



COVID-19 Literature Digest – 07/10/2020

Dear all,

This week's guest editor is Dr Sam Collins - Principal Public Health Scientist in Chemicals and Poisons at PHE and Programme Lead for the COVID-19 External Guidance Cell.

If you only read three papers this week...

Considerable work has been undertaken by PHE and others examining the associations between racial disparities and COVID-19 incidence and outcomes. This is a subject close to the heart of the Guidance Cell as we look to adapt our guidance and outputs to ensure that our key public health messages reach, are understood and are interpreted correctly by all communities. [Munoz-Price and colleagues](#) undertook a cross-sectional study of 2595 COVID-19 patients in a large mid-western healthcare system during the early stages of the pandemic. COVID-19 positivity was associated with Black race (odds ratio [OR], 5.37; 95%CI, 3.94-7.29; P = .001). Hospitalisation was associated with both Black race (OR, 1.85; 95%CI, 1.00-3.65; P = .04) and poverty (OR, 3.58; 95% CI, 1.08-11.80; P = .04). However, encouragingly there was no evidence of racial disparity in other indicators of disease severity including ICU admission and death, suggesting no inherent racial susceptibility to poor outcomes from this disease. It was proposed that the burden of disease within Black populations could be mitigated by reducing the rate of infection through already established measures adapted to the social economic status of these populations.

Next, we have a study from the United States examining COVID-19 cases in universities. As we have seen in several universities in the UK, [Wilson et al](#) examined a rapid rise in COVID-19 cases and clusters within two weeks of a North Caroline University opening to students. Not surprisingly, key settings of transmission were identified as student gatherings and congregated living settings. Although these findings are limited, they should help inform enhanced measures to reduce transmission within university settings such as reducing housing density, ensuring adherence to face covering guidance and testing strategies.

Finally, we have an unusual paper combining genetic risk factors and a part time interest of mine, anthropology. Several risk factors associated with poorer COVID-19 outcome have been identified e.g. age. More recently, a study of 3,199 hospitalised COVID-19 patients identified a major genetic risk factor for severe SARS-CoV-2 on chromosome 3. [Zeberg et al](#) showed that this core 50kb risk haplotype is inherited from Neanderthals and is present at different frequencies in populations across the globe. Highest frequency (30%) is seen in South Asia, with more than half of the Bangladeshi population carrying at least one copy of the Neanderthal risk haplotype. This is a very interesting observation and one hypothesis is that the risk haplotype has been positively selected in Bangladesh, perhaps as a defence mechanism against other pathogens. The risk haplotype is less frequent in European populations at an average 8% and strikingly absent in East Asian populations. The Neanderthal risk haplotype may be a significant contributor to severe COVID-19 disease. Current [data from the UK](#) supports this hypothesis, with patients of Bangladeshi origin having twice the risk of dying from COVID-19 than the general population (95% CI: 1.7-2.4). It will be interesting to determine what particular elements of the risk haplotype are associated with poorer COVID-19 outcomes and, when more complete data on outcomes is available, it's potential contribution to global deaths.

Sam

Please find [today's report](#) below.

PHE's COVID-19 Literature Digest has been produced since February 2020. A selection of our previous Digests [can be found here](#). This resource aims to highlight a small selection of recent COVID-19 papers that are relevant to UK settings, contains new data / insights or emerging trends. The Digest team generate a report three times per week (Mon, Wed, Fri), which includes both preliminary reports of work (preprints) that have NOT been peer-reviewed and research that has been subject to peer review and wider scrutiny. The Digest is very rapidly produced and does not claim to be a perfect product; the inclusion or omission of a publication should not be viewed as an endorsement or rejection by PHE. We do not accept responsibility for the availability, reliability or content of the items included in this resource.

To join our email distribution list please send a request to COVID.LitDigest@phe.gov.uk. If you are interested in papers relating to behaviour and social science please contact wncov.behaviour@phe.gov.uk to sign up to receive the PHE Behavioural Sciences Weekly Report.

