



COVID-19 Literature Digest – 06/11/2020

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). The reports include both preprints, which should be treated with caution as they are NOT peer-reviewed and may be subject to change, and also research that has been subject to peer review and wider scrutiny.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,

Bláthnaid Mahon, Emma Farrow

On behalf of the PHE COVID-19 Literature Digest Team

Report for 06.11.2020 (please note that papers that have **NOT been peer-reviewed** are highlighted in red).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
05.11.2020	Distinct antibody responses to SARS-CoV-2 in children and adults across the COVID-19 clinical spectrum	Nat Immunol / Article	<ul style="list-style-type: none">• Here, the authors show distinct antibody responses in children and adults after SARS-CoV-2 infection.• Adult COVID-19 cohorts had anti-spike (S) IgG, IgM and IgA antibodies, as well as anti-nucleocapsid (N) IgG antibody, while children with and without MIS-C had reduced breadth of anti-SARS-CoV-2-specific antibodies, predominantly generating IgG antibodies specific for the S protein but not the N protein.• Moreover, children with and without MIS-C had reduced neutralizing activity as compared to both adult COVID-19 cohorts, indicating a reduced protective serological response.• Results suggest a distinct infection course and immune response in children independent of whether they develop MIS-C, with implications for developing age-targeted strategies for testing and protecting the population.
04.11.2020	Lack of antibodies to SARS-CoV-2 in a large cohort of previously infected persons	Clin Infect Dis / Article	<ul style="list-style-type: none">• Analysed serologic data collected from health care workers and first responders in New York City and the Detroit metropolitan area with history of a positive SARS-CoV-2 RT-PCR test result and who were tested for IgG antibodies to SARS-CoV-2 spike protein at least 2 weeks after symptom onset.• In this population (n=2,547), approximately one in 16 persons lacked IgG antibodies. Absence of antibodies varied independently by illness severity, race/ethnicity, obesity, and immunosuppressive drug therapy. The proportion seronegative remained relatively stable among persons tested up to 90 days post symptom onset.
02.11.2020	SARS-CoV-2 responsive T cell numbers are associated with protection from COVID-19: A prospective cohort study in keyworkers	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none">• Prospective cohort study of 2,826 participants working in English hospitals and Fire and Police services.• Measured numbers of interferon-γ secreting, SARS-CoV-2 responsive T cells, and antibodies to SARS-CoV-2 proteins.• Of the participants with higher T cell responses, 367 (53%) had detectable antibodies against the N or S proteins. During a median of 118 days follow-up, 20 participants with lower T cell responses developed

			<p>COVID-19, compared with none in the population with high T cell responses.</p> <ul style="list-style-type: none"> • Concluded that peripheral blood SARS-CoV-2 responsive T cell numbers are associated with risk of developing COVID-19.
03.11.2020	A prospective study of risk factors associated with seroprevalence of SARS-CoV-2 antibodies in healthcare workers at a large UK teaching hospital	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Prospective sero-epidemiological study of healthcare workers (HCWs) at a UK teaching hospital; 410/5,698 (7.2%) staff tested positive for SARS-CoV-2 antibodies. • Seroprevalence higher in those working in designated COVID-19 areas (9.47% versus 6.16%). BAME staff had an aOR of 1.65 (95% CI 1.32-2.07; p<0.0001) compared to white staff; this increased risk was independent of COVID-19 area working. • Healthcare assistants (aOR 2.06 [95%CI 1.14-3.71]; p=0.016) and domestic and portering staff (aOR 3.45 [95% CI 1.07-11.42]; p=0.039) had significantly higher seroprevalence than other staff groups after adjusting for age, sex, ethnicity and COVID-19 working location. • Risk of SARS-CoV-2 infection amongst HCWs is heterogeneous and influenced by COVID-19 working location, role, age and ethnicity. Increased risk amongst BAME staff cannot be accounted for solely by occupational factors.
03.11.2020	Evolution of Antibody Immunity to SARS-CoV-2	bioRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Authors report on the humoral memory response in a cohort of 87 individuals assessed at 1.3 and 6.2 months after infection. • IgM, and IgG anti-SARS-CoV-2 spike protein RBD antibody titres decrease significantly; IgA less affected. Neutralizing activity in plasma decreases by five-fold. • Number of RBD-specific memory B cells is unchanged; display clonal turnover after 6.2 months; antibodies they express have greater somatic hypermutation, increased potency and resistance to RBD mutations, indicative of continued evolution of the humoral response. • Memory B cell response to SARS-CoV-2 evolves between 1.3 and 6.2 months after infection in a manner that is consistent with antigen persistence.

