Public Health England

COVID-19 Literature Digest – 24/08/2020

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
- Genomics
- Epidemiology and clinical - children and pregnancy
- Epidemiology and clinical - risk factors
- Epidemiology and clinical - other
- 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Please note that we are including preprints (highlighted in red), which are preliminary reports of work that have NOT been peer-reviewed.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
20.08.2020	High SARS-CoV-2 Seroprevalence in Children and Adults in the Austrian Ski Resort Ischgl	medRxiv (non-peer reviewed) / Article	• After a SARS-CoV-2 outbreak in Austrian ski resort Ischgl in early Mar, cross-sectional epidemiological study of Ischgl population (n= 1867), 79% included (n=1473, incl. 214 children). • High local seroprevalence of 42.4%, which was lower in individuals below the age of 18 (27.1%) than adults (45%). • Of seropositive individuals, 83.7% had not been diagnosed to have had SARS-CoV-2 infection previously. The clinical course was generally mild. • Mathematical modelling suggests that a drastic decline of newly

			infected individuals in Ischgl by the end of April occurred due to the dual impact from the non-pharmacological interventions (NPIs) and a significant immunization of the Ischgl population.
21.08.2020	[Neutralizing antibodies correlate with protection from SARS-CoV-2 in humans during a fishery vessel outbreak with high attack rate](#)	J Clin Microbiol / Article	• Recently included in the Digest as a pre-print (on 14 August 2020). • Describes an outbreak of COVID-19 on a fishing vessel associated with a high attack rate. Predeparture serological and viral RT-PCR testing along with repeat testing after return to shore was available for 120/122 persons on board over a median follow-up of 32.5 days. • A total of 104 individuals had an RT-PCR positive viral test, yielding an attack rate on board of 85.2%. • 3 crew members tested seropositive prior to the boat's departure and also had neutralizing and spike-reactive antibodies in follow-up assays. None of these crew members with neutralizing antibody titres showed evidence of viral infection or experienced any symptoms during the outbreak.
19.08.2020	[Self assessment overestimates historical COVID-19 disease relative to sensitive serological assays: cross sectional study in UK key workers](#)	medRxiv (non-peer reviewed) / Article	• Individuals recruited from: (A) Police and Fire and Rescue services (n=1147), (B) healthcare workers (n=1546) and (C) healthcare workers with previously positive virus detection (n=154) to measure association between self-reported signs and symptoms and SARS-CoV-2 seropositivity. • 943 of the 2847 participants (33%) reported belief they had had COVID-19, having experienced compatible symptoms. • Of these, 466 (49%) were seronegative on both Nucleoprotein (Roche) and Spike-protein (EUROIMMUN) antibody assays. • Self-reported belief of COVID-19 was common among our frontline worker cohort. About half of these individuals were seronegative, despite a high sensitivity of serology in this cohort.
21.08.2020	[An adenovirus-vectored COVID-19 vaccine confers protection from SARS-COV-2 challenge in rhesus macaques](#)	Nat Commun / Article	• The authors report the generation of a replication-incompetent recombinant serotype 5 adenovirus, Ad5-S-nb2, carrying a codon-optimized gene encoding Spike protein (S). • In mice and rhesus macaques, intramuscular injection with Ad5-S-nb2 elicits systemic S-specific antibody and cell-mediated immune (CMI) responses. • Intranasal inoculation elicits both systemic and pulmonary antibody responses but weaker CMI response. • At 30 days after a single vaccination with Ad5-S-nb2 either intramuscularly or intranasally, macaques are protected against COVID-19 challenge.

			• A subsequent challenge reveals that macaques vaccinated with a 10-fold lower vaccine dosage (1 × 10(10) viral particles) are also protected.

Genomics

Publication Date	Title / URL	Journal / Article type	Digest
18.08.2020	Retrospective screening of routine respiratory samples revealed undetected community transmission and missed intervention opportunities for SARS-CoV-2 in the United Kingdom	medRxiv (non-peer reviewed) / Article	• Data provides evidence for widespread community circulation of SARS-CoV2 in early Feb 2020 and into Mar that was undetected at the time due to restrictive case definitions informing testing policy. • Genome sequence data showed that many of these early cases were infected with a distinct lineage of the virus. Sequences obtained from the first officially recorded case in Nottinghamshire - a traveller returning from Daegu, South Korea - also clustered with these early UK sequences suggesting acquisition of the virus occurred in the UK and not Daegu. • Analysis of a larger sample of sequences obtained in the Nottinghamshire area revealed multiple viral introductions, mainly in late Feb and through Mar.

