COVID-19 Literature Digest – 16/12/2020

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, contain 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 The reports include both preprints, which should be treated with caution as they are NOT peer-reviewed and may be subject to change, and also research that has been subject to peer review and wider scrutiny.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, James Robinson
On behalf of the PHE COVID-19 Literature Digest Team
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Report for 16.12.2020 (please note that papers that have **NOT been peer-reviewed** are highlighted in red).

Serology and immunology

Publication Date	Title / URL	Journal / Article type	Digest
15.12.2020	SARS-CoV-2 antibody seroprevalence in the general population and high-risk occupational groups across 18 cities in Iran: a population-based cross-sectional study	Lancet Infectious Diseases / Article	• Assessed the seroprevalence of antibodies against SARS-CoV-2 in 18 cities of Iran as an indicator of the infection rate. • Among the 8902 individuals included in the analysis, 5372 had occupations with a high risk of exposure to SARS-CoV-2 and 3530 were recruited from the general population. • The overall population weight-adjusted and test performance-adjusted prevalence of antibody seropositivity in the general population was 17·1% (95% CI 14·6–19·5), implying that 4 265 542 (95% CI 3 659 043–4 887 078) individuals from the 18 cities included were infected by the end of April, 2020. • The overall population weight-adjusted and test performance-adjusted seroprevalence in the high-risk population was 20·0% (18·5–21·7) and showed little variation between the occupations included.
14.12.2020	Symptomatic SARS-CoV-2 reinfection of a health care worker in a Belgian nosocomial outbreak despite primary neutralizing antibody response	Clin Infect Dis / Article	• *This paper was previously included in the Digest as a preprint.* • Reinfection was confirmed in a young, immunocompetent health care worker, as viral genomes derived from the first and second episode belonged to different SARS-CoV-2 clades. • The symptomatic reinfection occurred after an interval of 185 days, despite the development of an effective humoral immune response following symptomatic primary infection. • Second episode milder and characterized by a fast rise in serum IgG and neutralizing antibodies. • Contact tracing and virus culture remained inconclusive, but the health care worker formed a transmission cluster with 3 patients and showed evidence of virus replication but not of neutralizing antibodies in her nasopharyngeal swabs.

Diagnostics and genomics

Publication Date	Title / URL	Journal / Article type	Digest
11.12.2020	Genomic epidemiology reveals transmission patterns and dynamics of SARS-CoV-2 in Aotearoa New Zealand	Nat Commun / Article	• Authors generate 649 SARS-CoV-2 genome sequences from infected patients in New Zealand with samples collected during 'first wave', representing 56% of all confirmed cases in this time period. • Despite its remoteness, viruses imported represented nearly all of the genomic diversity sequenced from global virus population. Data helped quantify effectiveness of public health interventions. • Effective reproductive number, Re of NZ's largest cluster decreased from 7 to 0.2 within first week of lockdown. Similarly only 19% of virus introductions resulted in ongoing transmission of more than one additional case. • Overall, these results demonstrate the utility of genomic pathogen surveillance to inform public health and disease mitigation.
14.12.2020	Update on new SARS-CoV-2 variant and how COG-UK tracks emerging mutations	COG-UK / News	• The variant contains a novel set of mutations associated with a lineage spreading rapidly in the South East of England (and more widely) that is the subject of ongoing investigations by the UK Public Health Agencies, coordinated by Public Health England and supported by COG-UK. • This variant carries a set of mutations including an N501Y mutation in the receptor binding motif of the Spike protein that the virus uses to bind to the human ACE2 receptor. • Efforts are under way to confirm whether or not any of these mutations are contributing to increased transmission. There is currently no evidence that this variant (or any other studied to date) has any impact on disease severity, or that it will render vaccines less effective, although both questions require further studies performed at pace.
14.12.2020	Recurrent emergence and transmission of a SARS-CoV-2 Spike deletion ΔH69/V70	bioRxiv (non-peer reviewed) / Article	• Reports recurrent, independent acquisitions and transmissions of the SARS-CoV-2 Spike double deletion ΔH69/ΔV70 following receptor binding mutations such as N501Y, N439K and Y453F. • Reports a sub-lineage of over 350 sequences bearing seven spike mutations across the RBD (N501Y, A570D), S1 (ΔH69/ΔV70) and S2 (P681H, T716I, S982A and D1118H) in England. • Presents data that ΔH69/ΔV70 increases Spike-mediated infectivity approximately two fold, and therefore may be a compensatory mechanism for putative antibody escape mutations in Spike. • Authors suggest enhanced surveillance for this deletion with and without RBD mutations should be considered as a priority.

