



COVID-19 Literature Digest – 14/08/2020

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- Serology and immunology
- Diagnostics
- Genomics
- Epidemiology and clinical - children and pregnancy
- Epidemiology and clinical - risk factors
- Epidemiology and clinical - other
- Infection control
- Miscellaneous
- Modelling
- 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Please note that we are including preprints (**highlighted in red**), which are preliminary reports of work that have NOT been peer-reviewed.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.

Serology and immunology

Publication Date	Title / URL	Journal / Article type	Digest
11.08.2020	Antibody prevalence for SARS-CoV-2 following the peak of the pandemic in England: REACT2 study in 100,000 adults	Imperial College London (non-peer reviewed) / Article	<ul style="list-style-type: none">• REACT-2 seroprevalence study using self-administered LFIA test for IgG among a random population sample of 100,000 adults in England, 20 June to 13 July 2020.• Completed questionnaires available for 109,076 participants, yielding 5,544 IgG positive results and adjusted, re-weighted prevalence of 6.0% (95% CI: 5.8, 6.1).

			<ul style="list-style-type: none"> • Highest prevalence in London (13.0% [12.3, 13.6]), among people of Black or Asian (mainly S. Asian) ethnicity (17.3% [15.8, 19.1] and 11.9% [11.0, 12.8] respectively), and those aged 18-24 years (7.9% [7.3, 8.5]). • One third (32.2%, [31.0-33.4]) of antibody positive individuals reported no symptoms. • Estimates 3.36 million (3.21, 3.51) people have been infected with COVID-19 in England to end June 2020, with an overall infection fatality ratio of 0.90% (0.86, 0.94).
10.08.2020	High prevalence of SARS-CoV-2 antibodies in care homes affected by COVID-19; a prospective cohort study in England	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • The authors report follow-up serological analysis in six London care homes which had previously experienced a COVID-19 outbreak among residents and staff. • RT-PCR testing for COVID-19 significantly underestimates the true extent of an outbreak in institutional settings. • More than two-thirds of residents and staff members had detectable antibodies against COVID-19 irrespective of their nasal swab RT-PCR positivity or symptoms status.
06.08.2020	Prevalence of SARS-CoV-2 Antibodies in Health Care Personnel in the New York City Area	Jama / Letter	<ul style="list-style-type: none"> • Found a 13.7% prevalence of SARS-CoV-2 antibodies in this large cohort study of HCP (n=40,329) in the greater NYC area.
12.08.2020	Clinical and laboratory evaluation of SARS-CoV-2 lateral flow assays for use in a national COVID-19 seroprevalence survey	Bmj Thorax / Article	<ul style="list-style-type: none"> • Lateral flow immunoassays (LFIAs) can deliver testing at scale. Sensitivity analysis was conducted on 276 non-hospitalised participants. • 95% of the infected cohort had detectable antibodies on at least one ELISA. LFA sensitivity was variable, but significantly inferior to ELISA in 8 out of 11 assessed. Of LFIAs assessed in both clinic and laboratory, finger-prick self-test sensitivity varied from 21% to 92% versus PCR-confirmed cases and from 22% to 96% versus composite ELISA positives. • Concordance between finger-prick and serum testing was at best moderate (kappa 0.56) and, at worst, slight (kappa 0.13). All LFIAs had high specificity (97.2%–99.8%).
12.08.2020	Usability and acceptability of home-based self-testing for SARS-CoV-2 antibodies for population surveillance	Clin Infect Dis / Article	<ul style="list-style-type: none"> • Assessed acceptability and usability of home-based self-testing for SARS-CoV-2 antibodies using lateral flow immunoassays (LFIA). • Carried out public involvement and pilot testing in 315 volunteers to improve usability. This informed the design of a nationally representative survey of adults in England using two LFIAs (LFIA1 and LFIA2) which were sent to 10,600 and 3,800 participants. • Impactful public involvement is feasible in a rapid response setting. Home self-testing with LFIAs can be used with a high degree of

