for facility residents, visitors, and staff were 54.5%, 50.0%, and 6.0%, respectively. The case fatality rate for residents was 33.7% (34 of 101). • Proactive steps by long-term care facilities to identify and exclude potentially infected staff and visitors, actively monitor for potentially infected patients, and implement appropriate infection prevention and control measures are needed to prevent the introduction of Covid-19.
18.05.2020	Changes in RT-PCR-positive SARS-CoV-2 rates in adults and children according to the epidemic stages	medRxiv (non-peer reviewed) / Article	• Prospective multicentre study involving 45 paediatric units, describing the trends of RT-PCR positive SARS-CoV-2 rates in children and adults according to the time of COVID-19 epidemic. • Out of 52,588 RT-PCR tests for SARS-CoV-2 performed, 6,490 in children and 46,098 in adults, the rate of positive tests for children was 2- to 7-fold less than that for adults. • These rates varied according to the time of the epidemic and were higher at the peak. The lower rates of positive test in children persisted during the surveillance period but varied according to the time in the epidemic.
21.05.2020	Report 23 - State-level tracking of COVID-19 in the United States	Imperial College / Report	• Model of the epidemics in the US at the state-level, using publicly available death data within a Bayesian hierarchical semi-mechanistic

			framework. • For each state, the time-varying reproduction number (the average number of secondary infections caused by an infected person) is estimated, the number of individuals that have been infected and the number of individuals that are currently infectious.
21.05.2020	Objective olfactory evaluation of self-reported loss of smell in a case series of 86 COVID-19 patients	Head & neck / article	• Eighty-six patients completed the study to investigate olfactory dysfunction (OD) in patients with mild COVID-19. • The most common symptoms were fatigue (72.9%), headache (60.0%), nasal obstruction (58.6%), and postnasal drip (48.6%). • Total loss of smell was self-reported by 61.4% of patients. Objective olfactory testing identified 41 anosmic (47.7%), 12 hyposmic (14.0%), and 33 normosmic (38.3%) patients. • There was no correlation between the objective test results and subjective reports of nasal obstruction or postnasal drip.
21.05.2020	Pulmonary Vascular Endothelialitis, Thrombosis, and Angiogenesis in Covid-19	New England Journal of Medicine / article	• Describes the morphologic and molecular changes in the peripheral lung of patients who have died from COVID-19, via a small case series of 7 lungs obtained during autopsy. • The vascular angiogenesis distinguished the pulmonary pathobiology of COVID-19 from that of equally severe influenza virus infection
10.05.2020	SARS-CoV-2 infection of the liver directly contributes to hepatic impairment in patients with COVID-19	Journal of hepatology	• In this study of 64 of 156 (41.0%) COVID-19 patients from two designated centres in China, liver enzyme abnormality was associated with disease severity. • SARS-CoV-2 infected hepatocytes displayed conspicuous mitochondrial swelling, endoplasmic reticulum dilatation, and glycogen granule decrease. Histologically, massive hepatic apoptosis and a certain binuclear hepatocytes were observed. • Both ultrastructural and histological evidence indicated a typical lesion of viral infection. • SARS-CoV-2 infection in liver is a crucial cause of hepatic impairment in COVID-19 patients. Hence, a surveillance of viral clearance in liver and long outcome of COVID-19 is required.
17.05.2020	COVID-19: the key role of pulmonary capillary leakage. An observational cohort study	medRxiv (non-peer reviewed) / Article	• Observational cohort study of 174 patients to investigate the hypothesis that hypoalbuminemia in COVID-19 patients is due to pulmonary capillary leakage and to test its correlation with indicators of respiratory function. • Serum albumin concentration was decreased in the whole cohort, with ICU patients displaying lower values than IMW (Intermediate Medicine ward) patients. Lower albumin values were found in patients belonging to a more compromised group.

