



COVID-19 Literature Digest – 27/11/2020

Dear all,

This week's guest editor is Dr James Rubin – Assistant Director of the Health Protection Research Unit in Emergency Preparedness and Response at King's College London. James's research focuses on how people understand and react to new and emerging health threats: everything from COVID-19 to Wifi.

If you only read three papers this week ...

Throughout the pandemic the Office for National Statistics has produced a remarkable range of data on how the public have been affected, and how they are reacting. Their [latest release](#), on survey data covering 11 to 15 November 2020 (during England's 'Lockdown 2.0') is worth your attention. The use of self-report to measure behaviour should be approached with appropriate caution, yet the rates measured suggest that most people continue to abide by most of the rules, most of the time. For example, frequent handwashing is reported by 89% of people and use of face coverings by 97%. Adherence to guidance is easier when it is understood – 65% of respondents thought it was easy or very easy to understand the current rules on lockdown in their local area.

Understanding current behaviour among the public is important, but how might adherence change over the coming weeks? In a set of focus groups with 51 UK residents conducted September to November 2020 designed to understand the possible reasons for non-adherence now and in the future, [Williams and colleagues](#) identified six themes, which are reported in a new preprint. Among these, the evidence of alert fatigue particularly caught my eye: the idea that continual changes to the rules and guidance has left people feeling "lost," "confused" or that it was "impossible to keep up." In the words of one participant, "It does feel like they are changing the rules like every week, and then people don't take them seriously, and I don't blame them..." It would be worth bearing alert fatigue in mind for future changes in guidance.

And finally, allow me to use guest editor's prerogative to tell you about the work of two students from my own Unit, described in a new preprint. Many of our strategies rely on people doing the right thing when they have symptoms of COVID-19. Yet some people with symptoms are still not asking for a test. Do people just not know what symptoms to look out for? In [a series of qualitative interviews](#) with 30 parents in the UK in April, Hodson and Woodland found that simply lacking knowledge was not the key problem for parents deciding what to do with a symptomatic child. Instead, parents go through a process of trying to make sense of the symptoms before acting. Is there some other, more normal explanation ("hayfever, or whatever")? Are the symptoms somehow unusual for that person ("we know each other, we'll know if something gets to that stage")? Is it best to err on the side of caution ("you're thinking 'is this the coronavirus?' I know that's a bit paranoid, but...")? And is it a fever, or 'just' a cough ("he'll be fine [...] Unless there was a temperature")? If we are to get more people to seek a test when symptomatic, some of these perceptions may need to be addressed.

James

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 27.11.2020 (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 |
|------------------|--|--|--|
| 26.11.2020 | Serology- and PCR-based cumulative incidence of SARS-CoV-2 infection in adults in a successfully contained early hotspot (CoMoLo study), Germany, May to June 2020 | Eurosurveillance / Rapid communication | <ul style="list-style-type: none">• Three months after a COVID-19 outbreak in Kupferzell, Germany, a population-based study (n = 2,203) found no RT-PCR-positives. IgG-ELISA seropositivity with positive virus neutralisation tests was 7.7% (95% confidence interval (CI): 6.5–9.1) and 4.3% with negative neutralisation tests.• Estimate 12.0% (95% CI: 10.4–14.0%) infected adults (24.5% asymptomatic), |

