Public Health England

COVID-19 Literature Digest – 28/10/2020

Dear all,

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a report three times per week (Mon, Wed, Fri), which includes both preliminary reports of work (preprints) that have NOT been peer-reviewed and research that has been subject to peer review and wider scrutiny.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 COVID19.behaviouralscience@phe.gov.uk to sign up to receive the PHE Behavioural Sciences Weekly Report.

Best wishes,

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On behalf of the PHE COVID-19 Literature Digest Team

Report for 28.10.2020 (please note that papers that have **NOT been peer-reviewed** are highlighted in red).

Sections:

Modelling
Overviews, comments and editorials (no digest)

Serology and immunology

Publication Date	Title / URL	Journal / Article type	Digest
26.10.2020	Declining prevalence of antibody positivity to SARS-CoV-2: a community study of 365,000 adults	medRxiv (non-peer reviewed) / Article	• Reports on REACT2 antibody positivity survey in England, with three cross-sectional surveys between late June and Sept 2020 (365,104 adults using a self-administered LFIA test for IgG). • There were 17,576 positive tests over the three rounds. • Antibody prevalence (adjusted and weighted) declined from 6.0% [5.8, 6.1], to 4.8% [4.7, 5.0] and 4.4% [4.3, 4.5], a fall of 26.5% [-29.0, -23.8] during the study. • Decline between rounds 1 and 3 in all age groups, with the highest prevalence of a positive result and smallest overall decline in positivity in the youngest age group (18-24 years: -14.9% [-21.6, -8.1]), and lowest prevalence and largest decline in the oldest group (75+ years: -39.0% [-50.8, -27.2]). • No change in antibody positivity in healthcare workers (+3.45% [-5.7, +12.7]). • Decline was largest in those who did not report a history of COVID-19, (-64.0% [-75.6, -52.3]), compared to -22.3% ([-27.0, -17.7]) in those with infection confirmed on PCR.
26.10.2020	Longitudinal observation and decline of neutralizing antibody responses in the three months following SARS-CoV-2 infection in humans	Nat Microbiol / Article	• Antibody responses to SARS-CoV-2 can be detected in most infected individuals 10–15 d after the onset of COVID-19 symptoms. • Sequential serum samples collected up to 94 d post onset of symptoms (POS) from 65 individuals: declining neutralizing antibody titres observed after an initial peak, magnitude of peak is dependent on disease severity. • Some individuals with high peak infective dose (ID50 > 10,000) maintained neutralizing antibody titres >1,000 at >60 d POS, some with lower peak ID50 had neutralizing antibody titres approaching baseline within the follow-up period. • A similar decline in neutralizing antibody titres was observed in a cohort of 31 seropositive healthcare workers. Results suggest vaccine boosters are required to provide long-lasting protection.

Vaccine development

Publication Date	Title / URL	Journal / Article type	Digest
27.10.2020	A booster dose enhances immunogenicity of the COVID-19 vaccine candidate ChAdOx1 nCoV-19 in aged mice	bioRxiv (non-peer reviewed) / Article	• The immunogenicity of the adenoviral vectored vaccine ChAdOx1 nCoV-19 (AZD-1222) in aged mice is tested. • A single dose of the vaccine induces cellular and humoral immunity in aged mice, but at a reduced magnitude than in younger adult mice. • A second dose enhances the immune response to this vaccine in aged mice, indicating that a prime-boost strategy may be a rational approach to enhance immunogenicity in older persons.

