



COVID-19 Literature Digest – 21/09/2020

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Please note that we are including preprints (**highlighted in red**), which are preliminary reports of work that have NOT been peer-reviewed.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

Serology and immunology

Publication Date	Title / URL	Journal / Article type	Digest
17.09.2020	A systematic review of antibody mediated immunity to coronaviruses: kinetics, correlates of protection, and association with severity	Nat Commun / Systematic review	<ul style="list-style-type: none"> • <i>This paper was previously included in the Digest as a preprint.</i> • Reviewed the scientific literature on antibody immunity to coronaviruses, including SARS-CoV-2. • Identified 491 manuscripts relevant to 5 focus areas: 1) antibody kinetics, 2) correlates of protection, 3) immunopathogenesis, 4) antigenic diversity and cross-reactivity, 5) population seroprevalence.

			<ul style="list-style-type: none"> • While further studies of SARS-CoV-2 are necessary to determine immune responses, evidence from other coronaviruses can provide clues and guide future research.
18.09.2020	Ultrasensitive high-resolution profiling of early seroconversion in patients with COVID-19	Nat Biomed Eng / Article	<ul style="list-style-type: none"> • Report a multiplexed assay for the fluorescence-based detection of seroconversion in infected individuals from less than 1 µl of blood, and as early as the day of the first positive nucleic acid test after symptom onset. • The assay uses dye-encoded antigen-coated beads to quantify the levels of immunoglobulin G (IgG), IgM and IgA antibodies against four SARS-CoV-2 antigens.

Diagnostics

Publication Date	Title / URL	Journal / Article type	Digest
15.09.2020	Universal screening for SARS-CoV-2 infection: a rapid review	Cochrane Database of Systematic Reviews / Rapid review	<ul style="list-style-type: none"> • Authors conducted a rapid review to assess (1) effectiveness of universal screening for SARS-CoV-2 infection compared with no screening; (2) accuracy of universal screening in people who have not presented to clinical care for symptoms of COVID-19. • Review highlights the uncertainty and variation in accuracy of screening strategies. A high proportion of infected individuals may be missed and go on to infect others; some healthy individuals may be falsely identified as positive, requiring confirmatory testing and potentially leading to the unnecessary isolation of these individuals. • Further studies need to evaluate the utility of rapid laboratory tests, combined screening, and repeated screening. More research is also needed on reference standards with greater accuracy than RT-PCR.
16.09.2020	Variation of SARS-CoV-2 viral loads by sample type, disease severity and time: a systematic review	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • A systematic review to describe whether SARS-CoV-2 viral loads (VLs) and cycle thresholds (CTs) vary by sample type, disease severity and symptoms duration. • VLs were higher in saliva and sputum than in nasopharyngeal and oropharyngeal swabs. • Combined naso/oropharyngeal swabs had lower CT values (i.e. higher VLs) than single site samples. • CT values were lower in asymptomatic individuals and patients with severe COVID-19 than among patients with moderate/mild symptoms.

			<ul style="list-style-type: none"> • Stool samples were reported positive for a longer period than other specimens.
18.09.2020	Sensitive fluorescence detection of SARS-CoV-2 RNA in clinical samples via one-pot isothermal ligation and transcription	Nat Biomed Eng / Article	<ul style="list-style-type: none"> • Report a highly sensitive and specific one-pot assay for the fluorescence-based detection of RNA from pathogens. • The assay, which can be performed within 30–50 min of incubation time and can reach a limit of detection of 0.1-attomolar RNA concentration, relies on a sustained isothermal reaction cascade producing an RNA aptamer that binds to a fluorogenic dye. • Also show that the assay can rapidly detect a range of viral and bacterial RNAs.
18.09.2020	Ultrasensitive and visual detection of SARS-CoV-2 using all-in-one dual CRISPR-Cas12a assay	Nat Commun / Article	<ul style="list-style-type: none"> • Authors present an All-In-One Dual CRISPR-Cas12a (AIOD-CRISPR) assay for one-pot, ultrasensitive, and visual SARS-CoV-2 detection. • Use low-cost hand warmer (~\$0.3) as an incubator, results in up to 20 min, enabling an instrument-free, visual SARS-CoV-2 detection at the point of care.