			acceptability and usability by adults, making them a good option for use in seroprevalence surveys.
11.08.2020	Systems biological assessment of immunity to mild versus severe COVID-19 infection in humans	Science / Article	<ul style="list-style-type: none"> • Analysed immune responses in 76 COVID-19 patients and 69 healthy individuals from Hong Kong and Atlanta. • In PBMCs of COVID-19 patients, there was reduced expression of HLA-DR and pro-inflammatory cytokines by myeloid cells, and impaired mTOR-signalling and IFN-α production by plasmacytoid DCs. • In contrast, there were enhanced plasma levels of inflammatory mediators, including EN-RAGE, TNFSF14, and oncostatin-M, which correlated with disease severity and increased bacterial products in human plasma. Single-cell transcriptomics revealed no type-I IFN, reduced HLA-DR in myeloid cells of severe patients, and transient expression of IFN-stimulated genes.
12.08.2020	Phase 1/2 study of COVID-19 RNA vaccine BNT162b1 in adults	Nature / Article	<ul style="list-style-type: none"> • Report the available safety, tolerability, and immunogenicity data from an ongoing placebo-controlled, observer-blinded dose escalation study among 45 healthy adults, 18 to 55 years of age, randomized to receive 2 doses, separated by 21 days, of 10 μg, 30 μg, or 100 μg of BNT162b1, a lipid nanoparticle-formulated, nucleoside-modified mRNA vaccine that encodes trimerized SARS-CoV-2 spike glycoprotein RBD. • Results support further evaluation of this mRNA vaccine candidate.
13.08.2020	Effect of an Inactivated Vaccine Against SARS-CoV-2 on Safety and Immunogenicity Outcomes: Interim Analysis of 2 Randomized Clinical Trials	Jama / Preliminary communication	<ul style="list-style-type: none"> • This inactivated COVID-19 vaccine had a low rate of adverse reactions and demonstrated immunogenicity, but longer-term assessment of safety and efficacy will require phase 3 trials.
10.08.2020	Effectiveness of booster BCG vaccination in preventing Covid-19 infection	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • All staff of the Emirates International Hospital (United Arab Emirates) were offered a booster BCG (bacille Calmette-Guerin) vaccine in early Mar 2020, then tested for Covid-19 infection by the end of June 2020. • Participants were divided into two groups: booster vaccinated (n=71), and unvaccinated (n=209). • The infection rate in the unvaccinated group was 8.6% versus zero in the booster vaccinated group.

Diagnostics

Publication Date	Title / URL	Journal / Article type	Digest
13.08.2020	Duration of infectiousness and correlation with RT-PCR cycle threshold values in cases of COVID-19, England, January to May 2020	Eurosurveillance / Rapid communication	<ul style="list-style-type: none"> • SARS-CoV 2 viral load in the upper respiratory tract peaks around symptom onset and infectious virus persists for 10 days in mild-to-moderate coronavirus disease (n = 324 samples analysed). • RT-PCR cycle threshold (Ct) values correlate strongly with cultivable virus. Probability of culturing virus declines to 8% in samples with Ct > 35 and to 6% 10 days after onset; it is similar in asymptomatic and symptomatic persons. • Asymptomatic persons represent a source of transmissible virus.
06.08.2020	Clinical Course and Molecular Viral Shedding Among Asymptomatic and Symptomatic Patients With SARS-CoV-2 Infection in a Community Treatment Center in the Republic of Korea	JAMA Intern Med / Original investigation	<ul style="list-style-type: none"> • Many individuals with SARS-CoV-2 infection remained asymptomatic for a prolonged period, and viral load was similar to that in symptomatic patients; therefore, isolation of infected persons should be performed regardless of symptoms.
10.08.2020	Point Prevalence Testing of Residents for SARS-CoV-2 in a Subset of Connecticut Nursing Homes	Jama / Letter	<ul style="list-style-type: none"> • In a sample of nursing homes in Connecticut with at least 1 COVID-19 case in the week preceding point prevalence surveys, 28% of residents tested positive, of which 78% remained asymptomatic and 10% were pre-symptomatic. • The proportion of asymptomatic residents is higher than in previous smaller survey studies of long-term care facilities, which found percentages of 50% to 55%.
13.08.2020	SARS-CoV-2 PCR testing of skin for COVID-19 diagnostics: a case report	The Lancet / Correspondence	<ul style="list-style-type: none"> • In summary, this case emphasises the use of SARS-CoV-2 PCR testing of skin biopsy samples as an additional diagnostic tool, helping to shed light on the actual prevalence of COVID-19 in the general population.