Diagnostics

Publication Date	Title / URL	Journal / Article type	Digest
26.10.2020	COVID-19 Serial Testing among Hospitalized Patients in a Midwest Tertiary Medical Center, July-September 2020	Clin Infect Dis / Article	• Implemented serial COVID-19 testing for inpatients with a negative test on admission to Iowa Hospitals and clinics (UIHC). • The conversion rate (negative to positive) on repeat testing was one percent. Identified patients during their incubation period and hospital-onset cases, rapidly isolated them, and potentially reduced exposures. • Serial testing and infectiousness determination were resource intensive.
25.10.2020	Viral load in community SARS-CoV-2 cases varies widely and temporally	medRxiv (non-peer reviewed) / Article	• Analysed all positive nose and throat swabs (n=1892) between 26 Apr-11 Oct 2020 from the UK national COVID-19 Infection Survey, tested by RT-PCR for the N, S and ORF1ab genes. • Ct values were lower in those reporting symptoms, with more genes detected, and in first (vs. subsequent) positives per-participant, with no evidence of independent effects of test characteristics ($p>0.20$). • Community SARS-CoV-2 infections show marked variation in viral load. Ct values could be a useful epidemiological early-warning indicator.
16.10.2020	Lessons from applied large-scale pooling of 133,816 SARS-CoV-2 RT-PCR tests	medRxiv (non-peer reviewed) / Article	• Report analysis of 133,816 samples collected April-Sept 2020, tested by pooling for the presence of SARS-CoV-2 (Israel). • Spared 76% of RNA extraction and RT-PCR tests, despite the reality of frequently changing prevalence rate (0.5%-6%). • Observed pooling efficiency and sensitivity that exceed theoretical predictions, which resulted from non-random distribution of positive samples in pools. • Overall, the findings strongly support the use of pooling for efficient large high throughput SARS-CoV-2 testing.

26.10.2020	Diagnostic value of cutaneous manifestation of SARS-CoV-2 infection	medRxiv (non-peer reviewed) / Article	• Assesses diagnostic value of new skin rashes in SARS-CoV-2 infection using longitudinal data from the COVID Symptom Study app (336,847 UK users) between 7 May and 22 June 2020, and data from an independent online survey on skin-related symptoms (11,546 surveyees). • Survey data found that in 17% of swab positive cases a rash was the initial presentation, and was the only clinical sign in in 21%. • The authors have established a free online library of high-quality curated photos to assist healthcare professionals (https://covidskinsigns.com).

Genomics

Publication Date	Title / URL	Journal / Article type	Digest
23.10.2020	Establishment & lineage dynamics of the SARS-CoV-2 epidemic in the UK	medRxiv (non-peer reviewed) / Article	• Reveal the fine-scale genetic lineage structure of this epidemic through analysis of 50,887 SARS-CoV-2 genomes, including 26,181 from the UK sampled throughout the country's first wave of infection. • Using large-scale phylogenetic analyses, combined with epidemiological and travel data, they quantify the size, spatio-temporal origins and persistence of genetically-distinct UK transmission lineages. • Rapid fluctuations in virus importation rates resulted in >1000 lineages; those introduced prior to national lockdown were larger and more dispersed. • Lineage importation and regional lineage diversity declined after lockdown, whilst lineage elimination was size-dependent.
26.10.2020	Spike mutation D614G alters SARS-CoV-2 fitness	Nature / Article	• *This paper was previously included in the Digest as a preprint.* • Engineered the D614G mutation in the USA-WA1/2020 strain and characterized its effect. • Hamsters infected with the G614 variant produced higher infectious titres in the nasal washes and trachea, but not lungs, confirming clinical evidence that the D614G mutation enhances viral loads in the upper respiratory tract of COVID-19 patients and may increases transmission. • Sera from D614-infected hamsters exhibit modestly higher neutralization titres against G614 virus than against D614 virus, indicating that (i) the mutation may not reduce the ability of vaccines in clinical trials to protect against COVID-19 and (ii) therapeutic antibodies should be tested against the circulating G614 virus.

Epidemiology and clinical – children / pregnancy

Publication Date	Title / URL	Journal / Article type	Digest
27.10.2020	COVID-19 associated arterial ischaemic stroke and multisystem inflammatory syndrome in children: a case report	Lancet Child & Adolescent Health / Case report	• Case report of a 9 yo girl with paediatric multisystem inflammatory syndrome temporally associated with COVID-19 who presented with acute ischaemic stroke.

