Public Health England

International EPI Cell Daily Evidence Digest – 20/05/2020

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:

- Serology and immunology
- Epidemiology and clinical - children and pregnancy
- Epidemiology and clinical - risk factors
- Epidemiology and clinical - other
- Infection control
- Treatment
- 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 <u>NOT</u> been peer-reviewed. They should not be relied on to guide clinical practice or health-related behaviour and should <u>NOT</u> be reported in news media as established information.

Serology and immunology

Publication Date	Title/URL	Journal/ Article type	Digest
18.05.2020	A preliminary study on serological assay for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in 238 admitted hospital patients	Microbes Infect / Article	• Evaluated diagnostic value of serological assay for SARS-CoV-2 via 238 hospital patients with confirmed or suspected SARS-CoV-2. • 194 (81.5%) of the serums were detected to be antibody (IgM and/or IgG) positive, significantly higher than positive rate of viral RNA (64.3%). • Antibody positive rates: very low in first five days after initial symptoms; rapid increase as disease progressed. After 10 days, jumped from below 50% to over 80%. Positive rates of viral RNA maintained above 60% in first 11 days then rapidly decreased. Overall, the suspected patients were most likely infected by SARS-CoV-2.

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			• The combination of serological assay can greatly improve the diagnostic efficacy. After 11th day, diagnosis for viral infection should be majorly dependent on serological assay.
13.05.2020	The infection fatality rate of COVID-19 inferred from seroprevalence data	medRxiv (not peer reviewed) / Article	• Population studies with sample size of at least 500 and published as peer-reviewed papers or preprints as of May 12, 2020 were retrieved from PubMed, preprint servers, and communications with experts. • Twelve studies were identified - seroprevalence estimates ranged from 0.113% to 25.9% and adjusted seroprevalence estimates ranged from 0.309% to 33%. • Infection fatality rates ranged from 0.03% to 0.50% and corrected values ranged from 0.02% to 0.40%. • Estimates of infection fatality rates inferred from seroprevalence studies tend to be much lower than original speculations made in the early days of the pandemic.
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. • Among these, 178 recombinant monoclonal antibodies were tested positive for antigen binding, and 17 strong binders to S1 or RBD were identified with Kd(EC50) below 1 nM. A substantial portion of these antibodies cross reacted with the SARS-CoV spike protein. • The study provides potent neutralization antibodies as clinical therapeutics candidates for further development.

Epidemiology and clinical – children and pregnancy

Publication Date	Title/URL	Journal/ Article type	Digest
19.05.2020	Septic shock presentation in adolescents with COVID-19	The Lancet Child & Adolescent Health / Correspondence	• Describe the clinical characteristics of three adolescents (10–12 years) who presented in septic shock, defined as a severe infection leading to cardiovascular dysfunction, two of whom had signs of peritonitis and multiple organ dysfunction syndrome (MODS), and who met the definition for paediatric multisystem inflammatory syndrome temporally associated with COVID-19. All had confirmed infection with SARS-CoV-2.
15.05.2020	Novel paediatric presentation of COVID-19 with ARDS and cytokine storm syndrome without respiratory symptoms	Lancet Rheumatol / Comment	• 14-year-old previously healthy individual who presented to institution with a 3-day history of pyrexia, abdominal pain, nausea, and vomiting, but without respiratory symptom • Not eligible for remdesivir compassionate use because SARS-CoV-2 PCR was

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			negative. Clinical features suggestive of COVID-19-associated cytokine storm syndrome, so 1,4 anti-inflammatory treatment with recombinant IL-1 receptor antagonist (anakinra) was initiated after multidisciplinary discussions. • First paediatric patient reported with cytokine storm syndrome presenting without respiratory symptoms on hospital admission who was successfully treated with IL-1 inhibition.
15.05.2020	Multisystem inflammatory syndrome in children and adolescents with COVID-19	World Health Organization / Scientific Brief	• Reports from Europe and North America have described clusters of children and adolescents requiring admission to intensive care units with a multisystem inflammatory condition with some features similar to those of Kawasaki disease and toxic shock syndrome. • Case reports and small series have described a presentation of acute illness accompanied by a hyperinflammatory syndrome, leading to multiorgan failure and shock. • There is an urgent need for collection of standardized data describing clinical presentations, severity, outcomes, and epidemiology. WHO has developed a preliminary case definition and case report form for multisystem inflammatory disorder in children and adolescents.
18.05.2020	Evidence and possible mechanisms of rare maternal-fetal transmission of SARS-CoV-2	J Clin Virol / Review	• 179 new-borns tested at birth from mothers with COVID-19, transmission suspected in 8 cases, 5 with positive nasopharyngeal SARS-CoV-2 RT-PCR and 3 with SARS-CoV-2 IgM. • Cases arise from maternal infection close to childbirth, no information about exposition during first or second trimester of pregnancy.