			• In a subset of 26 patients, analysis of bronchoalveolar lavage fluid (BALF) highlighted high protein concentrations, which were correlated to Interleukin-8 and Interleukin-10 BALF concentration. • Pulmonary capillary leak syndrome secondary to the hyperinflammatory state plays a key role in the pathogenesis of COVID-19 respiratory dysfunction and should be regarded as a therapeutic target.
20.05.2020	Neutrophil-to-lymphocyte ratio predicts critical illness patients with 2019 coronavirus disease in the early stage	Journal of translational medicine / article	• The study prospectively involved 61 patients with COVID-19 infection as a derivation cohort, and 54 patients as a validation cohort to screen the most useful predictive factor for critical illness caused by COVID-19. • Authors found that neutrophil-to-lymphocyte ratio (NLR) is a predictive factor for early-stage prediction of patients infected with COVID-19 who are likely to develop critical illness. • Patients aged ≥ 50 and having an NLR ≥ 3.13 are predicted to develop critical illness, and they should thus have rapid access to an intensive care unit if necessary.
20.05.2020	Elevated N-terminal pro-brain natriuretic peptide is associated with increased mortality in patients with COVID-19: systematic review and meta-analysis	Postgraduate medical journal / Original research	• This systematic review and meta-analysis aimed to assess the association between N-terminal pro-brain natriuretic peptide (NT-proBNP) and mortality in patients with COVID-19. • 967 patients from six studies were included. • Elevated NT-proBNP level was associated with increased mortality in COVID-19 pneumonia.
09.05.2020	Higher Temperature, Pressure, and Ultraviolet Are Associated with Less COVID-19 Prevalence: Meta-Regression of Japanese Prefectural Data	medRxiv (non-peer reviewed) / Article	• Meta-regression study of Japanese prefectural data to determine whether COVID-19 prevalence is modulated by meteorological conditions. • A slope of the meta-regression line was significantly negative for mean air temperature (coefficient, -0.134; P = 0.019), mean sea level air pressure (-0.351; P = 0.001), and mean daily maximum UV index (-0.908; P = 0.012), which indicated that COVID-19 prevalence decreased significantly as air temperature, air pressure, and UV index increased. • In conclusion, higher temperature, pressure, and UV may be associated with less COVID-19 prevalence, which should be confirmed by further epidemiological investigations taking other risk and protective factors of COVID-19 into account.

Treatment

Publication Date	Title/URL	Journal/Article type	Digest
21.05.2020	Clinical Outcomes in COVID-19 Patients Treated with Tocilizumab: An Individual Patient Data Systematic Review	Journal of Medical Virology / Research article	• In COVID-19 patients treated with tocilizumab, IL-6 levels are significantly elevated which are supportive of cytokine storm. • Following initiation of tocilizumab, there is elevation in the IL-6 levels and CRP levels dramatically decrease suggesting an improvement in this hyper-inflammatory state.
15.05.2020	Clinical evaluation of IFN beta1b in COVID-19 pneumonia: a retrospective study	medRxiv (non-peer reviewed) / Article	• Retrospective cohort study of 256 patients to assess the efficiency of IFN beta1b in COVID19, comparing the in-hospital mortality between patients who received IFN beta1b and patients who did not receive. • At admission, patients who did not receive interferon beta1b presented a greater number of comorbidities. The overall mortality rate was 24.6% (63/256). Twenty-two patients (20.8%) in the interferon group died and 41 (27.3%) in the control group (p=0.229). In the multivariate analysis, the predictors of in-hospital mortality were age, severity of clinical picture at admission and hydroxychloroquine treatment. • In hospitalized patients with COVID-19, interferon beta1b treatment was not associated to decrease in-hospital mortality.
21.05.2020	Anakinra in COVID-19: important considerations for clinical trials	The Lancet Rheumatology	• Anakinra inhibits the proinflammatory cytokines interleukin (IL)-1α and IL-1β and has been used with some success to treat macrophage activation syndrome caused by various inflammatory conditions. • The authors discuss ten ongoing clinical trials in COVID-19 with the drug anakinra and provide rationale for targeting hyperinflammation in COVID-19 and comment on different aspects of its use, patient selection, dosing, and outcome measures.

Social science

Publication Date	Title/URL	Journal/Article type	Digest
18.05.2020	Psychiatric and neuropsychiatric presentations associated with severe coronavirus infections: a systematic review and meta-analysis with comparison to the COVID-19 pandemic	The Lancet. Psychiatry / review	• If infection with SARS-CoV-2 follows a similar course to that with SARS-CoV or MERS-CoV, most patients should recover without experiencing mental illness. • SARS-CoV-2 might cause delirium in a significant proportion of patients in the acute stage. • Clinicians should be aware of the possibility of

			depression, anxiety, fatigue, post-traumatic stress disorder, and rarer neuropsychiatric syndromes in the longer term.
10.05.2020	Perinatal depressive and anxiety symptoms of pregnant women along with COVID-19 outbreak in China	American journal of obstetrics and gynecology / Article	• Cross-sectional study of 4124 pregnant women across China. Pregnant women assessed after the declaration of COVID-19 epidemic had significantly higher rates of depressive symptoms (26.0% vs 29.6%, P=0.02) than women assessed pre-epidemic announcement. • These women were also more likely to endorse thoughts of self-harm (P=0.005). The depressive rates were positively associated with the number of newly-confirmed COVID-19 cases (P=0.003), suspected infections (P=0.004), and death cases per day (P=0.001).
08.05.2020	Prevalence of depression, anxiety, and insomnia among healthcare workers during the COVID-19 pandemic: A systematic review and meta-analysis	Brain, behavior, and immunity / Systematic review	• Thirteen studies were included in the analysis with a combined total of 33062 participants. Anxiety was assessed in 12 studies, with a pooled prevalence of 23·2% and depression in 10 studies, with a prevalence rate of 22·8%. • A subgroup analysis revealed gender and occupational differences with female HCPs and nurses exhibiting higher rates of affective symptoms compared to male and medical staff respectively. Finally, insomnia prevalence was estimated at 38·9% across 4 studies.

