



COVID-19 Literature Digest – 25/09/2020

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
- Modelling
- Guidance, consensus statements and hospital resources (no digest)
- Overviews, comments and editorials (no digest)

Please note that we are including preprints (**highlighted in red**), which are preliminary reports of work that have NOT been peer-reviewed. They should not be relied on to guide clinical practice or health-related behaviour and should NOT be reported in news media as established information.

Serology and immunology

Publication Date	Title / URL	Journal / Article type	Digest
23.09.2020	Performance characteristics of five immunoassays for SARS-CoV-2: a head-to-head benchmark comparison	The Lancet Infectious Diseases / Article	<ul style="list-style-type: none">• Concluded that four commercial, widely available assays and a scalable 384-well ELISA can be used for SARS-CoV-2 serological testing to achieve sensitivity and specificity of at least 98%. The Siemens assay and Oxford immunoassay achieved these metrics without further optimisation.• This benchmark study in immunoassay assessment should enable refinements

			of testing strategies and the best use of serological testing resource to benefit individuals and population health.
24.09.2020	Sensitive Detection of SARS-CoV-2-Specific Antibodies in Dried Blood Spot Samples	Emerg Infect Dis / Dispatch	<ul style="list-style-type: none"> • <i>This paper was previously included in the Digest as a preprint.</i> • Dried blood spot (DBS) samples can be used for the detection of SARS-CoV-2 spike antibodies. DBS sampling is comparable to matched serum samples with a relative 98.1% sensitivity and 100% specificity. • Thus, DBS sampling offers an alternative for population-wide serologic testing in the coronavirus pandemic.
23.09.2020	Loss of Anti-SARS-CoV-2 Antibodies in Mild Covid-19	N Engl J Med / Correspondence	<ul style="list-style-type: none"> • A series of letters to the editor. • Letter 1: Convalescent plasma from 151 donors. Authors found that the IgA levels remained high until 50 to 60 days after the onset of symptoms and that the IgG levels remained elevated, with only a slight decrease, at 120 days after the onset of symptoms. • Letter 2: Convalescent plasma from 259 donors. Results suggest that there is a rapid reduction in anti-SARS-CoV-2 antibody levels in patients who have recovered from Covid-19 and highlight the need for a new antibody measurement at the time of plasmapheresis in studies of convalescent plasma. • Letter 3: 81 patients with Covid-19. Antibody titres tended to be higher in patients with severe disease than in those with mild or moderate disease. However, patients with moderate and severe disease, as well as those with mild disease, seemed to show a decrease in antibody titres after 60 days from the onset of symptoms. These results suggest that although antibody titres are higher in patients with a greater severity of disease, they will eventually decline.
23.09.2020	Serum antibody profile of a patient with COVID-19 reinfection	Clin Infect Dis / Article	<ul style="list-style-type: none"> • Patient with COVID-19 reinfection. Serum neutralizing antibody detected during the first episode but not at presentation of the second episode. • During reinfection, neutralizing antibody and high avidity IgG were found within 8 days after hospitalization, while IgM response was absent. • Results suggest that a 2-dose vaccine regimen may be required for individuals who do not have prior exposure to SARS-CoV-2.
16.09.2020	COVID-19 herd immunity in the Brazilian Amazon	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Authors show that the transmission of SARS-CoV-2 in Manaus, in the Brazilian Amazon, increased quickly during Mar and Apr and declined more slowly from May to Sept. • In June, one month following the epidemic peak, 44% of the population was seropositive for SARS-CoV-2, equating to a cumulative incidence of 52%, after correcting for the false-negative rate of the antibody test. The seroprevalence fell in July and Aug due to antibody waning. After correcting for this, they estimate a final epidemic size of 66%. • Concluded that although non-pharmaceutical interventions, plus a change in

			population behaviour may have helped to limit SARS-CoV-2 transmission in Manaus, the unusually high infection rate suggests that herd immunity played a significant role in determining the size of the epidemic.
21.09.2020	Dynamic Change of COVID-19 Seroprevalence among Asymptomatic Population in Tokyo during the Second Wave	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> Assessed changes in COVID-19 seroprevalence among asymptomatic employees working in Tokyo during the second wave. Out of the 350 individuals (mean + SD 42.5 + 10.0; range 19-69; 46.0 % female) who completed both offered tests, 21.4 % of those individuals who tested seronegative became seropositive and seroreversion was found in 12.2 % of initially seropositive participants. 81.1% of IgM positive cases at first testing became IgM negative in approximately one month. COVID-19 infection may have spread widely across the general population of Tokyo despite the very low fatality rate. Given the temporal correlation between the rise in seropositivity and the decrease in reported COVID-19 cases that occurred without a shut-down, herd immunity may be implicated.