Genomics

Publication Date	Title / URL	Journal / Article type	Digest
13.09.2020	Genome sequencing of sewage detects regionally prevalent SARS-CoV-2 variants	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Sequenced RNA directly from sewage collected by municipal utility districts in the San Francisco Bay Area to generate complete and near-complete SARS-CoV-2 genomes. • The major consensus SARS-CoV-2 genotypes detected in the sewage were identical to clinical genomes from the region. Using a pipeline for single nucleotide variant (SNV) calling in a metagenomic context, they characterized minor SARS-CoV-2 alleles in the wastewater and detected viral genotypes which were also found within clinical genomes throughout California. • Additional variants detected in wastewater have only been identified in genomes from patients sampled outside of CA, indicating that wastewater sequencing can provide evidence for recent introductions of viral lineages before they are detected by local clinical sequencing.

Epidemiology and clinical – children and pregnancy

Publication Date	Title / URL	Journal / Article type	Digest
16.09.2020	Characteristics and Maternal and Birth Outcomes of Hospitalized Pregnant Women with Laboratory-Confirmed COVID-19 — COVID-NET, 13 States, March 1–August 22, 2020	MMWR Morb Mortal Wkly Rep / Report	<ul style="list-style-type: none"> • Among 598 hospitalized U.S. pregnant women with COVID-19, 55% were asymptomatic at admission. • Severe illness occurred among symptomatic pregnant women, including intensive care unit admissions (16%), mechanical ventilation (8%), and death (1%). • Pregnancy losses occurred for 2% of pregnancies completed during COVID-19-associated hospitalizations and were experienced by both symptomatic and asymptomatic women.
16.09.2020	SARS-CoV-2 Infection Among Hospitalized Pregnant Women: Reasons for Admission and Pregnancy Characteristics — Eight U.S. Health Care Centers, March 1–May 30, 2020	MMWR Morb Mortal Wkly Rep / Report	<ul style="list-style-type: none"> • Investigated reasons for hospital admission, pregnancy-specific characteristics, and birth outcomes among pregnant women hospitalized with SARS-CoV-2 infections (n=105). • Prevalences of prepregnancy obesity and gestational diabetes were higher among pregnant women hospitalized for COVID-19–related illness (e.g., worsening respiratory status) than among those admitted for pregnancy-related treatment or procedures (e.g., delivery) and found to have COVID-19. • Intensive care was required for 30% (13 of 43) of pregnant women admitted for COVID-19, and one pregnant woman died from COVID-19.
18.09.2020	Infant Outcomes Following Maternal Infection with SARS-CoV-2: First Report from the PRIORITY Study	Clin Infect Dis / Article	<ul style="list-style-type: none"> • Among 263 initial infants enrolled in the U.S PRIORITY study, adverse outcomes - including preterm birth, NICU admission, difficulty breathing, apnea or upper or lower respiratory infection through 8 weeks of age - didn't differ between those born to mothers testing positive or negative for SARS-CoV-2. • PRIORITY's initial findings regarding infant health are reassuring. Further investigation with longer follow up periods and larger sample sizes are planned for the cohort.