Genomics

Publication Date	Title / URL	Journal / Article type	Digest
13.08.2020	Geographical and temporal distribution of SARS-CoV-2 clades in the WHO European Region, January to June 2020	Eurosurveillance / Rapid communication	<ul style="list-style-type: none"> • Show that the distribution of SARS-CoV-2 genetic clades over time and between countries and outline potential genomic surveillance objectives. • Applied three genomic nomenclature systems to all sequence data from the World Health Organization European Region available until 10

July 2020.

- Highlight the importance of real-time sequencing and data dissemination in a pandemic situation, compare the nomenclatures and lay a foundation for future European genomic surveillance of SARS-CoV-2.

Epidemiology and clinical - children and pregnancy

Publication Date	Title / URL	Journal / Article type	Digest
12.08.2020	COVID-19 in children: analysis of the first pandemic peak in England	Arch Dis Child / Article	<ul style="list-style-type: none">• The authors assessed disease trends, testing practices, community surveillance, case-fatality and excess deaths in children as compared with adults during the first pandemic peak in England between Jan and May 2020.• In children aged <16 years, 35,200 tests were performed and 1408 (4.0%) were positive for COVID-19, compared to 19.1%–34.9% adults.• Among 2,961 individuals presenting with ARI in primary care, 351 were children and 10 (2.8%) were positive compared with 9.3%–45.5% in adults.• Eight children died and four (case-fatality rate, 0.3%; 95% CI 0.07% to 0.7%) were due to COVID-19.• The authors suggest there was no evidence of excess mortality in children.
28.07.2020	Transmission of COVID-19 in school settings and interventions to reduce the transmission: a rapid review	Public Health England / Rapid review	<ul style="list-style-type: none">• This review included 9 studies: 3 epidemiological and 6 modelling studies (including 5 preprints) (search up to 18 June 2020).• There is limited and weak evidence from the 3 epidemiological studies that the transmission of COVID-19 within school settings is low.• There is weak evidence from 6 modelling studies that the re-opening of schools at a reduced capacity, particularly for younger children, may not be associated with a second epidemic wave.• The evidence base should be routinely monitored to capture new studies on transmission and interventions as they emerge.
14.08.2020	COVID-19-Associated Multisystem Inflammatory Syndrome in Children - United States, March-July 2020	MMWR Morb Mortal Wkly Rep / Report	<ul style="list-style-type: none">• Found that most cases of MIS-C have features of shock, with cardiac involvement, gastrointestinal symptoms, and significantly elevated markers of inflammation, with positive laboratory test results for COVID-19.

11.08.2020	Burden of illness in households with SARS-CoV-2 infected children	J Pediatric Infect Dis Soc / Article	<ul style="list-style-type: none"> • Investigated the dynamics of illness among household members of SARS-CoV-2 infected children that received medical care (n=32). • Identified 144 household contacts (HCs): 58 children and 86 adults. Forty-six percent of HCs developed symptoms consistent with COVID-19 disease. Child-to-adult transmission was suspected in 7 cases.
12.08.2020	COVID-19-associated apnea and circumoral cyanosis in a 3-week-old	BMC Pediatr / Case report	<ul style="list-style-type: none"> • First report of apnea and perioral cyanosis associated with COVID-19 in an infant. This case highlights a previously undocumented COVID-19 presentation and suggests that even mildly symptomatic infants warrant viral diagnostic testing in an effort to prevent further spread of the disease.