Best wishes,

Bláthnaid Mahon, Emma Farrow, James Robinson
On behalf of the PHE COVID-19 Literature Digest Team

Report for 07.10.2020 (please note that papers that have **NOT been peer-reviewed** are **highlighted in red**).

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Serology and immunology

Publication Date	Title / URL	Journal / Article type	Digest
03.10.2020	SARS-CoV-2 seroprevalence survey among 17,971 healthcare and administrative personnel at hospitals, pre-hospital services, and specialist practitioners in the Central Denmark Region	Clin Infect Dis / Article	<ul style="list-style-type: none"> • Authors found large differences in the prevalence of SARS-CoV-2 antibodies in 17,971 staff working in the healthcare sector within a small geographical area of Denmark. Half of all seropositive staff had been tested positive by PCR prior to this survey; overall seroprevalence was 3.4% (CI: 2.5%-3.8%). • Seroprevalence was higher in western area (11.9% vs 1.2%, difference: 10.7 percentage points, CI: 9.5-12.2). Here, emergency departments had highest seroprevalence (29.7%); departments without patients or with limited patient contact had lowest seroprevalence (2.2%). • This study raises awareness of precautions which should be taken to avoid in-hospital transmission. Regular testing of healthcare workers for SARS-CoV-2 should be considered to identify areas with increased transmission.
02.10.2020	A haemagglutination test for rapid detection of antibodies to SARS-CoV-2	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • The authors describe a red cell agglutination test for the detection of antibodies to the SARS-CoV-2 receptor binding domain (RBD). • The Haemagglutination Test (HAT) demonstrates a sensitivity of 90% and specificity of 99% for detection of antibodies after a PCR diagnosed infection. • HAT can be titrated, detects rising titres in the first five days of hospital admission, correlates well with a commercial test that detects antibodies to the RBD, and can be applied as a point of care test.

Diagnostics

Publication Date	Title / URL	Journal / Article type	Digest
01.10.2020	Effectiveness of tests to detect the presence of SARS-CoV-2 virus, and antibodies to SARS-CoV-2, to inform COVID-19 diagnosis: a rapid systematic review	BMJ Evid Based Med / Evidence synthesis	<ul style="list-style-type: none"> • A rapid systematic review with the aim of identifying evidence that could be used to answer the following research questions: (1) What is the clinical effectiveness of tests that detect the presence of SARS-CoV-2 to inform COVID-19 diagnosis? (2) What is the clinical effectiveness of tests that detect the presence of antibodies to the SARS-CoV-2 virus to inform COVID-19 diagnosis? • 38 studies on SARS-CoV-2 virus testing and 25 studies on SARS-CoV-2 antibody testing were identified. • Evidence is rapidly emerging on the effectiveness of tests for COVID-19 diagnosis and management, but important uncertainties about their effectiveness and most appropriate application remain.

03.10.2020	Diagnostic performance of the combined nasal and throat swab in patients admitted to hospital with suspected COVID-19	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • In a prospective, multi-centre, cohort study conducted in secondary and tertiary care hospitals in Scotland, the authors evaluated the combined nasal and throat swab with RT-PCR for SARS-CoV-2 in consecutive patients admitted to hospital with suspected COVID-19. • Enrolled 1,369 consecutive patients (68 [53-80] years, 47% women) who underwent a total of 3,822 tests (median 2 [1-3] tests per patient). • Concluded that in patients admitted to hospital, a single combined nasal and throat swab with RT-PCR for SARS-CoV-2 has excellent specificity, but limited diagnostic sensitivity for COVID-19. Diagnostic performance is significantly improved by repeated testing.
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Epidemiology and clinical – risk factors