Diagnostics

Publication Date	Title / URL	Journal / Article type	Digest
23.09.2020	Massive and rapid COVID-19 testing is feasible by extraction-free SARS-CoV-2 RT-PCR	Nat Commun / Article	<ul style="list-style-type: none"> Describe methods circumventing RNA extraction in COVID-19 testing by performing RT-PCR directly on heat-inactivated or lysed samples. The data, including benchmarking using 597 clinical patient samples and a standardised diagnostic system, demonstrate that direct RT-PCR is viable option to extraction-based tests. Using controlled amounts of active SARS-CoV-2, they confirm effectiveness of heat inactivation by plaque assay and evaluate various generic buffers as transport medium for direct RT-PCR.

Genomics

Publication Date	Title / URL	Journal / Article type	Digest
22.09.2020	Molecular Architecture of Early Dissemination and Massive Second Wave of the SARS-CoV-2	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> Sequenced the genomes of 5,085 SARS-CoV-2 strains causing two COVID-19 disease waves in metropolitan Houston, Texas, an ethnically diverse region with seven million residents.

	Virus in a Major Metropolitan Area		<ul style="list-style-type: none"> • Virtually all strains in the second wave have a Gly614 amino acid replacement in the spike protein, a polymorphism that has been linked to increased transmission and infectivity. • Patients infected with the Gly614 variant strains had significantly higher virus loads in the nasopharynx on initial diagnosis. • Found little evidence of a significant relationship between virus genotypes and altered virulence, stressing the linkage between disease severity, underlying medical conditions, and host genetics.
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Epidemiology and clinical – children and pregnancy

Publication Date	Title / URL	Journal / Article type	Digest
24.09.2020	Surveillance of COVID-19 school outbreaks, Germany, March to August 2020	Eurosurveillance / Rapid communication	<ul style="list-style-type: none"> • The authors analysed national surveillance system data on COVID-19 school outbreaks in Germany during different time periods. • After reopening, smaller outbreaks (average: 2.2/week) occurred despite low incidence in the general population. School closures might have a detrimental effect on children and should be applied only cautiously and in combination with other measures.

Epidemiology and clinical – risk factors

Publication Date	Title / URL	Journal / Article type	Digest
24.09.2020	Rapid risk assessment: Increased transmission of COVID-19 in the EU/EEA and the UK – twelfth update	European Centre for Disease Prevention and Control / Risk assessment	<ul style="list-style-type: none"> • In this update, the authors analyse the risk posed to the general population, vulnerable individuals, and healthcare provision by the current increase in COVID-19 case notification rates observed in the EU/EEA and the UK.
25.09.2020	Update: Characteristics of Health Care Personnel with COVID-19 - United States, February 12-July 16, 2020	MMWR Morb Mortal Wkly Rep / Report	<ul style="list-style-type: none"> • Among 2,633,585 U.S. COVID-19 cases reported individually to CDC during Feb 12–July 16, HCP status was available for 571,708 (22%) persons, among whom 100,481 (18%) were identified as HCP. • HCP with COVID-19 who died tended to be older, male, Asian, Black, and have an underlying medical condition when compared with HCP who did not die. • Nursing and residential care facilities were the most commonly reported job setting and nursing the most common single occupation type of HCP with COVID-19 in six jurisdictions.