Epidemiology and clinical – risk factors

Publication Date	Title / URL	Journal / Article type	Digest
18.09.2020	Thrombotic and haemorrhagic complications in critically ill patients with COVID-19: a multicentre observational study	Crit Care / Article	<ul style="list-style-type: none"> • Multicentre retrospective observational study evaluating all the COVID-19 patients received in four ICUs of four UK tertiary hospitals. • Critically ill COVID-19 patients experience high rates of venous and arterial thrombotic complications. Rates of bleeding may be higher than previously reported and re-iterate the need for randomised trials to better understand the risk-benefit ratio of different anticoagulation strategies.
18.09.2020	Interactions between SARS-CoV-2 and Influenza and the impact of coinfection on disease severity: A test negative design	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • To assess whether a coinfection was associated with severe SARS-CoV-2 outcome, the authors conducted univariable and multivariable analyses on the odds of death adjusted for age, sex, ethnicity, comorbidity and coinfection status. • The risk of testing positive for SARS-CoV-2 was 68% lower among influenza positive cases, suggesting possible pathogenic competition between the two viruses. • Patients with a coinfection had a risk of death of 5.92 (95% CI, 3.21-10.91) times greater than among those with neither influenza nor SARS-CoV-2 suggesting possible synergistic effects in coinfecting individuals. • The odds of ventilator use or death and ICU admission or death was greatest among coinfection patients showing strong evidence of an interaction effect compared to SARS-CoV-2/influenza acting independently.
18.09.2020	Risk Factors for COVID-19-associated hospitalization: COVID-19-Associated Hospitalization Surveillance Network and Behavioral Risk Factor Surveillance System	Clin Infect Dis / Article	<ul style="list-style-type: none"> • Authors sought to identify factors independently associated with COVID-19-associated hospitalizations in U.S. • Among 5,416 adults, hospitalization rates were higher among those with ≥ 3 underlying conditions (versus without), severe obesity, chronic kidney disease, diabetes, obesity, hypertension, and asthma, after adjusting for age, sex, and race/ethnicity. • Adjusting for presence of an individual underlying medical condition, higher hospitalization rates were observed for adults aged ≥ 65, 45-64 (versus 18-44 years), males (versus females), and non-Hispanic black and other race/ethnicities (versus non-Hispanic whites).
18.09.2020	The Impact of Sociodemographic Factors, Comorbidities and Physiologic Response on	Clin Infect Dis / Article	<ul style="list-style-type: none"> • Retrospective cohort study of 3,633 consecutive COVID-19 patients (mean age of 58 year) presenting to emergency departments within Metropolitan Detroit.

	30-day Mortality in COVID-19 Patients in Metropolitan Detroit		<ul style="list-style-type: none"> • Majority were female and black non-Hispanic. 64% required hospitalization, 56% of whom were black. Hospitalized patients were older, more likely to reside in a low-income area, and had a higher burden of comorbidities. • Those with comorbidities, advanced age, and physiological abnormalities on presentation had higher odds of death. Disparities in income or source of health insurance were not associated with outcomes. Black women had a lower risk of dying (odds ratio, 0.46; 95% confidence interval, 0.27 to 0.78).
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Epidemiology and clinical – other

Publication Date	Title / URL	Journal / Article type	Digest
17.09.2020	Clustering and superspreading potential of SARS-CoV-2 infections in Hong Kong	Nat Med / Article	<ul style="list-style-type: none"> • Using contact tracing data from 1,038 SARS-CoV-2 cases confirmed between 23 Jan and 28 Apr 2020 in Hong Kong, the authors identified and characterized all local clusters of infection. • They identified 4–7 superspreading events (SSEs) across 51 clusters (n = 309 cases) and estimated that 19% (95% confidence interval, 15–24%) of cases seeded 80% of all local transmission. Transmission in social settings was associated with more secondary cases than households when controlling for age (P = 0.002). • Decreasing the delay between symptom onset and case confirmation did not result in fewer secondary cases (P = 0.98), although the odds that an individual being quarantined as a contact interrupted transmission was 14.4 (95% CI, 1.9–107.2).
15.09.2020	COVID-19 epidemic severity is associated with timing of non-pharmaceutical interventions	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Using phylogenetic methods, the authors estimate the rate of early COVID-19 epidemic growth and proxy estimates of epidemic size (using 29,000 publicly available whole genome SARS-CoV-2 sequences from 57 locations). • The time elapsed between epidemic origin and maximum intervention is strongly associated with different measures of epidemic severity and explains 46% of variance in numbers infected at time of maximum intervention. • The R number is independently associated with epidemic severity. • In multivariable regression, epidemic severity was not associated with census population size.