| 15.12.2020 | Two mutations in the SARS-CoV-2 spike protein and RNA polymerase complex are associated with COVID-19 mortality risk | bioRxiv (non-peer reviewed) / Article | • Analyse 7,548 single stranded RNA-genomes of SARS-CoV-2 patients in the GISAID database, assessing each locus of the single stranded RNA of the SARS-CoV-2 virus for association with host/patient mortality using logistic regression.
• Two loci, at 12,053bp and 25,088bp, achieved genome-wide significance (p-values of 4.09e-09 and 4.41e-23, respectively).
• Mutations at 25,088bp occur in the S2 subunit of the SARS-CoV-2 spike protein, which plays a key role in viral entry of target host cells.
• Mutations at 12,053bp are within the ORF1ab gene, in a region encoding for the protein nsp7, which is necessary to form the RNA polymerase complex responsible for viral replication and transcription.
• Both mutations altered amino acid coding sequences, potentially imposing structural changes that could enhance viral infectivity and symptom severity. |

Epidemiology and clinical – children / pregnancy

Publication Date	Title / URL	Journal / Article type	Digest
15.12.2020	Factors Associated with Positive SARS-CoV-2 Test Results in Outpatient Health Facilities and Emergency Departments Among Children and Adolescents Aged <18 Years — Mississippi, September–November 2020	MMWR / Report	• Among children and adolescents aged <18 years in Mississippi, close contact with persons with COVID-19 and gatherings with persons outside the household and lack of consistent mask use in school were associated with SARS-CoV-2 infection, whereas attending school or child care was not associated with receiving positive SARS-CoV-2 test results.
15.12.2020	Neuroimaging manifestations in children with SARS-CoV-2 infection: a multinational, multicentre collaborative study	Lancet Child & Adolescent Health / Article	• An international call for cases of children with encephalopathy related to SARS-CoV-2 infection and abnormal neuroimaging findings was made. • 38 children with neurological disease related to SARS-CoV-2 infection were identified from France (n=13), the UK (n=8), the USA (n=5), Brazil (n=4), Argentina (n=4), India (n=2), Peru (n=1), and Saudi Arabia (n=1). • Concluded that acute-phase and delayed-phase SARS-CoV-2-related CNS abnormalities are seen in children. Recurring patterns of disease and atypical neuroimaging manifestations can be found and should be recognised being as potentially due to SARS-CoV-2 infection as an underlying aetiological factor. • Studies of paediatric specific cohorts are needed to better understand the effects of SARS-CoV-2 infection on the CNS at presentation and on long-term follow-up in children.

Epidemiology and clinical – risk factors

Publication Date	Title / URL	Journal / Article type	Digest
10.12.2020	[Reduction in all-cause mortality in COVID-19 patients on chronic oral anticoagulation: A population-based propensity score matched study](#)	Int J Cardiol / Article	• Italian population-based study of 4697 COVID-19 patients aged 65 years or older. All-cause mortality rate ratio significantly higher among non-anticoagulated patients (32.2% vs 26.5%, p = 0.036). • On time to event analysis, all-cause mortality was found lower among anticoagulated patients, although estimate was not statistically significant. (HR 0.81, 95%CI 0.65–1.01, p = 0.054). • Among elderly patients with COVID-19, those on chronic oral anticoagulant treatment for atrial fibrillation seem to be at lower risk of all-cause mortality compared to their propensity score matched non-anticoagulated counterpart.
14.12.2020	[Assessment of the risk of SARS-CoV-2 reinfection in an intense re-exposure setting](#)	Clin Infect Dis / Article	• Qatar cohort, 133,266 SARS-CoV-2 laboratory-confirmed cases with at least one PCR positive swab that is ≥45 days after a first-positive swab individually investigated for evidence of reinfection. • 243 persons (0.18%) had at least one subsequent positive swab ≥45 days after first-positive swab. Of these, 54 cases (22.2%) had strong or good evidence for reinfection. • Median time between first and reinfection swab was 64.5 days (range: 45-129). 23 (42.6%) diagnosed at a health facility suggesting presence of symptoms, 31 (57.4%) identified incidentally. • Reinfection risk was estimated at 0.02% (95% CI: 0.01-0.02%) and reinfection incidence rate at 0.36 (95% CI: 0.28-0.47) per 10,000 person-weeks. • SARS-CoV-2 reinfection can occur but is a rare phenomenon suggestive of protective immunity against reinfection that lasts for at least a few months post primary infection.
14.12.2020	[Readmission and Death After Initial Hospital Discharge Among Patients With COVID-19 in a Large Multihospital System](#)	Jama / Research Letter	• National cohort of 2179 U.S Veterans Affairs (VA) patients hospitalised with COVID-19: 678 (31.1%) treated in ICU, 279 (12.8%) mechanically ventilated, 1775 (81.5%) survived to discharge. • Within 60 days of discharge, 354 patients (19.9%) were readmitted, 162 (9.1%) died, 479 (27.0%) were readmitted or died. Most common readmission diagnoses were COVID-19 (30.2%), sepsis (8.5%), pneumonia (3.1%), and heart failure (3.1%). • Rates of readmission or death were higher than pneumonia or heart failure during the first 10 days after discharge, suggesting a period of heightened risk of clinical deterioration. • 27% of survivors were readmitted or died by 60 days after discharge, and this rate was lower than matched survivors of pneumonia or heart failure.