18.09.2020	Serial Testing for SARS-CoV-2 and Virus Whole Genome Sequencing Inform Infection Risk at Two Skilled Nursing Facilities with COVID-19 Outbreaks - Minnesota, April-June 2020	MMWR Morb Mortal Wkly Rep / Report	<ul style="list-style-type: none"> • Serial facility-wide testing at two Minnesota skilled nursing facilities (SNFs) identified COVID-19 cases among 64% of residents and 33% of HCP. • Genetic sequencing found facility-specific clustering of viral genomes from HCP and residents' specimens, suggesting interfacility transmission.
25.09.2020	Disparities in COVID-19 Incidence, Hospitalizations, and Testing, by Area-Level Deprivation - Utah, March 3-July 9, 2020	MMWR Morb Mortal Wkly Rep / Report	<ul style="list-style-type: none"> • During Mar 3–June 9, 2020, odds of SARS-CoV-2 infection in very high-deprivation areas of Utah were three times higher than those in very low-deprivation areas; rates of hospitalization and testing were also higher in higher-deprivation areas. • These areas were characterized by larger proportions of Hispanic and non-White residents, persons working in manual, essential, and public-facing sectors, more crowded housing, and food and health care insecurity.
22.09.2020	Ethnic differences in COVID-19 infection, hospitalisation, and mortality: an OpenSAFELY analysis of 17 million adults in England	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • A cohort study of 17,510,002 English adults (63% white, 6% south Asian, 2% black, 2% other, 1% mixed, and 26% unknown) investigated ethnic differences in the risk of COVID-19 infection, hospitalisation and mortality, adjusting for explanatory factors such as household size. • South Asian, black, and mixed groups were marginally more likely to be tested, and substantially more likely to test positive for SARS-CoV-2 compared with white adults. • Risk of COVID-19 mortality was increased by 25-56% in ethnic minority groups compared with white adults (south Asian HR 1.27; black HR 1.55; mixed HR 1.40; other HR 1.25).
24.09.2020	Assessment of Disparities in COVID-19 Testing and Infection Across Language Groups in Seattle, Washington	JAMA Netw Open / Research letter	<ul style="list-style-type: none"> • Authors evaluated the proportion of patients who completed testing and the proportion of positive cases using language as a surrogate for immigrant status. • 30 925 patients underwent testing. Non-English speakers overall less likely to have completed testing compared with English-speakers but the proportion tested varied across language groups. • Proportion of positive cases 4.6-fold higher among non-English speakers (18.6%; 95% CI, 16.8%-20.4%) compared with English speakers (4.0%; 95% CI, 3.8%-4.2%). This excess risk was observed across multiple languages and in the 3 largest non-English-speaking groups.
23.09.2020	Risk Factors for Hospitalization, Mechanical Ventilation, or Death Among 10 131 US Veterans With SARS-CoV-2 Infection	JAMA Netw Open / Original investigation	<ul style="list-style-type: none"> • Longitudinal cohort study: 88 747 patients tested for SARS-CoV-2 Feb 28 - May 14, followed up in June. 10 131 patients (11.4%) tested positive. • Most SARS-CoV-2 deaths associated with older age, male sex, and comorbidity burden. Many factors previously reported to be associated with mortality in smaller studies were not confirmed, such as obesity, Black race, Hispanic ethnicity, chronic obstructive pulmonary disease, hypertension, and smoking.

