Public Health England

COVID-19 Literature Digest – 20/11/2020

Dear all,

This week's guest editor is Professor Peter Bradley – PHE's Director of Health Intelligence / Chief Information Officer and NHS England Clinical Entrepreneur.

If you only read three papers this week….
As it is soon winter, my first paper, Seasonality and its impact on COVID-19, 22 October 2020 by NERVTAG and EMG, comments on the impact of seasonality on COVID-19. The paper suggests the direct effect of winter environmental conditions on transmission is likely to be small. It outlines that winter conditions will increase viral persistence on outdoor surfaces due to reduced temperatures and UV levels, in unheated indoor environments due to lower temperatures and in day-time outdoor aerosols due to reduced UV levels. However, the outdoor environment is not a dominant route of transmission for SARS-CoV-2, whereas indoor environmental conditions (where the vast majority of transmission is likely to occur) are more important. The authors note however, that co-infection with influenza viruses is likely to worsen the clinical course. There is no evidence, at present, to suggest that other physiological changes that may occur over winter will affect the severity of disease.

The second paper, Evidence summary for the incubation period of COVID-19, or time to first positive test, in individuals exposed to SARS-CoV-2 aims to shed light on the duration of the incubation period for Covid-19 and the time at which individuals first show symptoms. The review includes 98 studies; with 96 containing data relevant to the incubation period, and three with data on time to first positive test in asymptomatic individuals based on serial testing. The results of this analysis indicate that the median incubation period for COVID-19 is between five and six days. On average, approximately 95% of individuals who experience symptoms will do so by day 14, indicating that approximately 1 in 20 develop symptoms after this time. Approximately 82% to 87% of individuals will develop symptoms by day 10, indicating that approximately one in six develop symptoms at a later date. Some individuals may take 21 days or more to exhibit symptoms; however, there is considerable uncertainty associated with the tail of the distribution.

My final paper is a systematic review which asks At what times during infection is SARS-CoV-2 detectable and no longer detectable using RT-PCR-based tests? Individual participant data (IPD) from 32 longitudinal studies of RT-PCR test results in symptomatic SARS-CoV-2 are included. The study reports on 1619 test results from 1023 infected participants. Virus detection from nasopharyngeal sampling was 89% (95% confidence interval (CI) 83 to 93) at 0 - 4 days post-symptom, but this drops to 54% (95% CI 47 to 61) after 10 to 14 days. The duration of faecal and respiratory tract virus detection varied greatly within individual participants. For some, the virus was still detectable at 46 days post-symptom onset. On average, duration of detectable virus was longer with lower respiratory tract (LRT) sampling than upper respiratory tract (URT). Duration of faecal and respiratory tract virus detection varied greatly within individual participants. In some participants, the virus was still detectable at 46 days post-symptom onset. The authors conclude that RT-PCR can miss detection of people with SARS-CoV-2 infection, but early sampling minimises false negative diagnoses. Beyond 10 days post-symptom onset, LRT or faecal testing may be preferred sampling sites.

Peter

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

Report for 20.11.2020 (please note that papers that have **NOT been peer-reviewed** are highlighted in red).

Sections:

Serology and immunology
Vaccine development
Diagnostics and genomics
Epidemiology and clinical – children / pregnancy
Epidemiology and clinical – risk factors
Epidemiology and clinical – other
Transmission
Infection control / non-pharmaceutical interventions
Overviews, comments and editorials (no digest)

