COVID-19 Literature Digest – 02/10/2020

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a report three times per week (Mon, Wed, Fri), which includes both preliminary reports of work (preprints) that have NOT been peer-reviewed and research that has been subject to peer review and wider scrutiny.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Report for 02.10.2020 (please note that papers that have NOT been peer-reviewed are highlighted in red).

Sections:
Serology and immunology
Diagnostics
Genomics
Epidemiology and clinical – children / pregnancy
Epidemiology and clinical – risk factors
Epidemiology and clinical – other

Overviews, comments and editorials (no digest)
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| 01.10.2020       | Seroprevalence of SARS-CoV-2 antibodies in people with an acute loss in their sense of smell and/or taste in a community-based population in London, UK: An observational cohort study | PLoS Med / Article     | • The study aimed to determine the seroprevalence of SARS-CoV-2 antibodies in a community-based population (n=590; Mean age 39.4 years; 69.1% female) with acute loss of smell and/or taste, compare the frequency of COVID-19 associated symptoms, and evaluate whether smell or taste loss are indicative of COVID-19 infection.  
  • A total of 77.6% of 567 participants with acute smell and/or taste loss had SARS-CoV-2 antibodies; of these, 39.8% (n = 175) had neither cough nor fever.  
  • New loss of smell was more prevalent in participants with SARS-CoV-2 antibodies, compared with those without antibodies (93.4% versus 78.7%, p < 0.001), whereas taste loss was equally prevalent (90.2% versus 89.0%, p = 0.738).  
  • Seropositivity was 3 times more likely in participants with smell loss (OR 2.86; 95% CI 1.27-6.36; p < 0.001) compared with those with taste loss. |
| 30.09.2020       | SARS-CoV-2-derived peptides define heterologous and COVID-19-induced T cell recognition        | Nat Immunol / Article  | • Identified and characterized multiple dominant and subdominant SARS-CoV-2 HLA class I and HLA-DR peptides as potential T cell epitopes in COVID-19 convalescent and unexposed individuals.  
  • SARS-CoV-2-specific peptides enabled detection of post-infectious T cell immunity, even in seronegative convalescent individuals. Cross-reactive SARS-CoV-2 peptides revealed pre-existing T cell responses in 81% of unexposed individuals and validated similarity with common cold coronaviruses, providing a functional basis for heterologous immunity in SARS-CoV-2 infection.  
  • Together, the proposed SARS-CoV-2 T cell epitopes enable identification of heterologous and post-infectious T cell immunity and facilitate development of diagnostic, preventive and therapeutic measures for COVID-19. |
| 29.09.2020       | SARS-CoV-2 antibody testing in a UK population: detectable IgG for up to 20 weeks post infection | medRxiv (non-peer reviewed) / Article | • Analysis of a cohort of pre-pandemic and pandemic individuals (n=348 positive, n=510 negative) suggests SARS-CoV-2 IgG persists up to 140 days (20 weeks) post infection.  
  • The authors determine the sensitivity and specificity of the three commercial immunoassays used (EuroImmun; Sens. 98.9% [97.7-99.7%]; Spec. 99.2% [98.4-99.8%]; Roche; Sens. 99.4% [98.6-100%]; Spec. [96.7% [95.1-98.2%]; Abbott; Sens. 86.8% [83.1-90.2%; Spec. (99.2% [98.4-99.8%]). |
| 29.09.2020       | SARS-CoV-2 antibody responses in patients with aggressive haematological malignancies            | medRxiv (non-peer reviewed) / Article | • A study analysed longitudinal serum samples from ten hospitalised patients with aggressive haematological malignancy who were also on systemic anti-cancer treatment, collected up to 103 days post-onset of COVID-19 symptoms.  
  • The majority (8/9) of patients with confirmed SARS-CoV-2 infection seroconverted and developed antibodies to the major SARS-CoV-2 antigens (S1 and
N), with most (6/8) producing neutralising antibody responses.