Publication Date	Title / URL	Journal / Article type	Digest
05.10.2020	Change in obstetric attendance and activities during the COVID-19 pandemic	Lancet Infectious Diseases / Correspondence	<ul style="list-style-type: none"> • Investigated changes in obstetric attendance and activities at a large London teaching hospital during the first peak of the COVID-19 pandemic in the UK. • Compared the number of women booking for prenatal care, attendances at obstetric triage service for unscheduled care, and number of births at St George's University Hospital, London, UK, in two epochs: Feb 1–June 15, 2020, and Feb 1–June 15, 2019. • Findings suggest that the observed rise in stillbirths could be due to reduced care-seeking. A possible explanation for the greater fall in triage attendance (19%) than in births (6%) is that women might have perceived triage attendance as avoidable, whereas obviously labour and birth are not. However, it is possible that a small percentage of women opted for home deliveries or delivery in a private health-care setting, which would explain the slight decrease in birth rates.
01.10.2020	The Prognostic Value of Electrocardiogram at Presentation to Emergency Department in Patients With COVID-19	Mayo Clin Proc / Article	<ul style="list-style-type: none"> • Study analysed 1258 COVID-19 adults at three New York hospitals: does combining vital signs and electrocardiogram (ECG) analysis improve early prognostication? • Atrial fibrillation/flutter (odds ratio [OR], 2.5; 95% CI, 1.1 to 6.2), right ventricular strain (OR, 2.7; 95% CI, 1.3 to 6.1), and ST segment abnormalities (OR, 2.4; 95% CI, 1.5 to 3.8) were associated with death or mechanical ventilation at 48 hours. • In 108 patients without these ECG abnormalities and with normal respiratory vitals, only 5 (4.6%) died or required mechanical ventilation by 48 hours versus

			<p>68 of 216 patients (31.5%) having both ECG and respiratory vital sign abnormalities.</p> <ul style="list-style-type: none"> • Combination of abnormal respiratory vital signs and these ECG abnormalities accurately prognosticates early deterioration in patients with coronavirus disease 2019 and may assist with patient triage.
05.10.2020	Vitamin D status and seroconversion for COVID-19 in UK healthcare workers who isolated for COVID-19 like symptoms during the 2020 pandemic	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • A study of 392 NHS healthcare workers aimed to determine prevalence of vitamin D deficiency in staff who have isolated with symptoms suggestive of COVID-19 and relate this to vitamin D status. • Multivariate analysis revealed that BAME and COVID-19 seroconversion were independent predictors of vitamin D deficiency.
02.10.2020	COVID-19 severity in asthma patients: A multi-center matched cohort study	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • In this matched cohort study (n=562; matched 2686) from a large Boston-based healthcare system, asthma was associated with comparable risk of hospitalization (adjusted Hazard Ratios 0.99, 95% CI 0.80, 1.22) and mechanical ventilation (AHR 0.69, 95% CI 0.36, 1.29) but a lower risk of mortality (AHR 0.30, 95% CI 0.11, 0.80).

Epidemiology and clinical – other

Publication Date	Title / URL	Journal / Article type	Digest
05.10.2020	Adolescent with COVID-19 as the Source of an Outbreak at a 3-Week Family Gathering — Four States, June–July 2020	MMWR Morb Mortal Wkly Rep / Report	<ul style="list-style-type: none"> • During July–Aug 2020, four state health departments and CDC investigated a COVID-19 outbreak that occurred during a 3-week family gathering of five households in which an adolescent aged 13 years was the index and suspected primary patient; 11 subsequent cases occurred. • This outbreak highlights several important issues. <ul style="list-style-type: none"> - Children and adolescents can serve as the source for COVID-19 outbreaks within families, even when their symptoms are mild. - Provides evidence of the benefit of physical distancing as a mitigation strategy to prevent SARS-CoV-2 transmission. None of the six family members who maintained outdoor physical distance without face masks during two visits to the family gathering developed symptoms; the four who were tested for SARS-CoV-2 had negative test results. - Rapid antigen tests generally have lower sensitivity (84.0%–97.6%) compared with RT-PCR testing; negative results should be confirmed with RT-PCR if used for persons with high pretest probability of infection, such as those with a known exposure.

