



COVID-19 Literature Digest – 23/09/2020

The [Evidence Digest](#) continues after the “Top picks”.

Dear all,

This week’s guest editor is Dr Derren Ready – Consultant Clinical Scientist in Public Health Infections within PHE’s Field Services South West England Field Services team and Honorary Senior Lecturer at UCL and University of Bristol.

If you only read three papers this week...

Early in the pandemic I supported PHE’s contact tracing cell and for part of this work we asked people to self-isolate at home. As self-isolation is such a key component of our public health control measures it’s hard to realise that just over six months ago it was a new experience for us and more importantly for the first few people we spoke to. This [first paper](#) from Norway, by Steens et al, describes the adherence to quarantine requests which, in Norway, is directed to people with confirmed and probable COVID-19 infection and those returning from specific countries. Their findings show that the overall adherence to self-isolation requests is pretty low (42% of individuals followed the request to quarantine). Interestingly, in the early phase of the pandemic people were more likely to comply (66%) compared to more recent times (33 - 38%). Also, younger adults (aged 18-29 years) and people with symptoms of infection were most likely to adhere to the request. For me, this paper raises some interesting questions regarding the long-term success of public health measures. If people are weary of these measures and do not see the benefit of this control measure, how can we best communicate its value?

Since joining PHE in 2012 and more recently, whilst working in the adult social care cell, I have been interested in, and sometimes upset by, the disparity in attention given to different people in our society. This [next paper](#), by Rogers et al, looks at COVID-19 in some of our most vulnerable people; those living in homeless shelters. In this US paper, the risk of SARS-CoV-2 detection increased for those living in hostels by their age, with homeless people being more likely to be positive for SARS-CoV-2 if aged 60 years or older, when compared to those without SARS-CoV-2 detection (44.8% vs. 15.9%). Other local factors also influenced the likelihood of a positive PCR test, such as sleeping arrangements and resident density, with 86% of people with a positive test sleeping in a communal space rather than those able to distance themselves within a private or shared room. Unfortunately, in the UK we have significant numbers of older people who are homeless, so this paper reminds us to ensure that public health control measures are in place in hostels, to reduce the risk of COVID-19 transmission in these settings.

The [final paper](#), by Ben-Shmuel et al, returns me to one of my initial areas of microbiological research, which was understanding the role of the environment in the spread of infection, which for SARS-CoV-2 is far from clear. This interesting paper carried out sampling in patients’ rooms and demonstrated that viral RNA could be detected by PCR in 29 out of 55 samples tested (53%), with PCR cycles thresholds (ct) ranging from 30.0 - 39.8. These contaminated surfaces were mainly bed rails, ventilator touch-screens, staff computer accessories and taps. As a comparator, the team looked at environmental contamination in a hotel setting, which was occupied by mildly symptomatic or asymptomatic people. They found that 16 out of 42 (38%) samples yielded detectable levels of viral RNA with a ct ranging from 29.3 - 35.2 cycles, in this non-health care

setting. The research group also tested the viability of SARS-CoV-2 on non-porous surfaces using cell culture methods and reported viability for up to 3 days at room temperature. Although the importance of the environment to person transmission is well understood for other microbial pathogens, this indirect route of transmission still requires further study to help understand its significance for COVID-19.

Together, these research papers underline the importance of our key infection prevention and control measures of social distancing, good hygiene, isolation and environmental cleaning, which are designed to reduce transmission of COVID-19 infection to all our communities.

Derren

If you only read three papers this week...

This Evidence Digest is produced by the PHE COVID-19 Literature Digest Team as a resource for professionals working in public health. We do not accept responsibility for the availability, reliability or content of the items included in this resource and do not necessarily endorse the views expressed within them. The papers are organised under the following themes:

- Serology and immunology
- Diagnostics
- Genomics
- Epidemiology and clinical - risk factors
- Epidemiology and clinical - other
- Infection control
- Treatment
- Modelling
- Overviews, comments and editorials (no digest)

Please note that we are including preprints (**highlighted in red**), which are preliminary reports of work that have NOT been peer-reviewed. They should not be relied on to guide clinical practice or health-related behaviour and should NOT be reported in news media as established information.