Epidemiology and clinical – other

Publication Date	Title / URL	Journal / Article type	Digest
15.12.2020	REACT-1: real-time assessment of community transmission of coronavirus (COVID-19) in November 2020	Gov.uk / Official statistics	• REACT-1 is a series of community surveys of SARS-CoV-2 RT-PCR swab-positivity in England, designed to monitor the spread of the epidemic and thus increase situational awareness. • Prevalence fell from an average of 1.30% in mid-Oct to beginning Nov, to an average of 0.94% during the lockdown period, meaning it fell from 130 to 94 people infected per 10,000. • During the period 25 Nov to 3 Dec, SARS-CoV-2 virus was circulating with a slightly lower prevalence than between 13 Nov to 24 Nov with 91 in 10,000 infected.
14.12.2020	Epidemiological and cohort study finds no association between COVID-19 and Guillain-Barré syndrome	Brain / Article	• The epidemiology of GBS cases reported to the UK National Immunoglobulin Database was studied from 2016 to 2019 and compared to cases reported during the COVID-19 pandemic. • Although it is not possible to entirely rule out the possibility of a link, this study finds no epidemiological or phenotypic clues of SARS-CoV-2 being causative of GBS. • UK GBS incidence has fallen during pandemic; may be the influence of lockdown measures reducing transmission of GBS inducing pathogens such as *Campylobacter jejuni* and respiratory viruses.
14.12.2020	Pathological and molecular examinations of postmortem testis biopsies reveal SARS-CoV-2 infection in the testis and spermatogenesis damage in COVID-19 patients	Cell Mol Immunol / Correspondence	• Histological morphology of testes from five COVID-19 patients (compared to 3 uninfected controls). Degenerated germ cells (GCs) had sloughed into lumen of seminiferous tubules; in 4 cases, GC loss was massive, with only a few GCs left attached to the seminiferous tubules. • Molecular examinations suggest that SARS-CoV-2 infection triggers dynamic transcriptome alterations at the molecular level in testes during specific biological processes. • Findings provide direct evidence that SARS-CoV-2 can infect the testis and GCs, indicating potential impact of pandemic on spermatogenesis and male fertility. • Further study essential to reveal the underlying mechanism of SARS-CoV-2 infection of testicular cells and correlation of testis infection with the clinical course of COVID-19.
14.12.2020	Reduced mortality in New Zealand during the COVID-19 pandemic	Lancet / Correspondence	• Investigated the temporal association between public health measures and all-cause mortality in New Zealand, by comparing weekly death rates from 2015

			to 2020 using data from Stats NZ Tatauranga Aotearoa. • Reported weekly all-cause mortality in 2020 was similar to mortality in 2015–19 until week 17 (ie, the fifth week of public health measures) when mortality fell below historical rates, a trend which is still evident at week 42. • Continued reduction might be primarily due to the absence of an influenza epidemic in New Zealand in 2020. • Alternative factors, such as fewer deaths from road traffic accidents, occupational causes, air pollution, and postsurgical complications, might also have had a role in the reduction of all-cause mortality, although these effects would often manifest during, rather than after, a strict lockdown. • Finally, potential late adverse effects on mortality, resulting from reduced access to health care, have not become apparent.
15.12.2020	Impact of Population Growth and Aging on Estimates of Excess U.S. Deaths During the COVID-19 Pandemic, March to August 2020	Ann Intern Med / Original Research	• Pandemic resulted in an estimated 218 000 excess U.S deaths between Mar - Aug 2020, after changes in population size and age taken into account. 80% had COVID-19 as underlying cause. • Most excess non–COVID-19 deaths occurred in Apr, July, Aug; 34,900 (78%) in persons aged 25 to 64 years. Diabetes, Alzheimer disease, and heart disease caused the most non–COVID-19 excess deaths. • Accounting for population changes substantially reduced the excess non–COVID-19 death estimates, providing important information for guiding future clinical and public health interventions.