- The dynamics of antibody responses were broadly similar to that reported for the general population, except for a possible delay to seroconversion.

**30.09.2020**

**COVID-19 vaccine BNT162b1 elicits human antibody and T(H)1 T-cell responses**

*Nature / Article*

- Present antibody and T-cell responses after BNT162b1 vaccination from a second, non-randomized open-label phase 1/2 trial in healthy adults, 18-55 years of age.
- Two doses of 1 to 50 µg of BNT162b1 elicited robust CD4+ and CD8+ T-cell responses and strong antibody responses, with RBD-binding IgG concentrations clearly above those in a COVID-19 human convalescent sample (HCS) panel.
- Day 43 SARS-CoV-2 serum neutralising geometric mean titres were 0.7-fold (1 µg) to 3.5-fold (50 µg) those of the HCS panel.
- The robust RBD-specific antibody, T-cell and favourable cytokine responses induced by the BNT162b1 mRNA vaccine suggest multiple beneficial mechanisms with potential to protect against COVID-19.

**30.09.2020**

**LY-CoV555, a rapidly isolated potent neutralizing antibody, provides protection in a non-human primate model of SARS-CoV-2 infection**

*bioRxiv (non-peer reviewed) / Article*

- The authors report that high-throughput microfluidic screening of antigen-specific B-cells led to the identification of LY-CoV555, a potent anti-spike neutralizing antibody from a convalescent COVID-19 patient.
- Biochemical, structural, and functional characterization revealed high-affinity binding to the receptor-binding domain, ACE2 binding inhibition, and potent neutralizing activity.
- In a rhesus macaque challenge model, prophylaxis doses as low as 2.5 mg/kg reduced viral replication in the upper and lower respiratory tract.

**Diagnostics**

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<td>01.10.2020</td>
<td>SARS-CoV-2 samples may escape detection because of a single point mutation in the N gene</td>
<td><em>Eurosurveillance / Rapid communication</em></td>
<td>The authors found that a single nucleotide polymorphism (SNP) in the nucleoprotein gene of SARS-CoV-2 from a patient interfered with detection in a widely used commercial assay. Some 0.2% of the isolates in the EpiCoV database contain this SNP. Although SARS-CoV-2 was still detected by the other probe in the assay, this underlines the necessity of targeting two independent essential regions of a pathogen for reliable detection.</td>
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<td>30.09.2020</td>
<td>Real-time Screening of Specimen Pools for Coronavirus Disease 2019 (COVID-19) Infection at Sanya Airport, Hainan Island, China</td>
<td><em>Clin Infect Dis / Article</em></td>
<td>A 10:1 pooled test strategy on-site at an airport of China was pursued, resulting in increased test throughput, limited use of reagents, and increased testing efficiency without loss of sensitivity. This testing approach has the potential to reduce the need for contact tracing when the results are delivered first time.</td>
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Thoracic imaging tests for the diagnosis of COVID-19

- A systematic review and meta-analysis (84 studies) sought to determine the diagnostic accuracy of chest imaging (computed tomography (CT), X-ray and ultrasound) in people with suspected or confirmed COVID-19.
- Poor study quality and heterogeneity of included studies limit the ability to draw conclusions.
- Data indicates chest CT is sensitive but not specific for diagnosis in suspected patients.
- Accuracy estimates of chest X-ray and ultrasound of the lungs for the diagnosis of COVID-19 should be carefully interpreted due to limited data.