Serology and immunology

Publication Date	Title / URL	Journal / Article type	Digest
21.09.2020	SARS-CoV-2 Seroprevalence among Healthcare, First Response, and Public Safety	Emerg Infect Dis / Research	• Antibody testing of 16,403 participants in emergency medical service agencies and 27 hospitals in Detroit, USA May-June 2020: 6.9% had SARS-CoV-2 antibodies.

	Personnel, Detroit Metropolitan Area, Michigan, USA, May-June 2020		<ul style="list-style-type: none"> • Seropositivity associated with exposure to COVID-19 positive household members (adjusted odds ratio [aOR] 6.18, 95% CI 4.81-7.93) and working within 15 km of Detroit (aOR 5.60, 95% CI 3.98-7.89). • Nurse assistants (aOR 1.88, 95% CI 1.24-2.83) and nurses (aOR 1.52, 95% CI 1.18-1.95) more likely to be seropositive than physicians. • Working in a hospital emergency department increased the likelihood of seropositivity (aOR 1.16, 95% CI 1.002-1.35).
16.09.2020	Antigen-specific adaptive immunity to SARS-CoV-2 in acute COVID-19 and associations with age and disease severity	Cell / Article	<ul style="list-style-type: none"> • Completed a combined examination of all three branches of adaptive immunity at the level of SARS-CoV-2-specific CD4+ and CD8+ T cell and neutralizing antibody responses in acute and convalescent subjects. • Coordinated SARS-CoV-2-specific adaptive immune responses were associated with milder disease, suggesting roles for both CD4+ and CD8+ T cells in protective immunity in COVID-19. Notably, coordination of SARS-CoV-2 antigen-specific responses was disrupted in individuals > 65 years old. Scarcity of naive T cells was also associated with ageing and poor disease outcomes. • A parsimonious explanation is that coordinated CD4+ T cell, CD8+ T cell, and antibody responses are protective, but uncoordinated responses frequently fail to control disease, with a connection between ageing and impaired adaptive immune responses to SARS-CoV-2.
21.09.2020	Immune responses to SARS-CoV-2 infection in hospitalized pediatric and adult patients	Sci Transl Med / Research article	<ul style="list-style-type: none"> • Authors compared cytokine, humoral, cellular immune responses in paediatric (children & youth, age < 24 years) (n=65) and adult (n=60) COVID-19 patients. • Serum concentrations of IL-17A and IFN-γ, but not TNF-α or IL-6, were inversely related to age. • Adults mount more robust T cell response to viral spike protein; evidenced by increased expression of CD25+ on CD4+ T cells and frequency of IFN-γ+CD4+ T cells. • Findings demonstrate poor outcome in hospitalized COVID-19 adults compared to children may not be attributable to a failure to generate adaptive immune responses

Diagnostics

Publication Date	Title / URL	Journal / Article type	Digest
01.10.2020	Deep learning-based triage and analysis of lesion burden for COVID-19: a retrospective study with external validation	Lancet Digital Health / Article	<ul style="list-style-type: none"> • A deep learning algorithm for triaging patients with suspected COVID-19 at fever clinics was developed and externally validated. • Given its high accuracy across populations with varied COVID-19 prevalence, integration of this system into the standard clinical workflow could expedite identification of chest CT scans with imaging indications of COVID-19.