Vaccine development

Publication Date	Title / URL	Journal / Article type	Digest
31.10.2020	Elicitation of potent neutralizing antibody responses by designed protein nanoparticle vaccines for SARS-CoV-2	Cell / Article	<ul style="list-style-type: none"> • Describe the structure-based design of self-assembling protein nanoparticle immunogens that elicit potent and protective antibody

		<p>responses against SARS-CoV-2 in mice. The nanoparticle vaccines display 60 SARS-CoV-2 spike receptor-binding domains (RBDs) in a highly immunogenic array and induce neutralizing antibody titres ten-fold higher than the prefusion-stabilized spike despite a five-fold lower dose.</p> <ul style="list-style-type: none"> • Antibodies elicited by the RBD-nanoparticles target multiple distinct epitopes, suggesting they may not be easily susceptible to escape mutations, and exhibit a lower binding:neutralizing ratio than convalescent human sera, which may minimize the risk of vaccine-associated enhanced respiratory disease. • The high yield and stability of the assembled nanoparticles suggest that manufacture of the nanoparticle vaccines will be highly scalable.
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Diagnostics

Publication Date	Title / URL	Journal / Article type	Digest
02.11.2020	Understanding COVID-19 testing pathways in English care homes to identify the role of point-of-care testing: an interview-based process mapping study	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Study evaluated current testing pathways in care homes to explore the role of point-of-care tests (POCTs). Interviews with 10 staff from 8 English care homes. • Four main steps identified, and associated challenges: infection prevention, preparatory steps, swabbing procedure, and management of residents. • Swab-based testing is organisationally complex and resource-intensive in care homes. Flexibility needed to meet residents' needs, and provide rapid information to support care decisions. • POCT could help address gaps but complexity of the setting means each technology must be evaluated in context before widespread adoption in care homes.
30.10.2020	Analytical and Clinical Performance of the Panbio COVID-19 Antigen-Detecting Rapid Diagnostic Test	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Assessed the analytical and clinical performance of the Ag-RDT Panbio COVID-19 Ag Test (Abbott), using RT-qPCR as a reference test. • The Panbio COVID-19 Ag-RDT has high sensitivity for detecting the presence of SARS-CoV-2 in nasal or nasopharyngeal swabs of both, symptomatic and asymptomatic individuals. • The diagnostic performance of the test is particularly good in samples with viral loads associated with high risk of viral transmission (Ct <25), which show high positive and negative predictive values even when assuming a prevalence as low as 5%.

Genomics

Publication Date	Title / URL	Journal / Article type	Digest
03.11.2020	Revealing fine-scale spatiotemporal differences in SARS-CoV-2 introduction and spread	Nat Commun / Article	<ul style="list-style-type: none"> • Analysed 247 full-genome SARS-CoV-2 sequences from two nearby communities in Wisconsin, USA, and found surprisingly distinct patterns of viral spread. • Dane County had the 12th known introduction of SARS-CoV-2 in the US, but this did not lead to descendant community spread. Instead, the Dane County outbreak was seeded by multiple later introductions, followed by limited community spread. • In contrast, relatively few introductions in Milwaukee County led to extensive community spread. • Present evidence for reduced viral spread in both counties following the statewide “Safer at Home” order, which went into effect 25 Mar 2020. • Results suggest patterns of SARS-CoV-2 transmission may vary substantially even in nearby communities. Understanding these local patterns will enable better targeting of public health interventions.
24.10.2020	Identification of Required Host Factors for SARS-CoV-2 Infection in Human Cells	Cell / Article	<ul style="list-style-type: none"> • Performed a genome-scale CRISPR loss-of-function screen to identify host factors required for SARS-CoV-2 viral infection of human alveolar epithelial cells. Top-ranked genes cluster into distinct pathways, including the vacuolar ATPase proton pump, Retromer, and Commander complexes. • Using single-cell RNA-sequencing, they identify shared transcriptional changes in cholesterol biosynthesis upon loss of top-ranked genes. • Show that loss of RAB7A reduces viral entry by sequestering the ACE2 receptor inside cells. • Overall, this work provides a genome-scale, quantitative resource of the impact of the loss of each host gene on fitness/response to viral infection.
04.11.2020	The circulating SARS-CoV-2 spike variant N439K maintains fitness while evading antibody-mediated immunity	bioRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Observed that the N439K mutation resulted in immune escape from a panel of neutralizing monoclonal antibodies, including one in clinical trials, as well as from polyclonal sera from a sizeable fraction of persons recovered from infection. • Immune evasion mutations that maintain virulence and fitness such as N439K can emerge within SARS-CoV-2 S, highlighting need for ongoing molecular surveillance to guide development and usage of vaccines and therapeutics.