Genomics

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| 28.09.2020       | Large scale sequencing of SARS-CoV-2 genomes from one region allows detailed epidemiology and enables local outbreak management | medRxiv (non-peer reviewed) / Article | - The authors undertook whole genome sequencing of the SARS-CoV-2 genomes present in positive clinical samples from the UK county of Norfolk and surrounding areas, which have a stable, low-density population.  
- Genomes belonged to 26 distinct global lineages, indicating that there multiple separate introductions into the region.  
- One hundred genetically-distinct UK lineages were detected demonstrating local evolution, at a rate of ~2 SNPs per month, and multiple co-occurring lineages as the pandemic progressed.  
- Sixteen lineages in key workers which were not in patients were identified, indicating infection control measures were effective.  
- The D614G spike protein mutation which is linked to increased transmissibility dominates the samples, and rapidly confirmed relatedness of cases in an outbreak at a food processing facility. |
| 28.09.2020       | SARS-CoV-2 D614G Variant Exhibits Enhanced Replication ex vivo and Earlier Transmission in vivo | bioRxiv (non-peer reviewed) / Article | - The authors engineered SARS-CoV-2 variants harboring the D614G substitution in the S protein, with or without nanoluciferase.  
- The D614G variant replicates more efficiency in primary human proximal airway epithelial cells and is more fit than wildtype (WT) virus in competition studies.  
- With similar morphology to the WT virion, the D614G virus is also more sensitive to SARS-CoV-2 neutralizing antibodies.  
- Infection of human ACE2 transgenic mice and Syrian hamsters with the WT or D614G viruses produced similar titres in respiratory tissue and pulmonary disease.  
- However, the D614G variant exhibited significantly faster droplet transmission between hamsters than the WT virus, early after infection. |
| 30.09.2020 | The major genetic risk factor for severe COVID-19 is inherited from Neanderthals | Nature / Article | • Authors investigated if the genetic risk factor for severe COVID-19 is inherited from Neanderthals.  
• They state that the risk is conferred by a genomic segment of ~50 kb that is inherited from Neanderthals and is carried by ~50% of people in South Asia and ~16% of people in Europe today. |
| 30.09.2020 | The furin cleavage site of SARS-CoV-2 spike protein is a key determinant for transmission due to enhanced replication in airway cells | bioRxiv (non-peer reviewed) / Article | • SARS-CoV-2 has a unique polybasic insertion at the S1/S2 cleavage sites (CS), which the authors demonstrate can be cleaved by furin.  
• SARS-CoV-2 virus lacking the S1/S2 furin CS was shed to lower titres from infected ferrets and was not transmitted to cohoused sentinel animals, suggesting the polybasic CS is a key determinant for efficient SARS-CoV-2 transmission. |

### Epidemiology and clinical – children / pregnancy

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• COVID-19 incidence among adolescents aged 12–17 years (37.4 cases per 100,000 children) was approximately twice that in children aged 5–11 years (19.0).  
• Underlying conditions were more common among school-aged children with severe outcomes related to COVID-19.  
• Weekly incidence, SARS-CoV-2 test volume, and percentage of tests positive among school-aged children varied over time and by region of the United States. |

### Epidemiology and clinical – risk factors

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| 30.09.2020      | In-hospital cardiac arrest in critically ill patients with covid-19: multicenter cohort study | BMJ / Research | • A cohort study drawn from intensive care units at 68 hospitals across the United States investigated the incidence, risk factors, and outcomes associated with in-hospital cardiac arrest (IHCA) and cardiopulmonary resuscitation (CR) in critically ill adults with COVID-19 (n=5019).  
• 14.0% (701/5019) had IHCA, 57.1% (400/701) of whom received CR.  
• Patients who had IHCA were older (mean age 63 (standard deviation 14) v 60 (15) years), had more comorbidities, and were more likely to be admitted to a hospital with a smaller number of intensive care unit beds compared with those who did not have IHCA.  
• Patients who received CR were younger than those who did not (mean age 61 (standard deviation 14) v 67 (14) years). |
### Association of a Prior Psychiatric Diagnosis With Mortality Among Hospitalized Patients With Coronavirus Disease 2019 (COVID-19) Infection

JAMA Netw Open / Research letter

- A cohort study of 1685 patients (mean age 65.2 years; 52.6% male) hospitalized with COVID-19 in at 5 hospitals in Connecticut, USA, evaluated the association between prior psychiatric diagnosis and COVID-19–related mortality of hospitalised patients.
- Patients with a psychiatric diagnosis (n=473; 28% of the cohort) had a higher mortality rate compared with those with no psychiatric diagnosis, with 35.7% vs 14.7% of 2-week mortality and 40.9% vs 22.2% of 3-week mortality rate (P < .001) (and with 44.8% vs 31.5% of 4-week mortality rate).
- After controlling for demographic characteristics, other medical comorbidities, and hospital location, the risk of death remained significantly greater among patients with a psychiatric disorder (hazard ratio, 1.5; 95% CI, 1.1-1.9; P = .003).