Genomics

Publication Date	Title / URL	Journal / Article type	Digest
19.09.2020	Whole-genome sequencing to track SARS-CoV-2 transmission in nosocomial outbreaks	Clin Infect Dis / Article	<ul style="list-style-type: none"> • Authors applied whole virus genome sequencing (WvGS) to analyse transmission routes of SARS-CoV-2 in hospital-acquired (HA) COVID-19. • An investigation was undertaken for all HA cases of COVID-19 from March to April 2020 in an Irish tertiary referral centre. Fifty SARS-CoV-2 samples were analysed by WvGS and their phylogenetic relationship established. • WvGS identified transmission events previously undetected by epidemiological analysis and provided evidence for SARS-CoV-2 transmission between healthcare workers (HCW) and patients and among HCW themselves. • The majority of HA COVID-19 cases occurred in patients highly dependent on nursing care, suggesting the likely route of transmission was by close contact or droplet, rather than aerosol, transmission. Mortality among HA COVID-19 infections was recorded as 33%.
21.09.2020	Monitoring SARS-CoV-2 circulation and diversity through community wastewater sequencing	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • The authors examine the potential of using next-generation sequencing (NGS) of sewage samples to evaluate the diversity of SARS-CoV-2 at the community level from routine wastewater testing, and compared these results with the virus diversity in patients from the Netherlands and Belgium. • Phylogenetic analysis revealed the presence of viruses belonging to the most prevalent clades (19A, 20A and 20B) in both countries. • Combining genome consensus and LFV analyses, the authors found 57

			unique mutations in the SARS-CoV-2 genome which have not been described before.
21.09.2020	Free fatty acid binding pocket in the locked structure of SARS-CoV-2 spike protein	Science / Report	<ul style="list-style-type: none"> • 2.85 Å cryo-EM structure of SARS-CoV-2 spike (S) glycoprotein reveals receptor binding domains (RBDs) tightly bind essential free fatty acid (FFA) linoleic acid (LA) in three composite binding pockets. • LA binding stabilizes a locked S conformation giving rise to reduced ACE2 interaction in vitro. In human cells, LA supplementation synergizes with the COVID-19 drug remdesivir, suppressing SARS-CoV-2 replication. • Authors' structure directly links LA and S, setting the stage for intervention strategies targeting LA binding by SARS-CoV-2.

Epidemiology and clinical – risk factors

Publication Date	Title / URL	Journal / Article type	Digest
21.09.2020	Reinfection with SARS-CoV-2: considerations for public health response	European Centre for Disease Control and Prevention / Risk assessment	<ul style="list-style-type: none"> • The aim of this Threat Assessment Brief is to elucidate the characteristics and frequency of confirmed SARS-CoV-2 reinfection in the literature, to summarise the findings about SARS-CoV-2 infection and antibody development, and to consider the following questions: <ul style="list-style-type: none"> - How can a SARS-CoV-2 reinfection be identified? - How common are SARS-CoV-2 reinfections? - What is known about the role of reinfection in onward transmission? - What do these observations mean for acquired immunity?
22.09.2020	Coronavirus (COVID-19) related deaths by occupation, before and during lockdown, England and Wales: deaths registered between 9 March and 30 June 2020	Gov.uk / Official statistics	<ul style="list-style-type: none"> • 5,330 deaths involving COVID-19 in the working age population (20 to 64 yos) of England and Wales were registered Between 9 Mar and 30 June 2020. • Among men, four of the nine major occupation groups (elementary; caring, leisure and personal services; process, plant and machine operatives; and skilled trades) had statistically significantly higher rates of death involving COVID-19 both before and during lockdown. • Caring, leisure and other services was the only major occupation group to have a statistically significantly higher rate of death involving COVID-19 among women before and during lockdown.
21.09.2020	Sharing a household with children and risk of COVID-19: a study of over 300,000 adults living in healthcare worker households in Scotland	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • The authors used an occupational cohort comprising Scottish NHS healthcare workers and members of their households. The cohort was divided into adults who did not share a household with young children (n=241,266), and adults who shared a household with 1, 2 or 3+ young