Epidemiology and clinical - risk factors

Publication Date	Title / URL	Journal / Article type	Digest
13.08.2020	Does exposure to air pollution increase the risk of dying from the coronavirus (COVID-19)?	Office for National Statistics / Report	<ul style="list-style-type: none"> • Analysis examined the impact of long-term exposure to air pollution on COVID-19 deaths in England, with results pointing to a smaller effect than previous studies. • Polluted areas initially had higher rates of COVID-19 deaths, but this trend decreased as the death toll rose.
13.08.2020	Associations of type 1 and type 2 diabetes with COVID-19-related mortality in England: a whole-population study	The Lancet Diabetes & Endocrinology / Article	<ul style="list-style-type: none"> • An assessment of the independent effects of diabetes status, by type, on in-hospital death in England in patients with COVID-19 during the period from Mar 1 to May 11, 2020. • Results demonstrate that type 1 and type 2 diabetes are both independently associated with a significant increased odds of in-hospital death with COVID-19.
13.08.2020	Risk factors for COVID-19-related mortality in people with type 1 and type 2 diabetes in England: a population-based cohort study	The Lancet Diabetes & Endocrinology / Article	<ul style="list-style-type: none"> • An assessment of associations between risk factors and COVID-19-related mortality in people with type 1 and type 2 diabetes. • The authors conclude that increased COVID-19-related mortality was associated not only with cardiovascular and renal complications of diabetes but, independently, also with glycaemic control and BMI.
12.08.2020	Obesity and Mortality Among Patients Diagnosed With COVID-19: Results From an Integrated Health Care Organization	Ann Intern Med / Article	<ul style="list-style-type: none"> • Retrospective cohort study (n=6916) to determine the adjusted effect of BMI, associated comorbidities, time, neighbourhood-level sociodemographic factors, and other factors on risk for death due to COVID-19 in Southern California. • There was a J-shaped association between BMI and risk for death, even after adjustment for obesity-related comorbidities.

			<ul style="list-style-type: none"> • This risk was most striking among those aged 60 years or younger and men. • Increased risk for death associated with Black or Latino race/ethnicity or other sociodemographic characteristics was not detected.
11.08.2020	Is there a smoker's paradox in COVID-19?	BMJ Evid Based Med / Article	<ul style="list-style-type: none"> • The authors review existing literature to examine claims of a 'smoker's paradox', wherein smokers are protected from infection and severe complications of COVID-19. • Several biases and knowledge gaps which may give the false impression that smoking is protective in COVID-19. • At present, data supporting smoker's paradox claims are limited and questionable. • Plausible biologic mechanisms for a protective effect include an anti-inflammatory effect of nicotine, a blunted immune response in smokers and increased nitric oxide in the respiratory tract. • However, smoking may worsen susceptibility and prognosis in COVID-19, in a manner similar to other respiratory infections.
13.08.2020	Sex differential in COVID-19 mortality varies markedly by age	The Lancet /Correspondence	<ul style="list-style-type: none"> • Examined the sex ratio through the life course to see if the COVID-19 mortality sex-differential was the same at every age. • There was some variation across countries, although broadly the pattern was similar, and the numbers became too small for clear-cut interpretation.
11.08.2020	Racial and ethnic disparities in SARS-CoV-2 pandemic: analysis of a COVID-19 observational registry for a diverse US metropolitan population	BMJ Open / Article	<ul style="list-style-type: none"> • The authors analysed sociodemographic factors associated with higher likelihood of COVID-19 infection and explored mediating pathways for race and ethnic disparities in the COVID-19 pandemic. • Among 20,228 tested individuals, 1551 (7.7%) tested positive. • Non-Hispanic Black (NHB) and Hispanic ethnicity were associated with lower socioeconomic status and higher population density residence. • In the fully adjusted model, NHB and Hispanic ethnicity had a higher likelihood of infection. • Older individuals and males were at higher risk of infection.