23.09.2020	Association of Red Blood Cell Distribution Width With Mortality Risk in Hospitalized Adults With SARS-CoV-2 Infection	JAMA Netw Open / Original investigation	<ul style="list-style-type: none"> • A cohort study (1641 patients; mean age 62 years; 54% male) investigated potential association between mortality risk and elevated red blood cell distribution width (RDW) for COVID-19 patients being treated at 4 hospitals in Boston, Massachusetts. • Elevated RDW (>14.5%) was associated with an increased mortality risk in patients of all ages. • Patients whose RDW increased during hospitalization had higher mortality compared with those whose RDW did not change; for those with normal RDW, mortality increased from 6% to 24%, and for those with an elevated RDW at admission, mortality increased from 22% to 40%.
24.09.2020	Early predictors of in-hospital mortality in patients with COVID-19 in a large American cohort	Intern Emerg Med / Article	<ul style="list-style-type: none"> • Multicentred cohort study identifying patient characteristics and diagnostic markers present on initial evaluation associated with mortality in hospitalized COVID-19 patients. • 1461 patients were included in final analysis. • 327 patients died during hospitalization and 1134 survived to discharge. Median age was 62 years (IQR 50.0, 74.0) with 56% of hospitalized patients under the age of 65. 47% were female and 63% identified as African American. • In multivariable analysis, older age, admission respiratory status including elevated respiratory rate and oxygen saturation $\leq 88\%$, and initial laboratory derangements of creatinine > 1.33 mg/dL, alanine aminotransferase > 40 U/L, procalcitonin > 0.5 ng/mL, and lactic acid ≥ 2 mmol/L increased risk of in-hospital death.
22.09.2020	Etiology and antimicrobial resistance of secondary bacterial infections in patients hospitalized with COVID-19 in Wuhan, China: a retrospective analysis	Antimicrob Resist Infect Control / Research	<ul style="list-style-type: none"> • Retrospective study of 1495 hospitalized COVID-19 patients in Wuhan Union Hospital; 102 (6.8%) acquired secondary bacterial infections (SBIs). 49.0% (50/102) died during hospitalization. • Compared with severe patients, critical patients had higher chance of SBIs. 159 strains of bacteria isolated from SBIs, 136 (85.5%) were Gram-negative bacteria. • SBI incidence associated with severity of illness on admission. Gram-negative bacteria, especially <i>A. baumannii</i> and <i>K. pneumoniae</i>, were main bacteria. Resistance rates of the major isolated bacteria were generally high.
22.09.2020	Risk of adverse COVID-19 outcomes for people living with HIV: a rapid review and meta-analysis	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • A rapid review and meta-analysis assessed whether people living with HIV (PLWH) are at increased risk of COVID-19 mortality or adverse outcomes, and whether antiretroviral therapy (ART) influences this risk. Nineteen studies were included. • Evidence is emerging that suggests a moderately increased risk of COVID-19 mortality amongst PLWH. Further investigation into the relationship between COVID-19 outcomes and CD4+ T cell count, HIV viral load, ART and the use of TDF is warranted.

Epidemiology and clinical – other

Publication Date	Title / URL	Journal / Article type	Digest
23.09.2020	Respiratory disease in cats associated with human-to-cat transmission of SARS-CoV-2 in the UK	bioRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Case study of two cats from different COVID-19-infected households in the UK found to be infected with SARS-CoV-2. • High throughput sequencing of the virus from cat 2 revealed that the feline viral genome contained five single nucleotide polymorphisms (SNPs) compared to the nearest UK human SARS-CoV-2 sequence. • Analysis of the viral genome of cat 2 together with nine other feline-derived SARS-CoV-2 sequences from around the world revealed no shared cat-specific mutations. • Suggests human-to-cat transmission of SARS-CoV-2 occurred during the COVID-19 pandemic in the UK, with the infected cats developing mild or severe respiratory disease.
24.09.2020	Pathological features of COVID-19-associated myocardial injury: a multicentre cardiovascular pathology study	Eur Heart J / Article	<ul style="list-style-type: none"> • In an international multicentre study, cardiac tissue from the autopsies of 21 consecutive COVID-19 patients was assessed by cardiovascular pathologists. • In SARS-CoV-2 there are increased interstitial macrophages in a majority of the cases and multifocal lymphocytic myocarditis in a small fraction of the cases. • Other forms of myocardial injury are also present in these patients. The macrophage infiltration may reflect underlying diseases rather than COVID-19.
23.09.2020	Asymptomatic reinfection in two healthcare workers from India with genetically distinct SARS-CoV-2	Clin Infect Dis / Correspondence	<ul style="list-style-type: none"> • Report of COVID-19 reinfection in two healthcare workers in India (25 yo male and 28 yo female), as confirmed by genomic analysis.

Infection control

Publication Date	Title / URL	Journal / Article type	Digest
25.09.2020	COVID-19 Contact Tracing in Two Counties - North Carolina, June-July 2020	MMWR Morb Mortal Wkly Rep / Report	<ul style="list-style-type: none"> • During periods of high COVID-19 incidence in North Carolina, 48% of COVID-19 patients reported no contacts, and 25% of contacts were not reached in Mecklenburg County. In Randolph County, 35% of COVID-19 patients reported no contacts, and 48% of contacts were not reached. Median interval from index patient specimen collection to contact notification was 6 days. • Despite aggressive efforts by health departments, many COVID-19 patients do not report contacts, and many contacts cannot be reached. Improved timeliness