			<p>children (41,198, 23,783 and 3,850 respectively).</p> <ul style="list-style-type: none"> • Increased household exposure to young children was associated with an attenuated risk of testing positive for SARS-CoV-2 and appeared to also be associated with an attenuated risk of COVID-19 disease severe enough to require hospitalisation.
22.09.2020	Patterns of COVID-19 testing and mortality by race and ethnicity among United States veterans: A nationwide cohort study	PLoS Med / Article	<ul style="list-style-type: none"> • A cohort study of US Veterans receiving care (n=5,834,543; male=91%) examined associations between ethnicity and receipt of COVID-19 testing, positive test result, and 30-day mortality, with multivariable adjustment for demographic and clinical characteristics. • Black individuals were more likely to be tested (rate per 1,000 individuals: 60.0) than Hispanic (52.7) and White individuals (38.6). • While individuals from minority backgrounds were more likely to test positive, 30-day mortality did not differ by race/ethnicity.
19.09.2020	Characteristics and Outcomes of Individuals With Pre-existing Kidney Disease and COVID-19 Admitted to Intensive Care Units in the United States	Am J Kidney Dis / Original investigation	<ul style="list-style-type: none"> • 4,264 critically ill COVID-19 patients (143 dialysis; 521 chronic kidney disease [CKD]; 3,600 patients without CKD) admitted to ICUs at 68 U.S hospitals. • Half of dialysis and CKD patients died within 28-days of ICU admission versus 35% of patients without pre-existing kidney disease. Compared to patients without pre-existing kidney disease, dialysis patients had a higher risk of 28-day in-hospital death, while patients with CKD had an intermediate risk. • Highlights high mortality of severe COVID-19 patients with underlying kidney disease; safe and effective COVID-19 therapies needed for this vulnerable population.
19.09.2020	Outcomes Among Patients Hospitalized With COVID-19 and Acute Kidney Injury	Am J Kidney Dis / Original investigation	<ul style="list-style-type: none"> • Among 9657 patients hospitalized with COVID-19 in 13 New York hospitals, acute kidney injury (AKI) incidence rate was 38.4/1000 patient-days. • Incidence rates of in-hospital death among patients without AKI, with AKI not requiring kidney replacement therapy (AKI non-KRT) and with AKI receiving KRT (AKI-KRT) were 10.8, 31.1 and 37.5/1000 patient-days, respectively. • AKI in hospitalized patients with COVID-19 was associated with significant risk for death.
22.09.2020	Patient Trajectories Among Persons Hospitalized for COVID-19 : A Cohort Study	Ann Intern Med / Original research	<ul style="list-style-type: none"> • Retrospective cohort analysis of 832 consecutive COVID-19 admissions, 4 March to 24 April 2020, in five US hospitals - with follow-up through 27 June 2020. • A combination of demographic and clinical variables is strongly associated with severe COVID-19 disease or death and their early onset.

			<ul style="list-style-type: none"> • Patients had markedly different probabilities of disease progression on the basis of age, nursing home residence, comorbid conditions, obesity, respiratory symptoms, respiratory rate, fever, absolute lymphocyte count, hypoalbuminemia, troponin level, and C-reactive protein level and the interactions among these factors. • The COVID-19 Inpatient Risk Calculator (CIRC), using factors present on admission, can inform clinical and resource allocation decisions.
17.09.2020	Post-acute COVID-19 associated with evidence of bystander T-cell activation and a recurring antibiotic-resistant bacterial pneumonia	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • A case study describes a COVID-19 patient who developed recurring ventilator-associated pneumonia caused by a strain of <i>Pseudomonas aeruginosa</i> that acquired increasing levels of antimicrobial resistance (AMR) in response to COVID-19 treatment. • Immunological analysis of longitudinally-collected blood samples revealed escalating levels of T-cell activation targeting both bacteria and virus, with evidence of bystander-activation, a feature the authors suggest may have contributed to the continuing inflammation and prolonged requirement for ventilation.