### Epidemiology and clinical – other

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<td>01.10.2020</td>
<td><a href="https://www.gov.uk/government/publications/react-1-study-of-coronavirus-transmission-september-2020-results">React-1 study of coronavirus transmission: September 2020 results</a></td>
<td>Gov.uk / Official statistics</td>
<td>A representative cross-section of volunteers in England tested themselves with swabs between 18 and 26 Sep 2020. Swabs were analysed using PCR. Out of 84,610 swab results, 363 were positive. This was significantly higher than the prevalence of 0.125% (0.096%, 0.154%) measured during Aug 2020 and the highest observed prevalence of any round since this study started reporting in May. Subsequent rounds of React-1 will allow further accurate assessment of trends in prevalence and transmission.</td>
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<tr>
<td>29.09.2020</td>
<td><a href="https://www.cdc.gov_emergencies/COVID-19/npdh%E7%99%BC%E5%B8%83/npdhcoronavirus/2020-09-29-flight-associated-transmission-of-sars-cov-2.htm">Flight-Associated Transmission of Severe Acute Respiratory Syndrome Coronavirus 2 Corroborated by Whole-Genome Sequencing</a></td>
<td>Emerg Infect Dis / Research</td>
<td>Whole-genome sequencing was used to investigate potential transmission of SARS-CoV-2 during a domestic flight within Australia. Eleven passengers with SARS-CoV-2 infection and symptom onset within 48 hours of the flight were considered infectious during travel; 9 had recently disembarked from a cruise ship with a retrospectively identified SARS-CoV-2 outbreak.</td>
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Eight cases were considered flight associated with the distinct SARS-CoV-2 A2-RP strain; the remaining 3 cases (1 with A2-RP) were possibly flight associated. All 11 passengers had been in the same cabin with symptomatic persons who had primary, culture-positive, A2-RP cases. This investigation provides evidence of flight-associated SARS-CoV-2 transmission.

- 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.
- 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.

In this study, the US Army Public Health COVID-19 Task Force describes the results of an independent investigation of the shore-based USS Theodore Roosevelt (USS TR) outbreak response.
- Of 4085 USS TR sailors who disembarked, 736 had a diagnosis of SARS-CoV-2 (median age, 25 years; interquartile range, 22-31 years; 572 males [77.7%]).
- 590 sailors (80.2%) were characterized as symptomatic, with a median symptom duration of 7 days (interquartile range, 5-11 days).
- 146 sailors (19.8%) remained asymptomatic for the duration of the study period.
- Cough was observed for 677 person-days (13.6%), cold like symptoms for 483 person-days (9.7%), anosmia for 463 person-days (9.3%), headache for 438 person-days (8.8%), ageusia for 393 person-days (7.9%), and fever for 65 person-days (1.3%).

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<td>Epidemiology and transmission dynamics of COVID-19 in two Indian states</td>
<td>Science / Article</td>
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<td>01.10.2020</td>
<td>Symptom Characterization and Outcomes of Sailors in Isolation After a COVID-19 Outbreak on a US Aircraft Carrier</td>
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<td>Building a resilient NHS, for COVID-19 and beyond</td>
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<td>29.09.2020</td>
<td>Using critical information to strengthen pandemic preparedness: the role of national public health agencies</td>
<td>BMJ Glob Health / Analysis</td>
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<td>Covid-19: Universities roll out pooled testing of students in bid to keep campuses open</td>
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Produced by the PHE COVID-19 Literature Digest Team

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