04.10.2020	SARS-CoV-2 outbreak investigation in a German meat processing plant	EMBO Mol Med / Article	<ul style="list-style-type: none"> • Multifactorial investigation of a SARS-CoV-2 outbreak in a large meat processing complex in Germany. • Results suggest single index case transmitted SARS-CoV-2 to more than 60% of co-workers over distances of more than 8 meters, within a confined work area in which air is constantly recirculated and cooled. • Climate conditions, fresh air exchange rates, and airflow as factors that can promote efficient spread of SARS-CoV-2 via long distances and provide insights into possible requirements for pandemic mitigation strategies in industrial workplace settings.
06.10.2020	ISARIC COVID-19 Clinical Data Report: 4 October 2020	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • The authors present detailed analysis of data for COVID-19 positive individuals in the International Severe Acute Respiratory and emerging Infections Consortium (ISARIC) for whom data collection commenced on or before 14 Sept 2020 (n=88,463; Median age 72 years). • A total of 18% of patients were admitted to the ICU at some point during their illness. • Antibiotic use is high (82.2% of patients). • Fever, shortness of breath, a non-productive cough and fatigue were the most common symptoms. • Altered consciousness/confusion was relatively frequent (19,619/86,175) and most common in elderly patients. • Elderly patients are less likely to present with upper respiratory tract infection symptoms.
05.10.2020	Prevalence, management, and outcomes of SARS-CoV-2 infections in older people and those with dementia in mental health wards in London, UK: a retrospective observational study	Lancet Psychiatry / Article	<ul style="list-style-type: none"> • Describes the period prevalence, demographics, symptoms (and asymptomatic cases), management, and survival outcomes of COVID-19 in the older inpatient psychiatric population and people with young-onset dementia in five National Health Service Trusts in London, UK, from Mar 1 to Apr 30, 2020. • Of 344 inpatients, 131 (38%) were diagnosed with COVID-19 during the study period (period prevalence 38% [95% CI 33–43]). • The mean age of patients who had COVID-19 was 75.3 years (SD 8.2); 68 (52%) were women and 47 (36%) from ethnic minority groups. 16 (12%) of 131 patients were asymptomatic and 121 (92%) had one or more disease-related comorbidity. • 19 (15%) patients diagnosed with COVID-19 died during the study period, and their deaths were determined to be COVID-19 related.
30.09.2020	Epidemiology and transmission dynamics of COVID-19 in two Indian states	Science / Article	<ul style="list-style-type: none"> • Data from the Indian states of Tamil Nadu and Andhra Pradesh provide a detailed view into SARS-CoV-2 transmission pathways and mortality in a high-incidence setting.

			<ul style="list-style-type: none"> • Reported cases and deaths have been concentrated in younger cohorts than expected from observations in higher-income countries, even after accounting for demographic differences across settings. • Among 575,071 individuals exposed to 84,965 confirmed cases, infection probabilities ranged from 4.7-10.7% for low-risk and high-risk contact types. • Same-age contacts were associated with the greatest infection risk. Case-fatality ratios spanned 0.05% at ages 5-17 years to 16.6% at ages ≥85 years. Primary data are urgently needed from low-resource countries to guide control measures.
06.10.2020	Defining the role of asymptomatic and pre-symptomatic SARS-CoV-2 transmission: a living systematic review	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • This living review aims to critically appraise available data about secondary attack rates from people with asymptomatic and pre-symptomatic SARS-CoV-2 infection. • Of 928 studies identified, 19 were included. • Secondary attack rates from asymptomatic index cases ranged from 0% to 2.8% (9 studies). Pre-symptomatic secondary attack rates ranged from 0.7% to 31.8% (10 studies). • The highest secondary attack rates were found in contacts who lived in the same household as the index case. Other activities associated with transmission were group activities such as sharing meals or playing board games with the index case.
05.10.2020	Neuropathology of patients with COVID-19 in Germany: a post-mortem case series	Lancet Neurology / Article	<ul style="list-style-type: none"> • Investigated the brain tissue of patients who died from COVID-19 (n=43) for glial responses, inflammatory changes, and the presence of SARS-CoV-2 in the CNS. • In general, neuropathological changes in patients with COVID-19 seem to be mild, with pronounced neuroinflammatory changes in the brainstem being the most common finding. There was no evidence for CNS damage directly caused by SARS-CoV-2. • The generalisability of these findings needs to be validated in future studies as the number of cases and availability of clinical data were low and no age-matched and sex-matched controls were included.