Epidemiology and clinical – risk factors

Publication Date	Title / URL	Journal / Article type	Digest
27.10.2020	Residential context and COVID-19 mortality among adults aged 70 years and older in Stockholm: a population-based, observational study using individual-level data	Lancet Healthy Longevity / Article	• The aim of this study was to investigate how individual-level housing and neighbourhood characteristics are associated with COVID-19 mortality in older adults. • Of 279 961 individuals identified to be aged 70 years or older on Mar 12, 2020, and residing in Stockholm in Dec, 2019, 274 712 met the eligibility criteria and were included in the study population. • Between Mar 12 and May 8, 2020, 3386 deaths occurred, of which 1301 were reported as COVID-19 deaths. • Close exposure to working-age household members and neighbours is associated with increased COVID-19 mortality among older adults. Similarly, living in a care home is associated with increased mortality, potentially through exposure to visitors and care workers, but also due to poor underlying health among care-home residents.
26.10.2020	Pre-pandemic psychiatric disorders and risk of COVID-19: a UK Biobank cohort analysis	Lancet Healthy Longevity / Article	• Aimed to assess the association between pre-pandemic psychiatric disorders and the subsequent risk of COVID-19 using UK Biobank. • Included 421 014 UK Biobank participants in the study and assessed their COVID-19 status between Jan 31 and July 26, 2020. 50 809 participants were diagnosed with psychiatric disorders before the outbreak, while 370 205 participants had no psychiatric disorders. • Findings suggest that pre-existing psychiatric disorders are associated with an increased risk of COVID-19.
14.09.2020	COVID-19 risk and outcomes in patients with substance use disorders: analyses from electronic health records in the United States	Molecular Psychiatry / Article	• Retrospective case-control study of electronic health records (EHRs) data of 73,099,850 unique patients, of whom 12,030 had a diagnosis of COVID-19. • Findings identify individuals with SUD, especially with OUD and African Americans, as having increased risk for COVID-19 and its adverse outcomes.
27.10.2020	COVID-19 Outbreak Among a University's Men's and Women's Soccer Teams — Chicago, Illinois, July–August 2020	MMWR Morb Mortal Wkly Rep / Report	• Investigation of 17 COVID-19 cases among a university's men's and women's soccer team identified numerous social gatherings as possible transmission events. • Minimal mask use and social distancing resulted in rapid spread among students who live, practice, and socialize together.

Epidemiology and clinical – other

Publication Date	Title / URL	Journal / Article type	Digest
26.10.2020	Community prevalence of SARS-CoV-2 in England during April to September 2020: Results from the ONS Coronavirus Infection Survey	medRxiv (non-peer reviewed) / Article	• Analysis of 514,794 samples (nose and throat swabs) and questionnaires from 123,497 individuals aged 2 years and over, from a representative sample of private households in England- 26 Apr to 19 Sept 2020. • A total of 489 samples from 398 individuals were COVID-19 positive. • There was an initial decrease in positive tests between end of Apr and June, followed by low levels during the summer, before marked increases by Aug 2020. • Young adults were an important driver of the second period of increased positivity rates. • A large number of infections were asymptomatic (53%-70%, dependent on calendar time).
26.10.2020	Symptoms at presentation for patients admitted to hospital with Covid-19: results from the ISARIC prospective multinational observational study	medRxiv (non-peer reviewed) / Article	• Analyses international observational data from patients admitted to hospital with laboratory-confirmed Covid-19 (60,161 patients from 43 countries) to investigate symptoms variety by age and sex. • Fever (68%), cough (68%) and shortness of breath (63%) were the most prevalent symptoms, and prevalence was greater among patients aged 30 - 60 years (respectively 79%, 78%, 66%), and lower in children (≤18 years: 68%, 47%, 22%) and older adults (≥70 years: 61%, 62%, 61%). • The most sensitive case definition assessed was one or more of cough, shortness of breath, fever, muscle pains or sore throat, met by 92% of the whole cohort. • Regression models showed significant differences in symptoms with age, and considerable heterogeneity between countries.
25.10.2020	Baseline phenotype and 30-day outcomes of people tested for COVID-19: an international network cohort including >3.32 million people tested with real-time PCR and >219,000 tested positive for SARS-CoV-2 in South Korea, Spain and the United States	medRxiv (non-peer reviewed) / Article	• Characterises socio-demographics and comorbidity in 3,316,107 persons tested and 219,072 persons tested positive for COVID-19 in three countries (Spain, USA, South Korea) since Jan 2020, and key health outcomes in the month following a positive test. • Positive/tested ratio varied greatly geographically (2.2:100 to 31.2:100) and over time (from 50:100 in Feb-Apr to 6.8:100 in May-June). • Fever, cough and dyspnoea were the most common symptoms at presentation. • Between 4%-38% required admission and 1-10.5% died within a month of first positive test. • Disparity in testing practices led to variable baseline characteristics and outcomes.
24.10.2020	Few bacterial co-infections but frequent empiric antibiotic use in the early phase of hospitalized patients with COVID-19:	Infect Dis (Lond) / Article	• Aimed to determine the incidence of bacterial co-infections, antibiotic use and application of antimicrobial stewardship principles in hospitalized patients with COVID-19.