			of contact tracing, community engagement, and community-wide mitigation are needed to reduce SARS-CoV-2 transmission.
22.09.2020	Norwich COVID-19 Testing Initiative: feasibility project evaluation	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • This study aimed to pilot mass COVID-19 testing on a university research park (5,625 participants), to assess the feasibility and acceptability of scaling up to all staff and students. • Concluded that repeated self-testing is feasible and acceptable to a university population.
22.09.2020	Ability of fabric face mask materials to filter ultrafine particles at coughing velocity	BMJ Open / Original research	<ul style="list-style-type: none"> • Twenty commonly available fabrics and materials were evaluated for their ability to reduce air concentrations of ultrafine (0.02-0.1 µm) particles at coughing face velocities. • Average filtration efficiency of single layer fabrics and of layered combination was found to be 35% and 45%, respectively. • Face masks made from layered common fabric can help filter ultrafine particles and provide some protection for wearer when commercial face masks unavailable.

Treatment

Publication Date	Title / URL	Journal / Article type	Digest
24.09.2020	Risk of COVID-19-related death among patients with chronic obstructive pulmonary disease or asthma prescribed inhaled corticosteroids: an observational cohort study using the OpenSAFELY platform	The Lancet Respiratory Medicine / Article	<ul style="list-style-type: none"> • Assessed the association between inhaled corticosteroids (ICSs) and COVID-19-related death among people with COPD or asthma using linked electronic health records (EHRs) in England, UK. • Results do not support a major role for regular ICS use in protecting against COVID-19-related death among people with asthma or COPD. Observed increased risks of COVID-19-related death can be plausibly explained by unmeasured confounding due to disease severity.
23.09.2020	Decreased mortality in COVID-19 patients treated with Tocilizumab: a rapid systematic review and meta-analysis of observational studies	Clin Infect Dis / Article	<ul style="list-style-type: none"> • Review identified 10 studies comprising 1358 patients; 9 were of high quality. • Results: mortality 12% lower for COVID-19 patients treated with tocilizumab compared to COVID-19 patients not treated with tocilizumab. • Number needed to treat was 11, suggesting for every 11 (severe) COVID-19 patients treated with tocilizumab 1 death is prevented. These results require confirmation by randomized controlled trials.
24.09.2020	Human recombinant soluble ACE2 in severe COVID-19	The Lancet Respiratory Medicine / Case report	<ul style="list-style-type: none"> • A case report describing the first course of treatment with hrsACE2 of a patient with severe COVID-19.

Modelling

Publication Date	Title / URL	Journal / Article type	Digest
25.09.2020	Report 33 - Modelling the allocation and impact of a COVID-19 vaccine	Imperial College / Report	<ul style="list-style-type: none"> • Identified optimal vaccine allocation strategies within and between countries to maximise health (avert deaths) under constraints on dose supply. • Extended an existing mathematical model of SARS-CoV-2 transmission across different country settings to model the public health impact of potential vaccines, using a range of target product profiles developed by the World Health Organization. • Show that as supply increases, vaccines that reduce or block infection – and thus transmission – in addition to preventing disease have a greater impact than those that prevent disease alone, due to the indirect protection provided to high-risk groups.

Guidance and consensus statements

Publication Date	Title / URL	Journal / Article type
24.09.2020	Guidelines for the implementation of non-pharmaceutical interventions against COVID-19	European Centre for Disease Prevention and Control / Report

Overviews, comments and editorials

Publication Date	Title / URL	Journal / Article type
24.09.2020	Coronavirus (COVID-19) in 10 charts	Gov.uk / Official statistics
22.09.2020	COVID-19 clinical trials: learning from exceptions in the research chaos	Nat Med / Article
23.09.2020	Animal models for COVID-19	Nature / Review
23.09.2020	SARS-CoV-2 vaccines in development	Nature / Review
24.09.2020	Lessons learnt from easing COVID-19 restrictions: an analysis of countries and regions in Asia Pacific and Europe	The Lancet / Health policy
23.09.2020	As Their Numbers Grow, COVID-19 "Long Haulers" Stump Experts	JAMA / Medical news & perspectives
23.09.2020	The complexities of SARS-CoV-2 serology	The Lancet Infectious Diseases / Comment

24.09.2020

[Inhaled corticosteroids and COVID-19-related mortality: confounding or clarifying?](#)

The Lancet Respiratory Medicine / Comment

Produced by the PHE COVID-19 Literature Digest Team

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