			<ul style="list-style-type: none"> • The time elapsed between detection of initial COVID-19 cases to interventions was not associated with epidemic severity, indicating that many locations experienced long periods of cryptic transmission. • Concluded that locations where strong non-pharmaceutical interventions were implemented earlier experienced much less severe COVID-19 morbidity and mortality during the period of study.
18.09.2002	Coronavirus (COVID-19) related deaths by disability status, England and Wales: 2 March to 14 July 2020	ONS / Report	<ul style="list-style-type: none"> • Comparison of deaths where COVID-19 was mentioned on the death certificate by broad age group, sex and disability status, using linked census and mortality records on deaths registered up to 21 July 2020. • Disabled people (as defined) made up almost 6 in 10 (59%) of all deaths involving COVID-19 in this period; disabled people made up around 16% of the study population followed from the 2011 Census. • Among all deaths involving COVID-19 of males aged 9 to 64 years in this period, the proportion made up by disabled people (those limited a little or limited a lot in their day-to-day activities) was smallest at 39%; among all deaths involving COVID-19 of females aged 65 years and over in this period, the proportion made up by disabled people was largest, at 67% of these deaths.
14.09.2020	Tracing asymptomatic SARS-CoV-2 carriers among 3674 hospital staff:a cross-sectional survey	EClinicalMedicine / Article	<ul style="list-style-type: none"> • A total of 3764 hospital staff were included in this single-centre cross-sectional study: all received throat swab RT-PCR test, plasma COVID-19 IgM/IgG antibodies test and chest CT examination. 126 hospital staff had abnormal findings, and the proportion of asymptomatic infection accounted for 0.76% (28/3674). • Authors analysed the correlation between infection rates and gender, age, job position, work place and COVID-19 knowledge training of the staff.
19.09.2020	A Case of Early Re-infection with SARS-CoV-2	Clin Infect Dis / Letter	<ul style="list-style-type: none"> • The clinical, epidemiological, and sequencing data of this case suggest early re-infection with SARS CoV-2, only 51 days after resolution of initial infection. Importantly, this was observed in a young immunocompetent patient.
20.09.2020	A case of probable Parkinson's disease after SARS-CoV-2 infection	Lancet Neurol / Correspondence	<ul style="list-style-type: none"> • Parkinson's disease or parkinsonism have been described after infections by viruses, such as influenza A, Epstein-Barr virus, varicella zoster, hepatitis C virus, HIV. • Authors report a patient with probable Parkinson's disease, who was diagnosed after severe COVID-19 infection. • A genetic analysis for mutations associated with the disease was negative and the patient had no previous family history of Parkinson's disease.

18.09.2020	Measurement of SARS-CoV-2 RNA in wastewater tracks community infection dynamics	Nat Biotechnol / Article	<ul style="list-style-type: none"> • Measured SARS-CoV-2 RNA concentrations in primary sewage sludge in the New Haven, Connecticut, USA, metropolitan area during the COVID-19 outbreak in Spring 2020. • SARS-CoV-2 RNA was detected throughout the more than 10-week study and, when adjusted for time lags, tracked the rise and fall of cases seen in SARS-CoV-2 clinical test results and local COVID-19 hospital admissions. • Data shows the utility of viral RNA monitoring in municipal wastewater for SARS-CoV-2 infection surveillance at a population-wide level. In communities facing a delay between specimen collection and the reporting of test results, immediate wastewater results can provide considerable advance notice of infection dynamics.
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Infection control

Publication Date	Title / URL	Journal / Article type	Digest
15.09.2020	Adherence to the test, trace and isolate system: results from a time series of 21 nationally representative surveys in the UK (the COVID-19 Rapid Survey of Adherence to Interventions and Responses [CORSAIR] study)	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • The authors used a series of cross-sectional online surveys (31,787 participants) to investigate adherence to the UK's test, trace and isolate system over time. • Only 48.9% of participants identified key symptoms of COVID-19. • Self-reported adherence to test, trace and isolate behaviours was low (self-isolation 18.2%; requesting an antigen test 11.9%; intention to share details of close contacts 76.1%; quarantining 10.9%) and largely stable over time. • Non-adherence was associated with: men, younger age groups, having a dependent child in the household, lower socio-economic grade, greater hardship during the pandemic, and working in a key sector. • Practical support and financial reimbursement is likely to improve adherence. Targeting messaging and policies to men, younger age groups, and key workers may also be necessary.
18.09.2020	Transmission of Severe Acute Respiratory Syndrome Coronavirus 2 During Long Flight	Emerg Infect Dis / Research	<ul style="list-style-type: none"> • Investigated a cluster of cases among passengers on a 10-hour commercial flight. They traced 217 passengers and crew to their final destinations and interviewed, tested, and quarantined them. • Among the 16 persons in whom SARS-CoV-2 infection was detected, 12 (75%) were passengers seated in business class along with the only symptomatic person (attack rate 62%).