	results from a multicentre retrospective cohort study in The Netherlands		• Performed a retrospective observational study in four hospitals in the Netherlands from Mar to May 2020 including consecutive patients with PCR-confirmed COVID-19. • Concluded that on presentation to the hospital bacterial co-infections are rare, while empiric antibiotic use is abundant. • This implies that in patients with COVID-19 empiric antibiotic should be withheld. This has the potential to dramatically reduce the current overuse of antibiotics in the COVID-19 pandemic.
27.10.2020	Co-infection in critically ill patients with COVID-19: An observational cohort study from England	medRxiv (non-peer reviewed) / Article	• Describes incidence and nature of co-infection in critically ill adults with COVID-19 infection in England using a retrospective cohort study of 254 adults (median age 59 years; 64.6% male) with COVID-19 admitted to seven ICUs in England up to 18 May 2020. • A total of 139 clinically significant organisms were identified from 83 (32.7%) patients. • Bacterial co-infections were identified within 48 hours of admission in 14 (5.5%) patients. Proportion of pathogens detected increased with duration of ICU stay, consisting largely of Gram-negative bacteria, particularly *K. pneumoniae* and *E. coli*. • Patients with co-infections were more likely to die in ICU (crude OR 1.78,95% CI 1.03-3.08, p=0.04) compared to those without co-infections. • Found limited evidence for community-acquired bacterial co-infection in hospitalised adults with COVID-19, but a high rate of Gram-negative infection acquired during ICU stay.
26.10.2020	COVID-19–Associated Hospitalizations Among Health Care Personnel — COVID-NET, 13 States, March 1–May 31, 2020	MMWR Morb Mortal Wkly Rep / Report	• Analysis of COVID-19 hospitalization data from 13 sites indicated that 6% of adults hospitalized with COVID-19 were health care personnel (HCP). • Among HCP hospitalized with COVID-19, 36% were in nursing-related occupations, and 73% had obesity. • Approximately 28% of these patients were admitted to an intensive care unit, 16% required invasive mechanical ventilation, and 4% died.
20.10.2020	COVIDTrach; a prospective cohort study of mechanically ventilated COVID-19 patients undergoing tracheostomy in the UK	medRxiv (non-peer reviewed) / Article	• Evaluates outcomes of tracheostomy in 1605 intubated COVID-19 patients in 126 UK hospitals (the COVIDTrac cohort). • Median time from intubation to tracheostomy was 15 days (IQR 11, 21) and 285 (18%) patients died following the procedure. • 1229 (93%) of survivors had been successfully weaned from mechanical ventilation at censoring and 1049 (81%) had been discharged from hospital. • Six reports were received of operators testing positive for SARS-CoV-2 within two weeks following the procedure. • Suggests tracheostomy is safe in intubated COVID-19 patients and identifies clinical indicators of mortality.