Epidemiology and clinical - risk factors

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15.05.2020	Cardiovascular comorbidities, cardiac injury and prognosis of COVID-19 in New York City	Am Heart J / Research Letters	• Using Mt. Sinai (New York City) EMR health system data, retrospective analysis of 8438 COVID-19 patients seen March 1 - April 22 2020. Risk of intubation and of death rose as a function of increasing age and as a function of greater cardiovascular comorbidity. • Combining age and specific comorbidity markers suggests cardiovascular comorbidities increased relative risks for adverse outcomes most substantially in younger subjects with progressively diminishing relative effects at older ages.
16.05.2020	Cigarette smoke exposure and inflammatory signaling increase the	Developmental Cell / Article	• Cigarette smoke causes a dose-dependent upregulation of ACE2, the SARS-CoV-2 receptor, in rodent and human lungs. • Chronic smoking triggers the expansion of ACE2+ secretory cells. ACE2 is also

			upregulated by viral infections and interferon exposure. • Results may partially explain why smokers are particularly susceptible to severe SARS-CoV-2 infections.
	expression of the SARS-CoV-2 receptor ACE2 in the respiratory tract		
14.05.2020	Blacks/African Americans are 5 Times More Likely to Develop COVID-19: Spatial Modeling of New York City ZIP Code-level Testing Results	medRxiv (not peer reviewed) / Article	• The authors analysed positive COVID-19 testing results counts within New York City ZIP Code Tabulation Areas • The population and spatial patterns of COVID-19 infections differed by race, age, physical environment and health status. • Areas with large proportions of Black/African American residents are at markedly higher risk that is not fully explained by characteristics of the environment and pre-existing conditions in the population.
13.05.2020	Risk factors for adverse clinical outcomes in patients with COVID-19: A systematic review and meta-analysis	medRxiv (not peer reviewed) / Systematic review	• The authors performed a systematic review in PubMed from January 1 until April 19, 2020. • They identified 88 eligible articles, and they performed a total of 256 meta-analyses on the association of 98 unique risk factors with five clinical outcomes. • Elevated C-reactive protein (OR, 6.46; 95% CI, 4.85 - 8.60), decreased lymphocyte count (OR, 4.16; 95% CI, 3.17 - 5.45), cerebrovascular disease (OR, 2.84; 95% CI, 1.55 - 5.20), chronic obstructive pulmonary disease (OR, 4.44; 95% CI, 2.46 - 8.02), diabetes mellitus (OR, 2.04; 95% CI, 1.54 - 2.70), haemoptysis (OR, 7.03; 95% CI, 4.57 - 10.81), and male sex (OR, 1.51; 95% CI, 1.30 - 1.75) were associated with risk of severe COVID-19.
15.05.2020	Clinical Presentation of COVID19 in Dementia Patients	The journal of nutrition, health & aging / Article	• Italian study of patients hospitalized for COVID-19. Dementia diagnosed in 82 patients (13.1%); mortality rate 62.2% (51/82) compared to 26.2% (143/545) in subjects without dementia (p<0.001, Chi-Squared test). • Dementia diagnosis, especially in most advanced stages, represents an important risk factor for mortality in COVID-19 patients. Clinical presentation of COVID-19 in subjects with dementia is atypical, reducing early recognition of symptoms and hospitalization.
18.05.2020	Thrombotic risk in COVID-19: a case series and case-control study	Clin Med (Lond)	• Possible association between COVID-19 and thrombosis explored via three cases of thromboembolism refractory to heparin treatment, the incidence of VTE in an inpatient cohort, and a case-control study to identify risk factors associated with VTE. • Cohort of 274 confirmed (208) or probable (66) COVID-19 patients. 21 (7.7%) were diagnosed with VTE. D-dimer was elevated in both cases (confirmed VTE) and controls (no confirmed VTE) but higher levels were seen in confirmed VTE cases (4.1 vs 1.2 µg/mL, P<0.001). • Incidence of VTE high in hospitalised COVID-19 patients. Urgent clinical trials are needed to evaluate the role of anticoagulation in COVID-19. Monitoring of D-dimer and anti-factor Xa levels may be beneficial in guiding management.