			<ul style="list-style-type: none"> • Seating proximity was strongly associated with increased infection risk (risk ratio 7.3, 95% CI 1.2–46.2). They found no strong evidence supporting alternative transmission scenarios. • In-flight transmission that probably originated from 1 symptomatic passenger caused a large cluster of cases during a long flight. Guidelines for preventing SARS-CoV-2 infection among air passengers should consider individual passengers' risk for infection, the number of passengers traveling, and flight duration.
18.09.2020	In-Flight Transmission of Severe Acute Respiratory Syndrome Coronavirus 2	Emerg Infect Dis / Dispatch	<ul style="list-style-type: none"> • Four persons with SARS-CoV-2 infection had travelled on the same flight from Boston, Massachusetts, USA, to Hong Kong, China. • Their virus genetic sequences are identical, unique, and belong to a clade not previously identified in Hong Kong, which strongly suggests that the virus can be transmitted during air travel.
16.09.2020	Viable SARS-CoV-2 in the air of a hospital room with COVID-19 patients	Int J Infect Dis / Article	<ul style="list-style-type: none"> • Air samples collected in the hospital room of two COVID-19 patients, one ready for discharge, the other newly admitted, were subjected to RT-qPCR and virus culture. The genomes of the SARS-CoV-2 collected from the air and isolated in cell culture were sequenced. • Viable SARS-CoV-2 was isolated from air samples collected 2 to 4.8 m away from the patients. The genome sequence of the SARS-CoV-2 strain isolated from the material collected by the air samplers was identical to that isolated from the newly admitted patient. Estimates of viable viral concentrations ranged from 6 to 74 TCID50 units/L of air. • Patients with respiratory manifestations of COVID-19 produce aerosols in the absence of aerosol-generating procedures that contain viable SARS-CoV-2, and these aerosols may serve as a source of transmission of the virus.
18.09.2020	Clinical Impact, Costs, and Cost-Effectiveness of Expanded SARS-CoV-2 Testing in Massachusetts	Clin Infect Dis / Article	<ul style="list-style-type: none"> • Authors projected clinical/economic impact of alternative testing strategies on COVID-19 incidence and mortality in Massachusetts using a microsimulation model. • Testing people with any COVID-19-consistent symptoms would be cost-saving compared to testing only those whose symptoms warrant hospital care. Expanding PCR testing to asymptomatic people would decrease infections, deaths, and hospitalizations. • Despite modest sensitivity, low-cost, repeat screening of the entire population could be cost-effective in all epidemic settings.

Treatment

Publication Date	Title / URL	Journal / Article type	Digest
16.09.2020	Mortality outcomes with hydroxychloroquine and chloroquine in COVID-19: an international collaborative meta-analysis of randomized trials	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none">• A rapid meta-analysis (16 unpublished trials, 10 publications/preprints) found no benefit of hydroxychloroquine or chloroquine on the survival of COVID-19 patients.• For hydroxychloroquine, the confidence interval is compatible with increased mortality (OR 1.18) or negligibly reduced mortality (OR 0.99).• Findings have unclear generalisability to outpatients, children, pregnant women, and people with comorbidities.

Guidance and consensus statements

Publication Date	Title / URL	Journal / Article type
18.09.2020	A national consensus management pathway for paediatric inflammatory multisystem syndrome temporally associated with COVID-19 (PIMS-TS): results of a national Delphi process	Lancet Child & Adolescent Health / Review

Overviews, comments and editorials

Publication Date	Title / URL	Journal / Article type
16.09.2020	REGULAR MASS SCREENING FOR SARS-CoV-2 INFECTION IN CARE HOMES ALREADY AFFECTED BY COVID-19 OUTBREAKS: implications of false positive test results	J Infect / Letter
18.09.2020	Uruguay is winning against covid-19. This is how	Bmj / Feature
17.09.2020	Covid-19: Do many people have pre-existing immunity?	Bmj / Feature
18.09.2020	Severe COVID-19 Infections - Knowledge Gained and Remaining Questions	JAMA Intern Med / Editorial
18.09.2020	Artificial intelligence in COVID-19 drug repurposing	The Lancet Digital Health / Review

Produced by the PHE COVID-19 Literature Digest Team

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A selection of previous digests [can be found here](#)