Serology and immunology

Publication Date	Title / URL	Journal / Article type	Digest
19.11.2020	Options for the use of rapid antigen tests for COVID-19 in the EU/EEA and the UK	European Centre for Disease Prevention and Control / Technical report	• On 28 Oct 2020, a European Commission Recommendation on COVID-19 testing strategies, including the use of rapid antigen tests was published. That recommendation calls for EU/EEA Member States and the UK to agree on criteria to be used for the selection of rapid antigen tests, and to share and discuss information regarding the results of validation studies. • This ECDC document is intended to facilitate further discussions between Member States with the aim of reaching agreement on the criteria to be used for the selection of rapid antigen tests, as well as scenarios and settings during which it is appropriate to use rapid antigen tests. This document is also intended to support clinical validations of rapid antigen tests.
19.11.2020	Kinetics and seroprevalence of SARS-CoV-2 antibodies in children	Lancet Infectious Diseases / Correspondence	• Authors report the results of the second round of antibody testing in children from a prospective multicentre cohort study in the UK. • Results indicate antibody titres in children remain at a detectable level for at least 62 days; in this cohort mean antibody titres increased over time. This finding is consistent with data on adults.
18.11.2020	Antibodies to SARS-CoV-2 are associated with protection against reinfection	medRxiv (non-peer reviewed) / Article	• Investigated the incidence of SARS-CoV-2 PCR-positive results in seropositive and seronegative healthcare workers (HCWs) attending asymptomatic and symptomatic staff testing at Oxford University Hospitals, UK. • Baseline antibody status was determined using anti-spike and/or anti-nucleocapsid IgG assays and staff followed for up to 30 weeks. • A total of 12219 HCWs participated and had anti-spike IgG measured, 11052 were followed up after negative and 1246 after positive antibody results including 79 who seroconverted during follow up. • Concluded that prior SARS-CoV-2 infection that generated antibody responses offered protection from reinfection for most people in the six months following infection.
12.11.2020	Sex differences in the decline of neutralizing antibodies to SARS-CoV-2	medRxiv (non-peer reviewed) / Article	• Longitudinal study of sera from 308 RT-qPCR+ individuals with mild disease, collected at two time-points, up to 6 months post-onset of symptoms. • At month 1 (M1), males, individuals > 50 years of age or with a BMI > 25 exhibited higher levels of antibodies. • At month 3-6, anti-S antibodies persisted in 99% of individuals while anti-N IgG were measurable in only 59% of individuals. • Decline in anti-S and neutralising antibodies was faster in males than in females, independently of age and BMI. • Suggests some serology tests are less reliable over time and that the duration of

			protection after SARS-CoV-2 infection or vaccination will be different in women and men.
17.11.2020	Global seroprevalence of SARS-CoV-2 antibodies: a systematic review and meta-analysis	medRxiv (non-peer reviewed) / Article	• Aims to synthesise seroprevalence data from 338 global studies (2.3 million participants in 50 countries). • Seroprevalence was low in the general population (median 3.2%) and slightly higher in at-risk populations (median 5.4%). • Compared to White persons, Black persons (prevalence ratio [RR] 2.34) and Asian persons (RR 1.56) were more likely to be seropositive. • Health care workers had a 1.74x higher risk compared to the general population. • Seroprevalence estimates from national studies were median 11.9 (IQR 8.0 - 16.6) times higher than the corresponding SARS-CoV-2 cumulative incidence.
17.11.2020	Immune suppression in the early stage of COVID-19 disease	Nat Commun / Article	• Authors analyse 37 urine samples from healthy controls (10 samples); COVID-19 patients (14 samples); and non-COVID-19 pneumonia patients (13 samples) using quantitative proteomics. • Molecular changes suggest that immunosuppression and tight junction impairment occur in the early stage of COVID-19 infection. • Further subgrouping of COVID-19 patients into moderate and severe types shows that an activated immune response emerges in severely affected patients. • Data suggest more attention be paid to the dysregulation that occurs in the early onset of the infection.

Vaccine development

Publication Date	Title / URL	Journal / Article type	Digest
18.11.2020	Safety and immunogenicity of ChAdOx1 nCoV-19 vaccine administered in a prime-boost regimen in young and old adults (COV002): a single-blind, randomised, controlled, phase 2/3 trial	Lancet / Article	• Authors describe the safety and immunogenicity of this vaccine in a wider range of participants (previous report on young adults), including adults aged 70 years and older. • ChAdOx1 nCoV-19 appears to be better tolerated in older adults than in younger adults and has similar immunogenicity across all age groups after a boost dose. • Further assessment of the efficacy of this vaccine is warranted in all age groups and individuals with comorbidities.
21.11.2020	Notice of addendum to Article reporting Oxford trial of ChAdOx1 nCoV-19 vaccine	Lancet / Comment	• Authors have published the full standard operating procedures (SOPs) for the Oxford University-sponsored trials of the ChAdOx1 nCoV-19 vaccine in a new appendix to the original article.