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| | | | <p>six times more than notified. Full hotspot containment confirms the effectiveness of prompt protection measures. However, 88% naïve adults are still at high COVID-19 risk.</p> |
| 27.11.2020 | Decline in SARS-CoV-2 Antibodies After Mild Infection Among Frontline Health Care Personnel in a Multistate Hospital Network - 12 States, April-August 2020 | MMWR Morb Mortal Wkly Rep / Report | <ul style="list-style-type: none"> • Among 156 frontline health care personnel who had positive SARS-CoV-2 antibody test results in spring 2020, 94% experienced a decline at repeat testing approximately 60 days later, and 28% seroreverted to below the threshold of positivity. • Participants with higher initial antibody responses were more likely to have antibodies detected at the follow-up test than were those who had a lower initial antibody response. • SARS-CoV-2 antibodies decline over weeks following acute infection. Negative SARS-CoV-2 serologic results do not exclude previous infection, which has significant impacts on how serologic studies are interpreted. |
| 18.11.2020 | Serological follow-up of SARS-CoV-2 asymptomatic subjects | Sci Rep / Article | <ul style="list-style-type: none"> • Study to investigate the development and persistence of antibodies against SARS-CoV-2; 8 week follow up (from a positive nasal swab) with 31 asymptomatic subjects. • About 80% didn't present circulating immunoglobulins after 8 weeks; in more than 40%, no Ig against SARS-CoV-2 were detected at any time. • About two third of subjects with immunoglobulins at baseline did not present IgG against SARS-CoV-2 after 8 weeks. • In summary, majority of subjects who developed an asymptomatic SARS-CoV-2 infection do not present antibodies against the RBD-spike protein after 8 weeks of follow-up. These data should be taken into account for the interpretation of the serological evidences on SARS-CoV-2 that are emerging nowadays. |
| 23.11.2020 | Functional SARS-CoV-2-specific immune memory persists after mild COVID-19 | Cell / Article | <ul style="list-style-type: none"> • Longitudinal assessment of 15 individuals recovered from mild COVID-19 to determine if they develop and sustain multifaceted SARS-CoV-2-specific immunological memory. • Recovered individuals developed SARS-CoV-2-specific IgG antibodies, neutralizing plasma, memory B and memory T cells that persisted for at least three months. SARS-CoV-2-specific IgG memory B cells increased over time. • SARS-CoV-2-specific memory lymphocytes exhibited characteristics associated with potent antiviral function: memory T cells secreted cytokines and expanded upon antigen re-encounter, while memory B cells expressed receptors capable of neutralizing virus when expressed as monoclonal antibodies. • In summary, mild COVID-19 elicits memory lymphocytes that persist and display functional hallmarks of antiviral immunity. |

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| 19.11.2020 | Antibody response using six different serological assays in a completely PCR-tested community after a COVID-19 outbreak - The CoNAN study | Clinical Microbiology and Infection / Article | <ul style="list-style-type: none"> • 626 participants (71% of population in community Neustadt am Rennsteig, Germany; quarantined March 22 - April 5) enrolled for PCR- and antibody testing in the study. • Fifty-two out of 620 (8.4%) participants had antibodies against SARS-CoV-2 in at least two different assays. • 38 participants with previously PCR-confirmed SARS-CoV-2 infection - only 19 (50%) displayed anti-SARS-CoV-2 antibodies. • Antibody positive participants with symptoms compatible with a respiratory tract infection had significantly higher antibody levels than asymptomatic participants (EU-assay: Median 2.9 vs. 7.2 IgG-index, $p=0.002$; DS-assay: Median 45.2 vs. 143 AU/mL, $p=0.002$). Persisting viral replication was not detected. • Data questions relevance and reliability of IgG antibody testing to detect past SARS-CoV-2 infections six weeks after an outbreak. Assessing immunity should not only rely on antibody tests. |
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Diagnosics and genomics

| Publication Date | Title / URL | Journal / Article type | Digest |
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| 25.11.2020 | No evidence for increased transmissibility from recurrent mutations in SARS-CoV-2 | Nat Commun / Article | <ul style="list-style-type: none"> • This paper was previously included in the Digest as a preprint. • Tested whether any homoplasies observed in SARS-CoV-2 to date are significantly associated with increased viral transmission. • Developed a phylogenetic index to quantify the relative number of descendants in sister clades with and without a specific allele. • Applied this index to a curated set of recurrent mutations identified within a dataset of 46,723 SARS-CoV-2 genomes isolated from patients worldwide. • Recurrent mutations currently in circulation appear to be evolutionary neutral and primarily induced by the human immune system via RNA editing, rather than being signatures of adaptation. • At this stage the authors find no evidence for significantly more transmissible lineages of SARS-CoV-2 due to recurrent mutations. |