Epidemiology and clinical – risk factors

Publication Date	Title / URL	Journal / Article type	Digest
28.10.2020	Factors associated with COVID-19 in care homes and domiciliary care, and effectiveness of interventions: a rapid review	Public Health England / Rapid review	<ul style="list-style-type: none"> Reviewed: <ul style="list-style-type: none"> -factors associated with incidence, prevalence or transmission of COVID-19 within care homes and domiciliary care -interventions effective in minimising COVID-19 incidence, prevalence or transmission in care homes and domiciliary care 22 studies were identified. Multiple observational studies have consistently reported the use of temporary staffing and the movement of staff between different care homes, lack of sick pay provision for care home staff, 'for profit' ownership (US-based studies), lower quality ratings, and lower levels of trained nurses (amongst other factors) as being associated with increased levels of COVID-19. There is limited evidence on the effectiveness of interventions, and available evidence is weak. Routine testing with early intervention (1 study) and voluntary staff confinement (1 study) were associated with lower COVID-19 and descriptive studies reported the use of multiple consecutive strategies. Further research is needed, and studies that better infer causality.
27.10.2020	The Association between Influenza Vaccination and the Risk of SARS-CoV-2 Infection, Severe Illness, and Death: A Systematic Review of the Literature	Int J Environ Res Public Health / Systematic review	<ul style="list-style-type: none"> Reviewed the association between seasonal influenza vaccination and the risk of SARS-CoV-2 infection or complicated illness or poor outcome (e.g., severe disease, need for hospitalization or ventilatory support, or death) among COVID-19 patients. None of the studies that were reviewed (n = 12) found a significant increase in the risk of infection or in the illness severity or lethality, and some reported significantly inverse associations. Findings support measures aimed at raising influenza vaccination coverage in the coming months.
27.10.2020	High excess mortality in areas with young and socially vulnerable populations during the COVID-19 outbreak in Stockholm Region, Sweden	BMJ Glob Health / Article	<ul style="list-style-type: none"> Describe the distribution of excess mortality (EM) during the first weeks of the COVID-19 outbreak in the Stockholm Region, Sweden, according to age, sex and sociodemographic context. Living in areas characterised by lower socioeconomic status and younger populations was linked to excess mortality during the COVID-19 pandemic in the Stockholm Region. These conditions might have facilitated viral spread. Findings highlight the well-documented vulnerability linked to

			increasing age and sociodemographic context for COVID-19–related death.
03.11.2020	Explaining among-country variation in COVID-19 case fatality rate	Sci Rep / Article	<ul style="list-style-type: none"> • Attempted to identify key factors possibly explaining the variability in case fatality rate across countries. • In particular, countries with the highest values of DALYs lost to cardiovascular, cancer and chronic respiratory diseases had the highest values of COVID-19 CFR. • Among the demographic, economic and political variables, CFR was positively associated with share of the population over 70, GDP per capita, and level of democracy, while it was negatively associated with number of hospital beds ×1000. • Overall, these results emphasize the role of comorbidity and socio-economic factors as possible drivers of COVID-19 case fatality rate at the population level.
06.11.2020	Telework Before Illness Onset Among Symptomatic Adults Aged ≥18 Years With and Without COVID-19 in 11 Outpatient Health Care Facilities - United States, July 2020	MMWR Morb Mortal Wkly Rep / Report	<ul style="list-style-type: none"> • Adults who received positive test results for SARS-CoV-2 infection were more likely to report exclusively going to an office or school setting in the 2 weeks before illness onset, compared with those who tested negative, even among those working in a profession outside of the critical infrastructure.