Epidemiology and clinical - children and pregnancy

Publication Date	Title / URL	Journal / Article type	Digest
12.08.2020	SARS-CoV-2 infection and transmission in educational settings: cross-sectional analysis of clusters and outbreaks in England	Public Health England / Article	• This study found that SARS-CoV-2 infections and outbreaks were uncommon in educational settings during the first month after the easing of national lockdown in England. • The strong correlation with regional SARS-CoV-2 incidence emphasises the importance of controlling community transmission to protect educational settings. • Additional interventions should focus on reducing transmission in and among staff members.
20.08.2020	COVID-19 Pandemic Preparedness in a United Kingdom Tertiary and Quaternary Children`s Hospital: Tales of the Unexpected	medRxiv (non-peer reviewed) / Article	• Diverse group of 57 SARS-CoV-2 positive paediatric patients treated at a large UK tertiary/quaternary children's hospital. 70% non-Caucasian ethnicity; median age 9.3 years (IQR 5.16-13.48).

			• Four distinct groups identified: paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS) (54%), primary respiratory (18%), incidental (7%), and non-specific febrile illnesses with or without extra-pulmonary organ dysfunction (21%). • Groups presented in distinct chronological blocks - respiratory and other febrile illnesses predominating in first three weeks, followed almost exclusively by PIMS-TS cases. • PIMS-TS patients generally older (median 10.1 [8.7-13.9] vs. 3.4 years [0.1-8.2]), of non-Caucasian ethnicity (n=26 [84%] vs n=5 [50%]). 61% had no known COVID-19 contacts.

Epidemiology and clinical - risk factors

Publication Date	Title / URL	Journal / Article type	Digest
21.08.2020	COVID-19-associated hyperinflammation and escalation of patient care: a retrospective longitudinal cohort study	The Lancet Rheumatology / Article	• A retrospective cohort study of hospitalised adult COVID-19 patients (n=269) explored a specific phenotype of COVID-19-associated hyperinflammation (COV-HI), and its associations with escalation of respiratory support and survival. • A total of 90 (33%) patients met the COV-HI criteria at admission. • Despite having a younger median age and lower median Charlson Comorbidity Index scores, a higher proportion of patients with COV-HI on admission died during follow-up (36 [40%] of 90 patients) compared with the patients without COV-HI on admission (46 [26%] of 179). • Meeting the COV-HI criteria was significantly associated with the risk of next-day escalation of respiratory support or death (hazard ratio 2·24 [95% CI 1·62–2·87]) after adjustment for age, sex, and comorbidity.
18.08.2020	The Prognostic Value of Eosinophil Recovery in COVID-19: A Multicentre, Retrospective Cohort Study on Patients Hospitalised in Spanish Hospitals	medRxiv (non-peer reviewed) / Article	• Multicentre, retrospective, cohort study of 9,644 hospitalised COVID-19 patients to analyse effect of blood cell depletion and blood cell recovery on mortality due to COVID-19. • Increase in eosinophil count on 7th day of hospitalisation associated with better prognosis: lower mortality rates (5.2% vs 22.6% in non-recoverees, OR 0.234 [95% CI, 0.154 to 0.354]); lower complication rates, especially development of acute respiratory

			distress syndrome (8% vs 20.1%, p=0.000) and ICU admission (5.4% vs 10.8%, p=0.000). • Lymphocyte recovery was found to have no effect on prognosis. Treatment with inhaled or systemic glucocorticoids was not found to be a confounding factor. • Eosinophil recovery in COVID-19 patients is a reliable marker of a good prognosis that is independent of prior treatment.
20.08.2020	Clinical Characteristics and Outcomes of COVID-19 Positive Acute Coronary Syndrome Patients; a multisource Electronic Healthcare Records Study from England	medRxiv (non-peer reviewed) / Article	• This multisource national analysis of live data from England was designed to characterise the presenting profile and outcomes of patients hospitalized with acute coronary syndrome (ACS) and COVID-19 infection. • 1st March - 31st May, 517 (4.0%) COVID-19 ACS patients from a total of 12,958 ACS patients. • Compared to non-COVID-19 ACS patients: generally older, BAME ethnicity, more comorbid and unfavourable presenting characteristics. Less likely to receive invasive coronary strategy in the form of coronary angiography (67.7% vs 81.0%), PCI (30.2% vs 53.9%), dual antiplatelet medication 76.3% vs 88.0%), and other important secondary medication. Higher in-hospital (aOR 3.27 95%CI 2.41-4.42) and 30-day mortality (aOR 6.53 95%CI 5.1-8.36) • COVID-19 infection is prevalent but less frequent in ACS hospitalized patients; it's presence is associated with significant mortality hazard.