26.10.2020	A2B-COVID: A method for evaluating potential SARS-CoV-2 transmission events	medRxiv (non-peer reviewed) / Article	• Describes A2B-COVID, an approach for the rapid identification of linked cases of coronavirus infection which combines knowledge about infection dynamics, data describing the movements of individuals, and novel approaches to genome sequence data to assess whether or not cases of infection are consistent or inconsistent with linkage via transmission. • Applies A2B-COVID to analyse and compare data collected from two wards at Cambridge University Hospitals, showing qualitatively different patterns of linkage between cases on designated Covid-19 and non-Covid-19 wards.
26.10.2020	Long-term monitoring of SARS-CoV-2 in wastewater of the Frankfurt metropolitan area in Southern Germany	medRxiv (non-peer reviewed) / Article	• SARS-CoV-2 RNA concentration in raw sewage in the Frankfurt metropolitan area was monitored. • In Aug 2020 a resurgence in the SARS-CoV-2 RNA load was observed (3 x 10^13 copies/day), which represents similar levels compared to Apr (2 x 10^14 copies/day). • This corresponded with continuous increase in COVID-19 cases in Frankfurt since Aug, with an average of 28.6 incidences, compared to 28.7 incidences in Apr. • Different temporal dynamics were observed between different sampling points, indicating local dynamics in COVID-19 cases. • Suggests wastewater testing has potential as early warning system for SARS-CoV-2 infections and as a monitoring system to identify hotspots.
22.10.2020	Susceptibility of Raccoon Dogs for Experimental SARS-CoV-2 Infection	Emerg Infect Dis / Article	• 9 naive raccoon dogs infected - study demonstrates that raccoon dogs are susceptible to SARS-CoV-2 infection; can transmit virus to direct in-contact animals. • The raccoon dogs had only subtle clinical signs. Authors found evidence of viral replication and tissue lesions in only the nasal conchae. • Results indicate that affected farms may be reservoirs for SARS-CoV-2. Surveillance of susceptible animals needed; especially in China, key player in global fur production. • Also need to initiate large-scale epidemiologic field studies with historic samples that might elucidate the role of farmed animals in the current pandemic.

Infection control / non-pharmaceutical interventions

Publication Date	Title / URL	Journal / Article type	Digest
27.10.2020	COVID-19 Mitigation Behaviors by Age Group — United States, April–June 2020	MMWR Morb Mortal Wkly Rep / Report	• Self-reported engagement in mitigation behaviours (mask wearing, handwashing, physical distancing, crowd and restaurant avoidance, and cancellation of social activities) differed significantly by adult age group. • During Apr–June 2020, the prevalence of these behaviours was lowest among adults aged 18–29 years and highest among those aged >60 years. Whereas mask wearing increased over time, other reported mitigation behaviours decreased or remained unchanged.

Modelling

Publication Date	Title / URL	Journal / Article type	Digest
26.10.2020	Detecting COVID-19 infection hotspots in England using large-scale self-reported data from a mobile application	medRxiv (non-peer reviewed) / Article	• Modelling performed on longitudinal, self-reported data from users of the COVID Symptom Study app in England between 24 Mar and 29 Sept 2020 (2.6 million app users; 115 million daily symptom reports; 170,000 PCR test results). • Estimates of incidence and prevalence showed similar sensitivity to changes as two national community surveys: ONS and REACT. • The model highlighted regions before they were subject to local government lockdowns. • Between 12 May and 29 Sept between 35-80% of regions appearing in the Government's hotspot list were flagged. • Suggests self-reported data from mobile applications can be a cost-effective and agile resource to inform pandemic response.

Overviews, comments and editorials

Publication Date	Title / URL	Journal / Article type
27.10.2020	The UK Government's Vaccine Taskforce: strategy for protecting the UK and the world	Lancet / Comment
27.10.2020	Who should be prioritised for COVID-19 vaccines?	Lancet / Correspondence
27.10.2020	What defines an efficacious COVID-19 vaccine? A review of the challenges assessing the clinical efficacy of vaccines against SARS-CoV-2	Lancet Infectious Diseases / Review
08.10.2020	Rethinking the COVID-19 Pandemic: Back to Public Health	Ann Glob Health / Viewpoints
26.10.2020	Preventing the Spread of SARS-CoV-2 With Masks and Other "Low-tech" Interventions	Jama / Viewpoint
27.10.2020	Transparency assessment of COVID-19 models	Lancet Global Health / Correspondence
28.10.2020	Lessons from Sweden: where can older adults shelter from COVID-19?	Lancet Healthy Longevity / Comment

Produced by the PHE COVID-19 Literature Digest Team

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