Epidemiology and clinical – other

Publication Date	Title / URL	Journal / Article type	Digest
13.08.2020	Contact Settings and Risk for Transmission in 3410 Close Contacts of Patients With COVID-19 in Guangzhou, China: A Prospective Cohort Study	Ann Intern Med / Article	<ul style="list-style-type: none"> • A prospective cohort study in Guangzhou, China, evaluating risk for transmission of COVID-19 to close contacts (n=3410) in different settings between 13 Jan and 6 Mar 2020. • 127 were secondarily infected, and 8 of these were asymptomatic. • Compared with the household setting (10.3%), the secondary attack rate was lower for exposures in healthcare settings and on public transportation. • The secondary attack rate increased with the severity of index cases, from 0.3% for asymptomatic to 3.3% for mild, 5.6% for moderate, and 6.2% for severe or critical cases.
11.08.2020	Reducing nosocomial transmission of COVID-19: implementation of a COVID-19 triage system	Clin Med (Lond) / Article	<ul style="list-style-type: none"> • Of 662 inpatients with COVID-19 at an NHS Trust in South London, 45 (6.8%) were likely to have acquired COVID-19 in hospital. • These patients had no evidence of respiratory or influenza-like illness on admission and developed symptoms, with positive COVID-19 PCR test results, more than 7 days after admission (>14 days for 38 [5.7%] patients). • Forty (88.9%) had shared a ward with a confirmed COVID-19 case prior to testing positive. • Implementation of a triage system combining clinical assessment with rapid COVID-19 testing facilitated cohorting so that fewer susceptible patients were exposed to COVID-19 on shared wards.
03.08.2020	Coronavirus Disease 2019 Outcomes in French Nursing Homes That Implemented Staff Confinement With Residents	JAMA Netw Open / Article	<ul style="list-style-type: none"> • This cohort study including 17 nursing homes with staff self-confinement and 9513 nursing homes in a national survey found that nursing homes with staff self-confinement experienced lower mortality related to COVID-19 among residents and lower incidence of COVID-19 among residents and staff members than rates recorded in a national survey.
10.08.2020	Coronial autopsies identify the indirect effects of COVID-19	Lancet Public Health / Correspondence	<ul style="list-style-type: none"> • Of 67 autopsies done at John Radcliffe Hospital (Oxford, UK) during the first 2 months of lockdown, only two identified COVID-19 that was undiagnosed before death. • Reduced access to health-care systems associated with lockdown was identified as a probable contributory factor (six cases) or possible contributory factor (eight cases) to death. • Direct reference to financial or work pressures caused by COVID-19

			<p>was identified in three of ten cases of suicide.</p> <ul style="list-style-type: none"> • Deaths from drug and alcohol misuse significantly increased during the lockdown period in comparison to the same period in 2018, but it was not possible to identify whether individual cases were influenced by COVID-19 movement restrictions.
12.08.2020	Unspecific post-mortem findings despite multiorgan viral spread in COVID-19 patients	Crit Care / Article	<ul style="list-style-type: none"> • Autopsies of 17 COVID-19 patients revealed a great heterogeneity of COVID-19-associated organ injury and the remarkable absence of any specific viral lesions, even when RT-PCR identified the presence of the virus in many organs.
12.08.2020	SARS-CoV-2 Natural Transmission from Human to Cat, Belgium, March 2020	Emerg Infect Dis / Article	<ul style="list-style-type: none"> • In March 2020, a severe respiratory syndrome developed in a cat, 1 week after its owner received positive test results for SARS-CoV 2. • Viral RNA was detected in the cat's nasopharyngeal swab samples and vomitus or faeces; immunoglobulin against the virus was found in convalescent-phase serum. Human-to-cat transmission is suspected.