Diagnostics and genomics

Publication Date	Title / URL	Journal / Article type	Digest
19.11.2020	SARS-CoV-2, SARS-CoV, and MERS-CoV viral load dynamics, duration of viral shedding, and infectiousness: a systematic review and meta-analysis	Lancet Microbe / Article	• Systematic review to characterise viral load dynamics, duration of viral RNA shedding, and viable virus shedding of severe SARS-CoV-2 in various body fluids; compare SARS-CoV-2, SARS-CoV, and MERS-CoV viral dynamics. • Mean duration of SARS-CoV-2 RNA shedding: 17·0 days in upper respiratory tract, 14·6 days in lower respiratory tract, 17·2 days in stool, and 16·6 days in serum samples. • SARS-CoV-2 RNA shedding in respiratory and stool samples can be prolonged, but duration of viable virus is relatively short-lived. • SARS-CoV-2 titres in the upper respiratory tract peak in the first week of illness; that of SARS-CoV peaked at days 10–14; MERS-CoV peaked at days 7–10. • Early case finding and isolation, and public education on spectrum of illness and period of infectiousness are key to the effective containment of SARS-CoV-2.
19.11.2020	Routine laboratory testing to determine if a patient has COVID-19	Cochrane Database Syst Rev / Review	• Systematic review to assess diagnostic accuracy of routine laboratory testing as a triage test to determine if a person has COVID-19. Included 21 studies looking at 67 different routine laboratory tests for COVID-19. • None of the tests performed well enough to be a standalone diagnostic test for COVID-19 nor to prioritize patients for treatment.
18.11.2020	Detecting SARS-CoV-2 variants with SNP genotyping	bioRxiv (non-peer reviewed) / Article	• The authors evaluate their single nucleotide polymorphism (SNP) identification pipeline by developing a genotyping panel to detect variants-identified from SARS-CoV-2 sequences surveyed between Mar and May 2020, and tested this on 50 stored qRT-PCR positive SARS-CoV-2 clinical samples collected across the South West of the UK in April 2020. • The 50 samples split into 15 distinct genotypes and there was a 76% probability that any two randomly chosen samples from set of 50 would have a distinct genotype. • In a high throughput laboratory, qRT-PCR positive samples pooled into 384-well plates could be screened with marker panel at a cost of < £1.50 per sample. • The analysis pipeline is publicly available and will allow for marker panels to be updated periodically as viral genotypes arise or disappear from circulation.

Epidemiology and clinical – children / pregnancy

Publication Date	Title / URL	Journal / Article type	Digest
01.02.2021	Intrauterine Transmission of SARS-CoV-2	Emerg Infect Dis / Research letter (early release)	• Authors documented a case of fetal death associated with intrauterine transmission of SARS-CoV2. • Chronic histiocytic intervillositis, maternal and fetal vascular malperfusion, microglial hyperplasia, and lymphocytic infiltrate in muscle in the placenta and fetal tissue found. • Placenta and umbilical cord blood tested positive for the virus by PCR, confirming transplacental transmission.

Epidemiology and clinical – risk factors

Publication Date	Title / URL	Journal / Article type	Digest
19.11.2020	Rapid Risk Assessment: Increase in fatal cases of COVID-19 among long-term care facility residents in the EU/EEA and the UK	European Centre for Disease Prevention and Control / Risk assessment	• This risk assessment details the latest epidemiological data in the EU/EEA and the UK with a focus on older age groups and national reports of outbreaks among residents of LTCFs. All EU/EEA countries and the UK have experienced outbreaks among LTCF residents since Aug 2020.
20.11.2020	COVID-19 Outbreak - New York City, February 29-June 1, 2020	MMWR Morb Mortal Wkly Rep / Article	• Approximately 203,000 cases of confirmed COVID-19 reported in NYC during first 3 months of pandemic. Crude fatality rate among confirmed cases was 9.2% overall and 32.1% among hospitalized patients. • Highest incidence, hospitalization rates, and mortality among Black/African American and Hispanic/Latino persons, as well as those who were living in neighbourhoods with high poverty, aged ≥75 years, and with underlying medical conditions. • Using these data to prevent additional infections among NYC residents during subsequent waves of the pandemic, particularly among those at highest risk for hospitalization and death, is critical.
20.11.2020	Characterization of COVID-19 in Assisted Living Facilities - 39 States, October 2020	MMWR Morb Mortal Wkly Rep / Article	• Relatively little previously reported on COVID-19 among residents and staff members in U.S. assisted living facilities (ALFs). In 39 U.S states, 22% of ALFs reported one or more cases of COVID-19 among residents and staff members. • Among ALF residents with COVID-19, 21% died, compared with 3% who died among the general population with COVID-19.