Epidemiology and clinical – other

Publication Date	Title/URL	Journal/ Article type	Digest
19.05.2020	Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City: a prospective cohort study	The Lancet / Article	• Over 40 000 patients with COVID-19 have been hospitalised in New York City (NY, USA) as of April 28, 2020. Data on the epidemiology, clinical course, and outcomes of critically ill patients with COVID-19 in this setting are needed. • Critical illness among patients hospitalised with COVID-19 in New York City is common and associated with a high frequency of invasive mechanical ventilation, extrapulmonary organ dysfunction, and substantial in-hospital mortality.
18.05.2020	Coronavirus disease 2019 (SARS-CoV-2) and colonization of ocular tissues and secretions: a systematic review	Eye (Lond) / Review Article	• Review included 11 articles on presence of SARS-CoV-2 in cornea, conjunctiva, lacrimal sac, and tears. • Globally, three patients had conjunctivitis with a positive tear-PCR, 8 patients had positive tear-PCR in the absence of conjunctivitis, and 14 had conjunctivitis with negative tear-PCR. • Majority of available data is controversial, but cannot exclude that SARS-CoV-2 could both infect the eye and the surrounding structures.
19.05.2020	Olfactory Dysfunction and Sinonasal Symptomatology in COVID-19: Prevalence, Severity, Timing, and Associated Characteristics	Otolaryngol Head Neck Surg	• Included 103 patients diagnosed with COVID-19. Prevalence of Olfactory dysfunction (OD)-hyposmia or anosmia was 61.2%, • OD highly prevalent during COVID-19, occurring early and severely, often with loss of taste. Associated negatively with older age, positively with female sex. Patients with OD may also experience more severe shortness of breath.

Infection control

Publication Date	Title/URL	Journal/ Article type	Digest
13.05.2020	Can we use these masks? Rapid Assessment of the Inhalation Resistance Performance of Uncertified Medical Face Masks in the Context of Restricted Resources Imposed during a Public Health Emergency	medRxiv (not peer reviewed) / Article	• In this study, an experimental methodology for the assessment of the filtration performance of samples of real-world, uncertified, fluid resistant surgical masks was evaluated in the resource limited (lockdown) environment of the COVID-19 pandemic. • The results showed that the sample masks produced a pressure drop of between 26% to 58% compared to the control batch at the lower flow rate and 22% to 55% at the higher rate. • Critically, this method does not replace certification but it has enabled a public body to quickly make decisions; certify, re-assign, refund, thus saving time and resources.

Treatment

Publication Date	Title/URL	Journal/ Article type	Digest
19.05.2020	How can healthcare workers adapt non-pharmacological treatment – whilst maintaining safety – when treating people with COVID-19 and delirium?	Oxford COVID-19 Evidence Service / Treatments for COVID	• Delirium may be part of the spectrum of COVID-19 symptoms that patients present with. In some cases, the delirium may be severe and have a rapid onset. Clinicians should have a high level of suspicion of COVID-19 when considering a possible cause of the delirium. • Non-pharmacological interventions are the mainstay for the management of delirium in all settings; there is consistent evidence of benefit in the prevention of delirium. • Communication and care are compromised by the need for Personal Protection Equipment (PPE) in COVID-19. • Use of remote consultations may be necessary and is often feasible
19.05.2020	Famotidine Use is Associated with Improved Clinical Outcomes in Hospitalized COVID-19 Patients: A Propensity Score Matched Retrospective Cohort Study	medRxiv (not peer reviewed) / Article	• This study tested whether famotidine use is associated with improved clinical outcomes in patients with COVID-19 initially hospitalized to a non-intensive care setting. 1,620 hospitalized patients with COVID-19 were identified including 84 (5.1%) who received famotidine within 24 hours of hospital admission. • Use of famotidine was associated with reduced risk for death or intubation (adjusted hazard ratio (aHR) 0.42, 95% CI 0.21-0.85) and also with reduced risk for death alone (aHR 0.30, 95% CI 0.11-0.80). • Famotidine use is associated with reduced risk of intubation or death in hospitalized COVID-19 patients.
17.05.2020	Association of Angiotensin-Converting Enzyme Inhibitors and Angiotensin Receptor Blockers with the Risk of Hospitalization and Death in Hypertensive Patients with Coronavirus Disease-19	medRxiv (not peer reviewed) / Article	• In a national study, the authors evaluated the association of ACE inhibitors and ARB with coronavirus disease-19 (COVID-19) hospitalization and mortality among individuals with hypertension. • The use of ACE inhibitors and ARBs was not associated with the risk of hospitalization or mortality among those infected with SARS-CoV-2. • However, there was a nearly 40% lower risk of hospitalization with the use of ACE inhibitors in the Medicare population.