Infection control

Publication Date	Title / URL	Journal / Article type	Digest
05.10.2020	Scientific Brief: SARS-CoV-2 and Potential Airborne Transmission	Centers for Disease Prevention and Control / Scientific brief	<ul style="list-style-type: none"> • US CDC brief discussing the potential airborne transmission of SARS-CoV-2.
06.10.2020	Trends in COVID-19 Incidence After Implementation of Mitigation Measures — Arizona, January 22–August 7, 2020	MMWR Morb Mortal Wkly Rep / Report	<ul style="list-style-type: none"> • The number of COVID-19 cases in Arizona stabilized and then decreased after sustained implementation and enforcement of statewide and locally enhanced mitigation measures, beginning approximately 2 weeks after implementation and enforcement of mask mandates and enhanced sanitations practices began on June 17; further decreases were observed during July 13–Aug 7, after statewide limitations and closures of certain services and businesses. • Widespread implementation and enforcement of sustained community mitigation measures, including mask wearing, informed by state and local officials' continual data monitoring and collaboration can help prevent transmission of SARS-CoV-2 and decrease the numbers of COVID-19 cases.
05.10.2020	Crowding and the shape of COVID-19 epidemics	Nat Med / Letter	<ul style="list-style-type: none"> • Authors analysed highly resolved spatial variables in cities, together with case count data, to investigate the role of climate, urbanization and variation in interventions. • Degree to which COVID-19 cases are compressed into a short period of time (peakedness of the epidemic) is strongly shaped by population aggregation and heterogeneity, such that epidemics in crowded cities are more spread over time, and crowded cities have larger total attack rates than less populated cities.
02.10.2020	Testing mobile air purifiers in a school classroom: Reducing the airborne transmission risk for SARS-CoV-2	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Tested the efficiency and practicability of operating four air purifiers equipped with HEPA filters in a high school classroom while regular classes were taking place. • They monitored the aerosol number concentration for particles > 3 nm at two locations in the room, the aerosol size distribution in the range from 10 nm to 10 µm, PM10 and CO2 concentration. For comparison, they performed similar measurements in a neighbouring classroom without purifiers. • Measurements and calculation demonstrate that air purifiers represent a well suited measure to reduce the risks of airborne transmission of SARS-CoV-2 substantially. Staying for two hours in a closed room with a super infective

			person, they estimate that the inhaled dose is reduced by a factor of six when using air purifiers with a total air exchange rate of 5.7 h-1.
06.10.2020	COVID-SCORE: A global survey to assess public perceptions of government responses to COVID-19 (COVID-SCORE-10)	PLoS One / Article	<ul style="list-style-type: none"> • Authors developed a novel ten-item instrument that asks respondents to rate key aspects of their government's response to the pandemic (COVID-SCORE). • Heterogeneity in responses was observed across age, gender, education and income with the greatest amount of heterogeneity observed between countries. • National scores correlated with respondents' reported levels of trust in government and with country-level COVID-19 mortality rates. • Based on responses from 13,426 people randomly selected from general population in 19 countries, mean national scores ranged from 35.76 (Ecuador) to 80.48 (China) out of a maximum of 100 points.