Epidemiology and clinical – other

Publication Date	Title / URL	Journal / Article type	Digest
19.08.2020	Transmission dynamics of COVID-19 in household and community settings in the United Kingdom	medRxiv (non-peer reviewed) / Article	• Large scale UK household transmission study. A total of 233 households with two or more people were included with a total of 472 contacts. • Overall household secondary attack rate (SAR) was 37% (95% CI 31-43%) with a mean serial interval of 4.67 days, an R0 of 1.85 and a household reproduction number of 2.33. • Authors find lower secondary attack rates in larger households. SARs were highest when the primary case was a child. • Authors estimate a mean incubation period of around 4.5 days.

Date	Title	Source / Type	Summary
			• High rates of household COVID-19 transmission found in the UK emphasising the need for preventative measures in this setting. Careful monitoring of schools reopening is needed to monitor transmission from children.
21.08.2020	[Epidemiology of COVID-19 Outbreak on Cruise Ship Quarantined at Yokohama, Japan, February 2020](#)	Emerg Infect Dis / Research	• Assessed the epidemiology of an outbreak on a cruise ship, Feb 5–24, 2020. • The study population included persons on board on Feb 3 (2,666 passengers, 1,045 crew). Passengers had a mean age of 66.1 years and were 55% female; crew had a mean age of 36.6 years and were 81% male. • Of passengers, 544 (20.4%) were infected, 314 (57.7%) asymptomatic. Attack rates were highest in 4-person cabins (30.0%; n = 18). Of crew, 143 (13.7%) were infected, 64 (44.8%) asymptomatic. Passenger cases peaked Feb 7, and 35 had onset before quarantine. Crew cases peaked on Feb 11 and 13. The median serial interval between cases in the same cabin was 2 days. • This study shows that SARS CoV 2 is infectious in closed settings, that subclinical infection is common, and that close contact is key for transmission.
21.08.2020	[Asymptomatic Transmission of SARS-CoV-2 on Evacuation Flight](#)	Emerg Infect Dis / Dispatch	• A cohort study in a controlled environment measured asymptomatic transmission of COVID-19 on a flight from Italy to South Korea (310 passengers). • Results suggest stringent global regulations are necessary for the prevention of transmission of this virus on aircrafts.
23.08.2020	[Age-and sex-adjustment and the COVID-19 pandemic – transformative example from Italy](#)	International Journal of Epidemiology / Article	• The authors argue that not adjusting for age and sex undermines meaningful comparison between populations, especially when the age structure of populations differs markedly, such as for comparisons between low- and middle-income countries with high-income countries. • To illustrate this principle, data on age and sex distribution of the first 4993 COVID-19 deaths in Italy, recorded until 23 March 2020, are used to calculate age- and sex-standardized figures in each Italian region.
18.08.2020	[OxCOVID19 Database: a multimodal data repository for better understanding the global impact of COVID-19](#)	medRxiv (non-peer reviewed) / Article	• Oxford COVID-19 Database (OxCOVID19 Database) is a comprehensive source of information related to the COVID-19 pandemic. • This relational database contains time-series data on epidemiology, government responses, mobility, weather and more

| | | | across time and space for all countries at the national level, and for more than 50 countries at the regional level.
• The database is a freely available, daily updated tool that provides unified and granular information across geographical regions. |

Infection control

Publication Date	Title / URL	Journal / Article type	Digest
20.08.2020	Preventing within household transmission of COVID-19: Is self-isolation outside the home feasible and acceptable?	medRxiv (non-peer reviewed) / Article	• This research provides evidence that the provision of accommodation to support isolation outside the home is viewed as acceptable, feasible and necessary by many people who are concerned about infection transmission in the home.