Infection control

Publication Date	Title / URL	Journal / Article type	Digest
11.08.2020	Filtration Efficiency of Hospital Face Mask Alternatives Available for Use During the COVID-19 Pandemic	JAMA Intern Med / Original investigation	<ul style="list-style-type: none"> • This study found that when new N95 respirators are unavailable, N95 respirators past their expiration date; sterilized, used N95 respirators; and other less common respirators can be acceptable alternatives.

Miscellaneous

Publication Date	Title / URL	Journal / Article type	Digest
11.08.2020	Coronavirus: indexed data speed up solutions	Nature / Correspondence	<ul style="list-style-type: none"> • The authors has developed the COVID-19 Data Index (www.covid19dataindex.org). • Originally funded by the US National Institutes of Health as part of the Big Data to Knowledge project, the index hosts a metadata catalogue of COVID-19 data sets. • Update the COVID-19 Data Index daily.
12.08.2020	COVID-19, antibiotics and One Health: a UK environmental risk assessment	J Antimicrob Chemother / Letter	<ul style="list-style-type: none"> • Illustrate here data relevant to a single UK emergency hospital in different COVID-19 scenarios, providing environmental assessments

relevant to designing optimal drug use and waste management systems in a One Health context.

Treatment

Publication Date	Title / URL	Journal / Article type	Digest
12.08.2020	Effect of Convalescent Plasma on Mortality among Hospitalized Patients with COVID-19: Initial Three-Month Experience	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • The authors examined the effect of human convalescent plasma transfusion on 7 and 30-day mortality in a U.S. national cohort of 35,322 adult participants hospitalised with COVID-19. • The 7-day mortality rate was 8.7% [95% CI 8.3%-9.2%] in patients transfused within 3 days of COVID-19 diagnosis but 11.9% [11.4%-12.2%] in patients transfused 4 or more days after diagnosis (p=0.001). Similar findings were observed in 30-day mortality (21.6% vs. 26.7%, p=0.0001). • A gradient of mortality was seen in relation to IgG antibody levels in the transfused plasma. The pooled relative risk of mortality among patients transfused with high antibody level plasma units was 0.65 [0.47-0.92] for 7 days and 0.77 [0.63-0.94] for 30 days compared to low antibody level plasma units.
08.08.2020	An ultra-high affinity synthetic nanobody blocks SARS-CoV-2 infection by locking Spike into an inactive conformation	bioRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • The authors developed single-domain antibodies (nanobodies) that potentially disrupt the interaction between the COVID-19 Spike and ACE2. • Its properties may enable aerosol-mediated delivery directly to the airway epithelia, promising to yield a widely deployable, patient-friendly prophylactic and/or early infection therapeutic agent.

Modelling

Publication Date	Title / URL	Journal / Article type	Digest
04.08.2020	Fitting to the UK COVID-19 outbreak, short-term forecasts and estimating the reproductive number	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • The authors present an inference scheme employed for calibrating the Warwick COVID-19 model to the available public health data streams, which span hospitalisations, critical care occupancy, mortality and serological testing. • Compare how refinements to data streams and model structure impact estimates of epidemiological measures, including the estimated growth rate and daily incidence.

Overviews, comments and editorials

Publication Date	Title / URL	Journal / Article type
12.08.2020	Behind the headlines: Counting COVID-19 deaths	Public Health England / Blog
11.08.2020	Airborne Transmission of COVID-19	Clin Infect Dis / Article
13.08.2020	An Inactivated Virus Candidate Vaccine to Prevent COVID-19	Jama / Editorial
12.08.2020	COVID-19 and Severe Obesity: A Big Problem?	Ann Intern Med / Editorial
11.08.2020	Medicine is a social science: COVID-19 and the tragedy of residential care facilities in high-income countries	BMJ Glob Health / Comment
10.08.2020	A need for open public data standards and sharing in light of COVID-19	Lancet Infect Dis / Correspondence
10.08.2020	Digital public health and COVID-19	Lancet Public Health / Comment

Produced by the PHE COVID-19 Literature Digest Team

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