Treatment

Publication Date	Title / URL	Journal / Article type	Digest
05.10.2020	Lopinavir–ritonavir in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial	Lancet / Article	<ul style="list-style-type: none"> • Report the results of a randomised trial to assess whether lopinavir–ritonavir improves outcomes in patients admitted to hospital with COVID-19. • Between Mar 19, 2020, and June 29, 2020, 1616 patients were randomly allocated to receive lopinavir–ritonavir and 3424 patients to receive usual care. • In patients admitted to hospital with COVID-19, lopinavir–ritonavir was not associated with reductions in 28-day mortality, duration of hospital stay, or risk of progressing to invasive mechanical ventilation or death. • These findings do not support the use of lopinavir–ritonavir for treatment of patients admitted to hospital with COVID-19.
05.10.2020	Remdesivir for Adults With COVID-19 : A Living Systematic Review for an American College of Physicians Practice Points	Ann Intern Med / Review	<ul style="list-style-type: none"> • Aimed to evaluate the effectiveness and harms of remdesivir for COVID-19. Four randomized trials were included. • In hospitalized adults with COVID-19, remdesivir probably improves recovery and reduces serious adverse events and may reduce mortality and time to clinical improvement. • For adults not receiving mechanical ventilation or extracorporeal membrane oxygenation, a 5-day course of remdesivir may provide similar benefits to and fewer harms than a 10-day course. • Low-certainty evidence with few published trials, including 1 preliminary

report and 2 open-label trials. Trials excluded pregnant women and adults with severe kidney or liver disease.

Modelling

Publication Date	Title / URL	Journal / Article type	Digest
02.10.2020	Investigating the potential benefit that requiring travellers to self-isolate on arrival may have upon the reducing of case importations during international outbreaks of influenza, SARS, Ebola virus disease and COVID-19	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • A model presented in a previous paper suggested airport arrivals screening alone delivered only minimal reduction in the risk of COVID-19 case importation, with a detection rate of 12.0%. • The authors present a brief modification to take account of the added impact that quarantining incoming travellers may have. • Primary data suggests requiring all travellers to undergo 5 days of self-isolation on arrival, after which they are tested again, has the potential to increase rate of detection for travellers infected with COVID-19 to 81.7%. • Extending the period of self-isolation to 14 days increases the potential detection rate to 99.5%.

Guidance and consensus statements

Publication Date	Title / URL	Journal / Article type
06.10.2020	Infection prevention and control and preparedness for COVID-19 in healthcare settings - fifth update	European Centre for Disease Prevention and Control / Technical report
Sept. 2020	Pandemic fatigue: Reinvigorating the public to prevent COVID-19	WHO Europe / Policy framework

Overviews, comments and editorials

Publication Date	Title / URL	Journal / Article type
06.10.2020	Comparing methods used in the COVID-19 Infection Survey and NHS Test and Trace, England	Gov.uk / Official statistics
05.10.2020	How achievable are COVID-19 clinical trial recruitment targets? A UK observational cohort study and trials registry analysis	BMJ Open / Article
28.09.2020	The Exclusion of Older Persons From Vaccine and Treatment Trials for Coronavirus Disease 2019—Missing the Target	JAMA Internal Medicine / Letter
06.10.2020	The changing demographics of COVID-19	Lancet Respiratory Medicine / News
05.10.2020	Antiviral monotherapy for hospitalised patients with COVID-19 is not enough	Lancet / Comment

05.10.2020	Should Remdesivir Be Used for the Treatment of Patients With COVID-19? Rapid, Living Practice Points From the American College of Physicians (Version 1)	Ann Intern Med / Clinical Guidelines
05.10.2020	MIS-C: post-infectious syndrome or persistent infection?	Lancet Infectious Diseases / Correspondence
05.10.2020	Catch me if you can: SARS-CoV-2 detection in brains of deceased patients with COVID-19	Lancet Neurology / Comment
05.10.2020	Why misinterpretation of electron micrographs in SARS-CoV-2-infected tissue goes viral	Lancet / Correspondence
05.10.2020	Power of and power over COVID-19 response guidelines	Lancet / Correspondence

Produced by the PHE COVID-19 Literature Digest Team

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