Transmission

Publication Date	Title / URL	Journal / Article type	Digest
14.12.2020	Household Transmission of SARS-CoV-2: A Systematic Review and Meta-analysis	JAMA Netw Open / Original investigation	• Meta-analysis of 54 studies with 77 758 participants: estimated household secondary attack rate 16.6% (95% CI, 14.0%-19.3%), higher than observed secondary attack rates for SARS-CoV and MERS. • Controlling for differences across studies, secondary attack rates higher in households from symptomatic index cases than asymptomatic index cases, to adult contacts than to child contacts, to spouses than to other family contacts, and in households with 1 contact than households with 3 or more contacts. • Findings suggest that given that individuals with suspected or confirmed infections are being referred to isolate at home, households will continue to be a significant transmission venue.

Treatment

Publication Date	Title / URL	Journal / Article type	Digest
14.12.2020	Treatment of COVID-19 with remdesivir in the absence of humoral immunity: a case report	Nat Commun / Article	• Authors report the use of remdesivir in a patient with COVID-19 and the prototypic genetic antibody deficiency X-linked agammaglobulinaemia (XLA). • Despite evidence of complement activation and a robust T cell response, the patient developed persistent SARS-CoV-2 pneumonitis, without progressing to multi-organ involvement. • This unusual clinical course and relatively stable baseline allowed the detailed assessment of clinical, virological and immune responses during two independent challenges with remdesivir. • Over two independent courses of treatment, authors observe a temporally correlated clinical and virological response, leading to clinical resolution and viral clearance, with no evidence of acquired drug resistance. • Therefore provide evidence for the antiviral efficacy of remdesivir in vivo, and its potential benefit in selected patients.
10.12.2020	Azithromycin in Hospitalised Patients with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial	medRxiv (non-peer reviewed) / Article	• In a randomised controlled trial between 7 Apr and 27 Nov 2020, 2582 patients were randomly allocated to receive 500 mg azithromycin once daily for 10 days or until discharge, and 5182 patients received usual care alone. • In total, 496 (19%) patients allocated to azithromycin and 997 (19%) patients allocated to usual care died within 28 days (rate ratio 1.00; p=0.99). • Consistent results were seen in all pre-specified patient sub-groups. • There was no difference in duration of hospitalisation (median 12 days vs. 13 days) or proportion of patients discharged from hospital alive within 28 days (60% vs. 59%; rate ratio 1.03; p=0.29). • Among those not on invasive mechanical ventilation at baseline, there was no difference in the proportion meeting the composite endpoint of invasive mechanical ventilation or death (21% vs. 22%; risk ratio 0.97; p=0.54). • Authors suggest azithromycin use in hospitalised COVID-19 patients should be restricted to patients where there is a clear antimicrobial indication.

Modelling

Publication Date	Title / URL	Journal / Article type	Digest
11.12.2020	Individual and community-level risk for COVID-19 mortality in the United States	Nat Med / Letter	• Authors developed a general population risk calculator for COVID-19 mortality based on various sociodemographic factors and pre-existing conditions for the US population.

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			• Validation analyses using 54,444 deaths from 7 June to 1 Oct 2020 show that the model is well calibrated for the US population. • Model can identify relatively small fractions of population (e.g. 4.3%) that might experience a disproportionately large number of deaths (e.g. 48.7%), but wide variation in risk across communities. • Web-based risk calculator and interactive maps for viewing community-level risks available at http://covid19risktools.com/.
07.12.2020	Model-informed COVID-19 vaccine prioritization strategies by age and serostatus	medRxiv (non-peer reviewed) / Article	• Authors demonstrate a mathematical model to compare five age-stratified vaccine prioritisation strategies. • A transmission-blocking vaccine prioritised to adults ages 20-49 years minimised cumulative incidence, but mortality and years of life lost were minimised in most scenarios when the vaccine was prioritised to adults >60 years old. • Serological tests to redirect doses to seronegative individuals improved marginal impact of each dose while partially addressing existing inequities in COVID-19 impact. • Maximum impact prioritisation strategies were broadly consistent across countries, transmission rates, vaccination rollout speeds, and estimates of naturally acquired immunity.

Guidance and consensus statements

Publication Date	Title / URL	Journal / Article type
14.12.2020	Defining and managing COVID-19-associated pulmonary aspergillosis: the 2020 ECMM/ISHAM consensus criteria for research and clinical guidance	Lancet Infectious Diseases / Review

Overviews, comments and editorials

Publication Date	Title / URL	Journal / Article type
14.12.2020	Coronavirus and ethnicity: a summary of what we know	Gov.uk / Official statistics
15.12.2020	Concerns and motivations about COVID-19 vaccination	Lancet Infectious Diseases / Comment
14.12.2020	Buyer beware: inflated claims of sensitivity for rapid COVID-19 tests	Lancet / Correspondence
14.12.2020	COVID-19 vaccine and Guillain-Barré syndrome: let's not leap to associations	Brain / Commentary

Produced by the PHE COVID-19 Literature Digest Team

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