Epidemiology and clinical – children / pregnancy

| Publication Date | Title / URL | Journal / Article type | Digest |
|------------------|--|---------------------------|---|
| 25.11.2020 | Report 37 - Children's role in the COVID-19 pandemic: as systematic review of susceptibility, severity, and transmissibility | Imperial College / Report | <ul style="list-style-type: none"> • This systematic review of early studies synthesises evidence on the susceptibility of children to SARS-CoV-2 infection, the severity and clinical outcomes in children with SARS-CoV-2 infection, and the transmissibility of SARS-CoV-2 by children. • Pooled estimate of the proportion of test positive children who were asymptomatic was 21.1% (95% CI: 14.0 - 28.1%), based on 13 included studies, and the proportion of children with severe or critical symptoms was 3.8% (95% CI: 1.5 - 6.0%), based on 14 included studies. • They did not identify any studies designed to assess transmissibility in children and found that susceptibility to infection in children was highly variable across studies. |
| 24.11.2020 | Symptoms associated with a positive result for a swab for SARS-CoV-2 infection among children in Alberta | Cmaj / Article | <ul style="list-style-type: none"> • Authors analysed results for 2463 children who underwent testing for SARS-CoV-2 infection: 1987 with positive result (476 negative) with 714 (35.9%) reported being asymptomatic. • Two common symptoms - cough (24.5%), rhinorrhea (19.3%) - also common in negative test results; not predictive of positive test (positive LR 0.96, 95% confidence interval [CI] 0.81–1.14, and 0.87, 95% CI 0.72–1.06, respectively). • Symptoms most strongly associated with a positive SARS-CoV-2 swab result were anosmia/ageusia, nausea/vomiting, headache and fever. The positive LR for combination of anosmia/ageusia, nausea/vomiting and headache was 65.92 (95% CI 49.48–91.92). |

Epidemiology and clinical – risk factors

| Publication Date | Title / URL | Journal / Article type | Digest |
|------------------|--|------------------------------|--|
| 23.11.2020 | Retrospective cohort study of admission timing and mortality following COVID-19 infection in England | BMJ Open / Original research | <ul style="list-style-type: none"> • Study investigating if timing of hospital admission is associated with risk of mortality for COVID-19 patients in England; factors associated with a longer interval between symptom onset and hospital admission. • Timing was an independent predictor of mortality following adjustment for age, sex, comorbidities, ethnicity and obesity. Each additional day between symptom onset and hospital admission was associated with a 1% increase in mortality risk (HR 1.01; p<0.005). • Most likely to have an increased interval between symptom onset and hospital admission: healthcare workers; individuals from a BAME background; |

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| | | | <p>patients with obesity.</p> <ul style="list-style-type: none"> • Strategies to identify and admit patients with high-risk and those showing signs of deterioration in a timely way may reduce the consequent mortality from COVID-19, and should be explored. |
| 25.11.2020 | Characterisation of 22445 patients attending UK emergency departments with suspected COVID-19 infection: Observational cohort study | PLoS One / Article | <ul style="list-style-type: none"> • Aimed to characterise patients attending emergency departments with suspected COVID-19, including subgroups based on sex, ethnicity and COVID-19 test results. • Undertook a mixed prospective and retrospective observational cohort study in 70 emergency departments across the UK. • Concluded that important differences exist between patient groups presenting to the emergency department with suspected COVID-19. Adults and children differ markedly and require different approaches to emergency triage. Admission and adverse outcome rates among adults suggest that policies to avoid unnecessary ED attendance achieved their aim. Subsequent COVID-19 confirmation confers a worse prognosis and greater need for organ support. |