Modelling

Publication Date	Title/URL	Journal/Article type	Digest
18.05.2020	Understanding the spreading patterns of COVID-19 in UK and its impact on exit strategies	medRxiv (non-peer reviewed) / Article	• Prior to lockdown the spread of COVID-19 in UK is found to be exponential (exponent 0.207). Lockdown has dramatically slowed down the spread of COVID-19 in UK, and even more significantly, has changed the growth in the total number of infected from exponential to quadratic. This significant change is due to a transition from a mobility-driven epidemic spreading to a spatial epidemic which is dominated by slow growth of spatially isolated clusters of infected population. • Study results strongly indicate that, to avoid a return to exponential growth of COVID-19 (also known as second wave), mobility restrictions should not be prematurely lifted. Instead mobility should be kept restricted while new measures, such as wearing of masks and contact tracing, get implemented in order to prevent health services becoming overwhelmed due to a resurgence of exponential growth.

18.05.2020	A spatial model to optimise predictions of COVID-19 incidence risk in Belgium using symptoms as reported in a large-scale online survey	medRxiv (non-peer reviewed) / Article	• Modelling study to understand spatial dynamics of COVID-19 spread in Belgium. • The authors analyse data of COVID-19 symptoms, as self-reported in a weekly online survey, which is open to all Belgian citizens. They predict symptoms' incidence using binomial models for spatially discrete data, and introduce these as a covariate in the spatial analysis of COVID-19 incidence, as reported by the Belgian government during the days following a survey round. • The symptoms' incidence predictions explain a significant proportion of the variation in the relative risks based on the confirmed cases, and exceedance probability maps of the symptoms' incidence and the confirmed cases' relative risks pinpoint the same high-risk region.
13.05.2020	Analysis of the time and age dependence of the case-fatality-ratio for COVID-19 in seven countries with a high total-to-positive test ratio suggests that the true CFR may be significantly underestimated for the United States in current models	medRxiv (non-peer reviewed) / Article	• Modelling study to explain increases in reported CFR and IFR, concluding that the large rise in the reported CFR is due to the delay time between infection/diagnosis and fatality with COVID-19. • The linear model based on age specific CFR values provides an alternative method for calculating the true CFR in other regions. Most of the variation in CFR between countries was dependent on case age distribution, which must be considered in measures for mitigating the extensive impacts of the pandemic.
18.05.2020	Who should we test for COVID-19? A triage model built from national symptom surveys	medRxiv (non-peer reviewed) / Article	• In response to global limitations in testing capacity, the authors devised a model that estimates the probability of an individual to test positive for COVID-19 based on answers to 9 simple questions regarding age, gender, presence of prior medical conditions, general feeling, and the symptoms fever, cough, shortness of breath, sore throat and loss of taste or smell. • The model provides statistically significant predictions on held-out individuals and achieves a positive predictive value (PPV) of 46.3% at a 10% sensitivity. As the tool can be used online and without the need of exposure to suspected patients, it may have worldwide utility in combating COVID-19.

Guidance, consensus statements

Publication Date	Title/URL	Journal/Article type

21.05.2020	COVID-19 rapid evidence summary [ES24]: angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) in people with or at risk of COVID-19	NICE / Evidence summary
21.05.2020	COVID-19 rapid evidence summary [ES25]: Long-term use of non-steroidal anti-inflammatory drugs (NSAIDs) for people with or at risk of COVID-19	NICE / Evidence summary
21.05.2020	COVID 19 rapid evidence summary [ES26]: Anakinra for COVID-19 associated secondary haemophagocytic lymphohistiocytosis	NICE / Evidence summary
21.05.2020	Medtech innovation briefing [MIB217]: Cytokine adsorption devices for treating respiratory failure in people with COVID-19	NICE / MIB

Produced by the PHE COVID-19 Literature Digest Team

Bláthnaid Mahon, Caroline De Brún, Nicola Pearce-Smith, Ruth Muscat, Rachel Gledhill, Emma Farrow, Cath Hayes, Paul Rudd