Transmission

Publication Date	Title / URL	Journal / Article type	Digest
26.09.2020	Transmission of COVID-19 on Public Transport: a rapid review	Public Health England / Rapid review	<ul style="list-style-type: none"> • Four studies identified reporting on the transmission of COVID-19 on trains (n=3) and buses (n=2) (search up to 24 Aug 2020). • There is weak and limited evidence from China and India that transmission on public transport may occur. • Further research is needed to examine the potential for transmission of COVID-19 on public transport.
26.09.2020	Transmission of COVID-19 in school settings and interventions to reduce the transmission: a rapid review [Update 1]	Public Health England / Rapid review	<ul style="list-style-type: none"> • Updated review on: <ul style="list-style-type: none"> -Transmission of COVID-19 within school settings -Effectiveness of interventions to reduce the transmission of COVID-19 within school settings • Limited evidence from 2 observational studies suggests that keeping schools open for children younger than 15 years old is not associated with higher infection rates in these children. • Consistent with their previous review, evidence from modelling studies

			<p>suggests that the reopening of schools at reduced capacity is not associated with a second epidemic wave; and that contact tracing strategies are required to control community transmission in case of full return to school.</p> <ul style="list-style-type: none"> • It is essential to closely monitor the transmission of COVID-19 via school-based surveillance such as the PHE SKID study, and further research is needed on the transmission of COVID-19 in schools and on the effectiveness of school-based interventions.
11.04.2020	Household Transmission of SARS-COV-2: Insights from a Population-based Serological Survey	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Population-based serosurvey in Geneva, Switzerland; 4,524 household members five years and older from 2,267 households enrolled April-June 2020. • Infection risk from exposure to single infected household member was four-times that of extra-household exposures over first wave; young children had a lower risk from infection. • Asymptomatic infections are far less likely to transmit than symptomatic ones but do cause infections. • While the small households in Geneva limit the contribution of household spread, household transmission likely plays a greater role in other settings.
02.11.2020	High attack rates of SARS-CoV-2 infection through household-transmission: a prospective study	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Prospective case-ascertained study of 112 households (291 participants) in Bergen, Norway: demographic and clinical data from index cases / household members. • Sera collected 6-8 weeks after index case symptom onset, to measure SARS-CoV-2-specific antibodies. 45% overall household attack rate assessed by seroconversion; 47% if also including RT-PCR positives. • Serological assays provide more accurate estimates of household secondary attack rate than RT-PCR, especially amongst children who have a lower RT-PCR positivity rate. • Children equally susceptible to infection as adults, but elderly show higher attack rates. Negative RT-PCR or lack of symptoms are not sufficient to rule out infection in household members.

Infection control / non-pharmaceutical interventions

Publication Date	Title / URL	Journal / Article type	Digest
06.11.2020	Network Characteristics and Visualization of COVID-19 Outbreak in a Large Detention Facility in the United States - Cook County, Illinois, 2020	MMWR Morb Mortal Wkly Rep / Report	<ul style="list-style-type: none"> • Analysis of detained person and staff member movements during a COVID-19 outbreak at Cook County Jail in Illinois found fewer connections among detained persons with COVID-19 than expected, suggesting that interventions and medical isolation practices were effective at reducing transmission. • Higher than expected connections were identified in staff member networks, suggesting occurrence of additional transmission and areas of focus for transmission interruption.
04.11.2020	Intranasal fusion inhibitory lipopeptide prevents direct contact SARS-CoV-2 transmission in ferrets	bioRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Designed a dimeric lipopeptide fusion inhibitor that blocks critical first step of infection for emerging coronaviruses and document that it completely prevents SARS-CoV-2 infection in ferrets. • Daily intranasal administration to ferrets completely prevented SARS-CoV-2 direct-contact transmission during 24-hour co-housing with infected animals, under stringent conditions that resulted in infection of 100% of untreated animals. • These lipopeptides are highly stable and non-toxic and thus readily translate into a safe and effective intranasal prophylactic approach to reduce transmission of SARS-CoV-2.

Treatment

Publication Date	Title / URL	Journal / Article type	Digest
05.11.2020	Effect of pre-exposure use of hydroxychloroquine on COVID-19 mortality: a population-based cohort study in patients with rheumatoid arthritis or systemic lupus erythematosus using the OpenSAFELY platform	Lancet Rheumatology / Article	<ul style="list-style-type: none"> • Evaluated the effectiveness of hydroxychloroquine for prevention of COVID-19 mortality, as opposed to treatment for the disease. • Found no evidence of a difference in COVID-19 mortality among people who received hydroxychloroquine for treatment of rheumatological disease before the COVID-19 outbreak in England.

Overviews, comments and editorials

Publication Date	Title / URL	Journal / Article type
05.11.2020	Spotlight on COVID-19 rapid guidance: NICE's experience of producing rapid guidelines during the pandemic	J Public Health (Oxf) / Article

Produced by the PHE COVID-19 Literature Digest Team

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