Epidemiology and clinical – other

Publication Date	Title / URL	Journal / Article type	Digest
01.10.2020	Routine haematological parameters in COVID-19 prognosis	Lancet Haematology / Correspondence	<ul style="list-style-type: none"> • Analysed data from 210 consecutive patients with COVID-19 who were admitted to a tertiary care hospital in Austria between Mar 3 and June 13, 2020. 61 (29%) patients developed severe to critical disease requiring intensive care treatment, and 47 (22%) patients died in hospital. • In this cohort, haematological parameters did not allow prediction of patient outcome. • The authors aim to raise awareness that these routine parameters, despite giving guidance on the overall health of the patient, might not always accurately indicate COVID-19-related complications.
01.10.2020	Clinical features of COVID-19 mortality: development and validation of a clinical prediction model	Lancet Digital Health / Article	<ul style="list-style-type: none"> • Using the development dataset (n=3841) and a systematic machine learning framework, the authors developed a COVID-19 mortality prediction model that showed high accuracy (AUC=0.91) when applied to test datasets of retrospective (n=961) and prospective (n=249) patients. • This model was based on three clinical features: patient's age,

minimum oxygen saturation over the course of their medical encounter, and type of patient encounter (inpatient vs outpatient and telehealth visits).

Infection control

Publication Date	Title / URL	Journal / Article type	Digest
16.09.2020	In-flight transmission of COVID-19 on flights to Greece: an epidemiological analysis	Travel Med Infect Dis / Article	<ul style="list-style-type: none"> • Authors investigated 18 international flights (2224 passengers/110 crew members), and present 5 cases of probable in-flight transmission in Greece. • Air travel has played a central role in the progression of the COVID-19 pandemic. However, there are scarce data about in-flight transmission. • Efforts should be placed in order to ensure the prompt implementation of appropriate infection control measures on board.
18.09.2020	Potential sources, modes of transmission and effectiveness of prevention measures against SARS-CoV-2	J Hosp Infect / Review	<ul style="list-style-type: none"> • Review current evidence on possible sources for SARS-CoV-2, including evaluation of transmission risks and effectiveness of applied prevention measures. • Air and inanimate surfaces may be sources; however, viral RNA has been inconsistently detected. • SARS-CoV-2 RNA detected on PPE / in blood, urine, eyes, gastrointestinal tract and pets, but these sources are thought to play a negligible role for transmission. • Prevention measures - e.g. hand washing, face masks, gloves - are analysed for their expected protective effect.

Treatment

Publication Date	Title / URL	Journal / Article type	Digest
21.09.2020	Long-term hydroxychloroquine use in patients with rheumatic conditions and development of SARS-CoV-2 infection: a retrospective cohort study	Lancet Rheumatology / Article	<ul style="list-style-type: none"> • Authors examine whether 10,703 patients with rheumatological conditions receiving chronic hydroxychloroquine therapy are at less risk of COVID-19 than 21,406 patients not receiving hydroxychloroquine. • Hydroxychloroquine was not associated with a preventive effect against SARS-CoV-2 infection in a large group of patients with rheumatological conditions.