Modelling

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19.04.2020	Mandated Bacillus Calmette-Guérin (BCG) vaccination predicts flattened curves for the spread of COVID-19	medRxiv (not peer reviewed) / Article	• The authors compared countries that mandated BCG vaccination at least until 2000, with countries that did not (129 countries in total). • Linear mixed models revealed a significant effect of mandated BCG policies on the growth rate of both cases and deaths after controlling for median age, gross domestic product per capita, population density, population size, net migration rate, and various cultural dimensions (e.g., individualism and the tightness vs. looseness of social norms). • The analysis suggested that mandated BCG vaccination can be effective in the fight against COVID-19.
15.05.2020	The impact of COVID-19 on African American communities in the United States	medRxiv (not peer reviewed) / Article	• The objective was to understand the impact of the density of African American communities (defined as the percentage of African Americans in a county) on COVID-19 prevalence and death rate within the three most populous counties in each U.S. state and territory (n=152). • There was a direct association between African American density and COVID-19 prevalence; COVID-19 prevalence increased 5% for every 1% increase in county AA density. • There was also an association between county AA density and COVID-19 deaths, such; the death rate increased 2 per 100,000 for every percentage increase in county AA density (p=.02) • These study findings indicate that communities with a high African American density have been disproportionately burdened with COVID-19.
19.05.2020	Agent-Based Simulation for Evaluation of Contact-Tracing Policies Against the Spread of SARS-CoV-2	medRxiv (not peer reviewed) / Article	• In order to quantify the benefits of tracing and similar policies, the authors have developed an agent-based model that not only validly depicts the spread of the disease, but allows for exploratory analysis of containment policies. • This paper describes the model, and performs case studies where the model is used to quantify impact of contact tracing.
19.05.2020	Reproducing SARS-CoV-2 epidemics by region-specific variables and modeling contact tracing App containment	medRxiv (not peer reviewed) / Article	• The authors built an expanded SIR model of COVID-19 epidemics that accounts for region-specific population densities, and used it to test the impact of a contact-tracing app in a number of scenarios. • The results showed that, in support of efficient isolation of symptomatic cases, app-mediated contact-tracing can improve containment and achieve successful epidemic mitigation even with a relatively small fraction of the population using it, and, with increasing penetrance of its adoption, suppression. • However, when regional differences in population density are taken into consideration, the epidemic can be significantly harder to contain in higher density areas, highlighting potential limitations of this intervention in specific contexts.

| 19.05.2020 | [Predictors of COVID-19 incidence, mortality, and epidemic growth rate at the country level](#) | medRxiv (not peer reviewed) / Article | • The authors examined COVID-19 cases and deaths reported up to May 2, 2020 across 205 countries and territories in relation to weather data collected from capital cities for the eight weeks prior to and four weeks after the date of the first reported case, as well as country/territory-level population, geographic, and planetary data.
• Lower temperature (p<0.0001), lower humidity (p=0.006), higher altitude (p=0.0080), higher percentage of urban population (p<0.0001), increased air travellers (p=0.00019), and higher prevalence of obesity (p<0.0001) were strong independent predictors of national COVID-19 incidence, mortality, and epidemic growth rate.
• The results of this ecologic analysis demonstrate that global COVID-19 burden and timing of country-level epidemic growth can be predicted by weather and population factors; cool, dry, and higher altitude environments, as well as more urban and obese populations, may be conducive to more rapid epidemic spread. |

Guidelines and consensus statements

Publication Date	Title/URL	Journal/ Article type
16.05.2020	[Allergic respiratory disease care in the COVID-19 era: a EUFOREA statement](#)	World Allergy Organization Journal / Article
10.05.2020	[Contact tracing in the context of COVID-19](#)	World Health Organization / Interim guidance
13.05.2020	[Laboratory biosafety guidance related to coronavirus disease (COVID-19)](#)	World Health Organization / Interim guidance
16.05.2020	[Cleaning and disinfection of environmental surfaces in the context of COVID-19](#)	World Health Organization / Interim guidance
18.05.2020	[Overview of Public Health and Social Measures in the context of COVID-19](#)	World Health Organization / Interim guidance
15.05.2020	[Preparedness and response to Pediatric CoVID-19 in European Emergency Departments: a survey of the REPEM and PERUKI networks](#)	Ann Emerg Med
14.05.2020	[COVID-19 management in a UK NHS Foundation Trust with a High Consequence Infectious Diseases centre: a detailed descriptive analysis](#)	medRxiv (not peer reviewed) / Article

Produced by the PHE COVID-19 Literature Digest Team

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