Epidemiology and clinical – other

Publication Date	Title / URL	Journal / Article type	Digest
12.11.2020	REACT-1 round 6 updated report: high prevalence of SARS-CoV-2 swab positivity with reduced rate of growth in England at the start of November 2020	Imperial College London / Working paper	• Overall weighted prevalence of infection in the community in England during round 6 was 1.3% or 130 people per 10,000 infected, up from 60 people per 10,000 in the round 5 report, with corresponding R number estimated at 1.2. • Rapid growth in the South observed in the first half of round 6 was no longer apparent in the second half of round 6. • A decline in prevalence in Yorkshire and The Humber was also observed during this period. • Comparing the first and second halves of round 6, there was a suggestion of decline in weighted prevalence in participants aged 5 to 12 years and in those aged 25 to 44 years. • While prevalence remained high, in the second half of round 6 there was suggestion of a slight fall then rise that was seen nationally and also separately in both the North and the South.

Transmission

Publication Date	Title / URL	Journal / Article type	Digest
18.11.2020	SARS-CoV-2 Transmission between Mink (Neovison vison) and Humans, Denmark	Emerg Infect Dis / Article	• In Denmark, SARS-CoV-2 has spread rapidly among farmed mink, resulting in some respiratory disease. In this study of 3 mink farm, infections occurred with little clinical disease or increase in death, making it difficult to detect the spread of infection; thus, mink farms could represent a serious, unrecognized animal reservoir for SARS-CoV-2. • Full-length virus genome sequencing revealed novel virus variants in mink. These variants subsequently appeared within the local human community.
17.11.2020	Secondary transmission of COVID-19 in preschool and school settings after their reopening in northern Italy: a population-based study	medRxiv (non-peer reviewed) / Article	• Population-based study including all consecutive COVID-19 primary cases leading to an investigation in 36 educational institutions (8 preschools, 10 primary and 18 secondary schools) from 1 Sept to 15 Oct 2020 in Reggio Emilia province, Italy. • A total of 994 students and 204 teachers were tested following notification of 43 cases (38 students and 5 teachers). • Of these, 10 students and two teachers created 39 secondary cases: an attack rate of 3.9%. • There were no secondary cases among teachers/staff. • Secondary transmission occurred in one primary school and 8 secondary schools. • The majority of secondary cases did not report any previous close contact with a positive case. Clusters ranged from one to 22 secondary cases.

Infection control / non-pharmaceutical interventions

Publication Date	Title / URL	Journal / Article type	Digest
01.02.2021	COVID-19 Infection Control Measures in Long-Term Care Facility, Pennsylvania, USA	Emerg Infect Dis / Research letter (early release)	• Authors report a surveillance exercise at a long-term care facility in Pennsylvania, USA. • After introduction of a testing strategy and other measures, this facility had a 17-fold lower coronavirus disease case rate compared with those of neighbouring facilities. • Despite some limitations, this study suggests that a proper testing strategy coupled with other measures may result in protection of vulnerable populations.
18.11.2020	Effectiveness of Adding a Mask Recommendation to Other Public Health Measures to Prevent SARS-CoV-2 Infection in Danish Mask Wearers : A Randomized Controlled Trial	Ann Intern Med / Original research	• Authors assess whether recommending surgical mask use outside the home reduces wearers' risk for SARS-CoV-2 infection in a setting where masks were uncommon and not among recommended public health measures. • Recommendation to wear surgical masks to supplement other public health measures did not reduce infection rate among wearers by more than 50% in a community with modest infection rates, some degree of social distancing, and uncommon general mask use. The data were compatible with lesser degrees of self-protection. • **Limitations:** Inconclusive results, missing data, variable adherence, patient-reported findings on home tests, no blinding, and no assessment of whether masks could decrease disease transmission from mask wearers to others.

Overviews, comments and editorials

Publication Date	Title / URL	Journal / Article type
18.11.2020	Pfizer / BioNTech COVID-19 vaccine: MHRA statement	Gov.uk / News story
19.11.2020	Urgent actions and policies needed to address COVID-19 among UK ethnic minorities	Lancet / Comment
19.11.2020	Ct values and infectivity of SARS-CoV-2 on surfaces	Lancet Infectious Diseases / Correspondence
18.11.2020	Rapid Response to an Outbreak in Qingdao, China	NEJM / Correspondence
18.11.2020	A Proposed Framework and Timeline of the Spectrum of Disease Due to SARS-CoV-2 Infection: Illness Beyond Acute Infection and Public Health Implications	JAMA / Viewpoint

Produced by the PHE COVID-19 Literature Digest Team

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