Epidemiology and clinical – other

| Publication Date | Title / URL | Journal / Article type | Digest |
|------------------|---|--|---|
| 26.11.2020 | Epidemiology and public health response in early phase of COVID-19 pandemic, Veneto Region, Italy, 21 February to 2 April 2020 | Eurosurveillance / Research | <ul style="list-style-type: none"> • This paper describes the public health response and epidemiology of SARS-CoV-2 infections in the Veneto Region from 21 Feb to 2 Apr 2020. • In the Veneto Region, the strict social distancing measures imposed by the Italian government were supported by thorough case finding and contact tracing, as well as well-defined roles for different levels of care. |
| 26.11.2020 | Impact of the COVID-19 pandemic on testing services for HIV, viral hepatitis and sexually transmitted infections in the WHO European Region, March to August 2020 | Eurosurveillance / Rapid communication | <ul style="list-style-type: none"> • Present preliminary results of a COVID-19 impact assessment on testing for HIV, viral hepatitis and sexually transmitted infections in the WHO European Region. • Analysed 98 responses from secondary care (n = 36), community testing sites (n = 52) and national level (n = 10). Compared to pre-COVID-19, 95% of respondents report decreased testing volumes during Mar–May and 58% during June–Aug 2020. • Reasons for decreases and mitigation measures were analysed. |
| 27.11.2020 | Where has all the influenza gone? The impact of COVID-19 on the circulation of influenza and other respiratory viruses, Australia, March to September 2020 | Eurosurveillance / Rapid communication | <ul style="list-style-type: none"> • The coronavirus disease pandemic was declared in Mar 2020, as the southern hemisphere’s winter approached. Australia expected co-circulation of SARS-CoV-2, influenza and other seasonal respiratory viruses. However, influenza notifications were 7,029 (Mar–Sept) compared with an average 149,832 for the same period in 2015–2109, despite substantial testing. |

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| | | | <ul style="list-style-type: none"> Restrictions on movement within and into Australia may have temporarily eliminated influenza. Other respiratory pathogens also showed remarkably changed activity in 2020. |
| 25.11.2020 | Estimated incidence of COVID-19 illness and hospitalization - United States, February-September, 2020 | Clin Infect Dis / Article | <ul style="list-style-type: none"> CDC study estimating U.S. cumulative incidence SARS-CoV-2 infections, symptomatic illnesses, and hospitalizations. Nationally reported confirmed case counts adjusted for sources of under-detection based on testing practices in inpatient and outpatient settings and assay sensitivity. Estimated that 1 of every 2.5 (95% Uncertainty Interval (UI): 2.0–3.1) hospitalized infections and 1 of every 7.1 (95% UI: 5.8–9.0) non-hospitalized illnesses nationally reported. Multipliers applied to reported cases along with data on prevalence of asymptomatic infection from published systematic reviews: estimate that 2.4 million hospitalizations, 44.8 million symptomatic illnesses, and 52.9 million total infections may have occurred in the U.S. population from Feb 27–Sept 30, 2020. |

Transmission

| Publication Date | Title / URL | Journal / Article type | Digest |
|------------------|---|------------------------|--|
| 24.11.2020 | Transmission heterogeneities, kinetics, and controllability of SARS-CoV-2 | Science / Article | <ul style="list-style-type: none"> Detailed patient and contact tracing data in Hunan, China, found 80% of secondary infections traced back to 15% of SARS-CoV-2 primary infections, indicating substantial transmission heterogeneities. Transmission risk scales positively with duration of exposure and closeness of social interactions. Lockdown period increases transmission risk in the family and households, while isolation and quarantine reduce risks across all contacts. Reconstructed infectiousness profile of a typical SARS-CoV-2 patient peaks just before symptom presentation. Modelling indicates need for synergistic efforts of case isolation, contact quarantine, and population-level interventions. |

Overviews, comments and editorials

| Publication Date | Title / URL | Journal / Article type |
|------------------|---|--|
| 28.11.2020 | A tribute to some of the doctors who died from COVID-19 | Lancet / Obituary |
| 06.11.2020 | The Dental Team: An Additional Resource for Delivering Vaccinations | Front Med (Lausanne) / Opinion article |

Produced by the PHE COVID-19 Literature Digest Team

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