Treatment

Publication Date	Title / URL	Journal / Article type	Digest
21.08.2020	Effect of Remdesivir vs Standard Care on Clinical Status at 11 Days in Patients With Moderate COVID-19: A Randomized Clinical Trial	JAMA / Article	• In a randomised, open-label, phase 3 trial that included 584 patients with moderate COVID-19, the day 11 clinical status distribution measured on a 7-point ordinal scale was significantly better for those randomized to a 5-day course of Remdesivir (median length of treatment, 5 days) compared with those randomised to standard care. • The difference for those randomised to a 10-day course (median length of treatment, 6 days) compared with standard care was not significantly different.
17.08.2020	RNA-Based COVID-19 Vaccine BNT162b2 Selected for a Pivotal Efficacy Study	medRxiv (non-peer reviewed) / Article	• Healthy adults 18–55 and 65–85 years randomized in an ongoing, observer–blinded dose–escalation study to receive 2 doses at 21-day intervals of i. placebo or either ii. BNT162b1 (encodes a secreted trimerized SARS–CoV–2 receptor-binding domain) or iii. BNT162b2 (encodes a prefusion stabilized membrane-anchored SARS–CoV–2 full-length spike). • The 2 vaccine candidates elicited similar dose-dependent SARS–CoV–2–neutralizing geometric mean titres (GMTs), comparable to or higher than the GMT of a panel of SARS–CoV–2

convalescent sera. BNT162b2 was associated with less systemic reactogenicity, particularly in older adults.
• Results support selection of the BNT162b2 vaccine candidate for Phase 2/3 large–scale safety and efficacy evaluation, currently underway.

Modelling

Publication Date	Title / URL	Journal / Article type	Digest
21.08.2020	Modeling Contact Tracing Strategies for COVID-19 in the Context of Relaxed Physical Distancing Measures	JAMA Netw Open / Article	• A mathematical model to examine the potential for contact tracing to reduce the spread of COVID-19 in the context of relaxed physical distancing is discussed, using different assumptions for case detection, tracing, and quarantine efficacy. • When community detection of symptomatic index cases and tracing of contacts were less than 50%, simulated contract tracing programs did not reduce Rt by more than 10%. • In scenarios with rates of detection and tracing both greater than 50%, testing asymptomatic contacts increased the program benefit by a median factor of 1.28 (range, 1.04-2.07). • The contact tracing scenario with the greatest benefit reduced Rt by 46%. • The degree to which contract tracing efforts could compensate for relaxed physical distancing and maintain Rt less than 1.0 is analysed.
20.08.2020	Engagement and adherence trade-offs for SARS-CoV-2 contact tracing	medRxiv (non-peer reviewed) / Article	• Authors use an existing branching process model to examine which aspects of contact tracing adherence should be prioritised. An inverse relationship between self-isolation adherence and self-reporting engagement is considered, assuming that increasingly strict self-isolation policies will result in fewer individuals self-reporting to the programme. • Policies that increase the average duration of self-isolation, or that increase the probability that people self-isolate at all, at the expense of reduced self-reporting rate, will not decrease the risk of a large outbreak and may increase the risk, depending on the strength of the trade-off. • These results suggest that policies to increase self-isolation

			adherence should be implemented carefully. Policies that increase self-isolation adherence at the cost of self-reporting rates should be avoided.
09.06.2020	An imperfect tool: COVID-19 'test & trace' success relies on minimising the impact of false negatives and continuation of physical distancing	medRxiv (non-peer reviewed) / Article	• Authors extend an existing branching process contact tracing model, adding diagnostic testing and refining parameter estimates. Poor test sensitivity potentially reduces the efficacy of contact tracing, due to false-negative results impacting quarantine. • They show that, counter-intuitively, faster testing could also reduce operational test sensitivity, exacerbating this effect. • If sensitivity-based risks are mitigated, the authors find that contact tracing can facilitate control, but small changes in the population reproduction number (1.3 to 1.5) could impact contact tracing feasibility.

Overviews, comments and editorials

Publication Date	Title / URL	Journal / Article type
23.08.2020	Statement from the UK Chief Medical Officers on schools and childcare reopening	Department of Health and Social Care / Press release
18.08.2020	Resurgence of covid-19 in Japan	BMJ / Editorial
21.08.2020	Efficacy of Remdesivir in COVID-19	Jama / Editorial
21.08.2020	Apples and oranges: international comparisons of COVID-19 observational studies in ICUs	The Lancet Respiratory Medicine / Comment
21.08.2020	Delving beneath the surface of hyperinflammation in COVID-19	The Lancet Rheumatology / Comment

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