Modelling

Publication Date	Title / URL	Journal / Article type	Digest
16.09.2020	OpenABM-Covid19 - an agent-based model for non-pharmaceutical interventions against COVID-19 including contact tracing	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • The authors present OpenABM-Covid19: an open-source, agent-based simulation of the epidemic which includes detailed age-stratification and realistic social networks. • Although parameterised to UK demographics, it can easily be re-parameterised for other countries. • OpenABM-Covid19 can evaluate non-pharmaceutical interventions, including contact tracing, and simulate a population of 1 million people in seconds per day. • The Python interface allows scientists and policymakers to simulate dynamic packages of interventions.
21.09.2020	Effects of Cocooning on Coronavirus Disease Rates after Relaxing Social Distancing	Emerg Infect Dis / Research letter	<ul style="list-style-type: none"> • By using a model capturing high-risk populations and transmission rates estimated from U.S hospitalization data, authors found that postponing relaxation will only delay future disease waves. • Cocooning vulnerable populations can prevent overwhelming medical surges.
17.09.2020	Report 32 - Age groups that sustain resurging COVID-19 epidemics in the United States	Imperial College / Report	<ul style="list-style-type: none"> • Considering dynamics for the US, the authors analysed aggregated, age-specific mobility trends from more than 10 million individuals and link these mechanistically to age-specific COVID-19 mortality data. • Estimate that, until Aug, 63.4% [60.9%-65.5%] of SARS-CoV-2 infections in the US originated from adults aged 20-49, while 1.2% [0.8%-1.8%] originated from children aged 0-9. • In areas with continued, community-wide transmission, the transmission model predicts that re-opening kindergartens and elementary schools could facilitate spread and lead to additional COVID-19 attributable deaths over a 90-day period. • These findings indicate that targeting interventions to adults aged 20-49 are an important consideration in halting resurgent epidemics and preventing COVID-19-attributable deaths when kindergartens and elementary schools reopen.
20.09.2020	COVID-19 healthcare demand and mortality in Sweden in response to non-pharmaceutical mitigation and suppression scenarios	Int J Epidemiol / Article	<ul style="list-style-type: none"> • Contrast the consequences of different responses to COVID-19 within Sweden, the resulting demand for care, intensive care, the death tolls and the associated direct healthcare related costs. • The results of this study highlight the impact of different combinations of non-pharmaceutical interventions, especially moderate physical

			<p>distancing in combination with more effective isolation of infectious individuals, on reducing deaths, health demands and lowering healthcare costs.</p> <ul style="list-style-type: none"> • In less effective mitigation scenarios, the demand on ICU beds would rapidly exceed capacity, showing the tight interconnection between the healthcare demand and physical distancing in society.
22.09.2020	Short-term and long-term health impacts of air pollution reductions from COVID-19 lockdowns in China and Europe: a modelling study	Lancet Planetary Health / Article	<ul style="list-style-type: none"> • Assessed the implications of different lockdown measures on air pollution levels in Europe and China, as well as the short-term and long-term health impact. • Results indicate that lockdown interventions led to substantial reductions in fine particulate matter (PM2.5) concentrations in China and Europe. • They estimated that tens of thousands of premature deaths from air pollution were avoided, although with significant differences observed in Europe and China. • Findings suggest that considerable improvements in air quality are achievable in both China and Europe when stringent emission control policies are adopted.

Overviews, comments and editorials

Publication Date	Title / URL	Journal / Article type
22.09.2020	COVID-19 testing in the UK	Lancet Respiratory Medicine / Editorial
21.09.2020	Covid-19: What's going wrong with testing in the UK?	BMJ / Briefing
22.09.2020	Pooled saliva samples for COVID-19 surveillance programme	Lancet Respiratory Medicine / Spotlight
21.09.2020	The UCL Ventura CPAP device for COVID-19	Lancet Respiratory Medicine / Spotlight
01.10.2020	Prediction models for COVID-19 clinical decision making	Lancet Digital Health / Comment
23.09.2020	ECDC launches new COVID-19 situation dashboard	European Centre for Disease Control and Prevention / News
21.09.2020	COVID19-world: a shiny application to perform comprehensive country-specific data visualization for SARS-CoV-2 epidemic	BMC Med Res Methodol / Article
21.09.2020	A Decision-Making Algorithm for Children With Suspected Coronavirus Disease 2019	JAMA Pediatr / Comment & response
21.09.2020	Evaluation of the COVID-19 response in Spain: principles and requirements	Lancet Public Health / Correspondence
21.09.2020	Tracking COVID-19 with wastewater	Nat Biotechnol / News & views
01.10.2020	The online anti-vaccine movement in the age of COVID-19	Lancet Digital Health / News

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