



International EPI Cell Evidence Digest – 10/08/2020

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
- clinical - children and pregnancy
- 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Please note that we are including preprints (**highlighted in red**), which are preliminary reports of work that have NOT been peer-reviewed.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 |
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| 03.08.2020 | Risk of COVID-19 in health-care workers in Denmark: an observational cohort study | Lancet Infect Dis / Article | <ul style="list-style-type: none">• An observational cohort study of 29,295 Danish health-care workers investigated the prevalence of antibodies against COVID-19 and the proportion of seroconverted health-care workers with previous symptoms of COVID-19.• The prevalence of health-care workers with antibodies against COVID-19 was low but higher than in blood donors.• The risk of COVID-19 infection in health-care workers was related to exposure to infected patients.• More than half of seropositive health-care workers reported symptoms attributable to COVID-19. |

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| 03.08.2020 | Repeated leftover serosurvey of SARS-CoV-2 IgG antibodies, Greece, March and April 2020 | Eurosurveillance / Rapid communication | <ul style="list-style-type: none"> • A serosurvey of IgG antibodies against SARS-CoV-2 was performed during Mar and Apr 2020. • Among 6,586 leftover sera, 24 (0.36%) were positive, with higher prevalence in females, older individuals and residents of large urban areas. Seroprevalence was estimated at 0.02% and 0.25%, respectively, in Mar and Apr, infection fatality rate at 2.66% and 0.54%. • The authors findings confirm low COVID-19 incidence in Greece and possibly the effectiveness of early measures. |
| 06.08.2020 | Morphogenesis and cytopathic effect of SARS-CoV-2 infection in human airway epithelial cells | Nat Commun / Article | <ul style="list-style-type: none"> • The authors characterise the replication dynamics, cell tropism and morphogenesis of COVID-19 in organotypic human airway epithelial (HAE) cultures. • COVID-19 replicates efficiently and infects both ciliated and secretory cells in HAE cultures. In comparison, HCoV-NL63 replicates to lower titres and is only detected in ciliated cells. • COVID-19 shows a similar morphogenetic process as other coronaviruses but causes plaque-like cytopathic effects in HAE cultures. • Cell fusion, apoptosis, destruction of epithelium integrity, cilium shrinking and beaded changes are observed in the plaque regions. |
| 06.08.2020 | Single-cell analysis of two severe COVID-19 patients reveals a monocyte-associated and tocilizumab-responding cytokine storm | Nat Commun / Article | <ul style="list-style-type: none"> • The authors employed single-cell analysis of the immune cell composition of two severe-stage COVID-19 patients prior to and following tocilizumab-induced remission, identifying a monocyte subpopulation that contributes to the inflammatory cytokine storms. • Although tocilizumab treatment attenuates the inflammation, immune cells, including plasma B cells and CD8(+) T cells, still exhibit robust humoral and cellular antiviral immune responses. |

Epidemiology and clinical - children and pregnancy

| Publication Date | Title / URL | Journal / Article type | Digest |
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| 10.08.2020 | Objectives for COVID-19 testing in school settings | European Centre for Disease Prevention and Control / Technical report | <ul style="list-style-type: none"> • The aim of this document is to provide an overview of major aspects of testing, contact tracing, contact identification and contact follow-up in school settings within the EU/EEA countries and the UK. |
| 04.08.2020 | Multisystem Inflammatory Syndrome in Children (MIS-C) Associated with SARS-CoV-2: A Systematic Review | J Pediatr / Article | <ul style="list-style-type: none"> • Systematic review by members of the CDC to develop a more comprehensive description of multisystem inflammatory syndrome in children (MIS-C), a novel syndrome linked to COVID-19. Eight studies were identified representing a total of 440 MIS-C cases. |

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| | | | <ul style="list-style-type: none"> • Median age of patients ranged from 7.3 to 10 years, and 59% of patients were male. • The proportion of patients with positive results for COVID-19 RT-PCR tests ranged from 13 to 69% and for serology, from 75 to 100%. • MIS-C patients had high prevalence of gastrointestinal (87%), dermatologic/mucocutaneous (73%), and cardiovascular (71%) symptoms. • Prevalence of cardiovascular, neurologic, and respiratory system involvement significantly differed by study inclusion criteria. • All studies reported elevated C-reactive protein, interleukin-6, and fibrinogen levels for at least 75% of patients in each study. |
| 03.08.2020 | Transmission of SARS-CoV-2 in Australian educational settings: a prospective cohort study | Lancet Child Adolesc Health / Article | <ul style="list-style-type: none"> • A study of COVID-19 transmission among children and staff in schools and early childhood education and care (ECEC) settings in the Australian state of New South Wales (NSW). • 15 schools and ten ECEC settings had children (n=12) or adults (n=15) attend while infectious, with 1448 contacts monitored. Of these, 633 (43.7%) of 1448 had nucleic acid testing, or antibody testing, or both, with 18 secondary cases identified (attack rate 1.2%). • Five secondary cases (three children; two adults) were identified (attack rate 0.5%; 5/914) in three schools. • No secondary transmission occurred in nine of ten ECEC settings among 497 contacts. However, one outbreak in an ECEC setting involved transmission to six adults and seven children (attack rate 35.1%; 13/37). • Suggests COVID-19 transmission rates were low in NSW educational settings during the first COVID-19 epidemic wave, consistent with mild infrequent disease in the 1.8 million child population. |
| 07.08.2020 | Transmission dynamics of SARS-CoV-2 within families with children in Greece: a study of 23 clusters | J Med Virol / Article | <ul style="list-style-type: none"> • A study of the transmission dynamics of COVID-19 within 23 families with children in Greece (66 adults, 43 children). • The median attack rate per cluster was 60% (range: 33.4%-100%). An adult member with COVID-19 was the first case in 21 (91.3%) clusters. There was no evidence of child-to-adult or child-to-child transmission. • Children were more likely to have asymptomatic COVID-19 infection compared to adults (40% versus 10.5%, p-value=0.021). • Adults were more likely to develop a severe clinical course compared to children (8.8% versus 0%, p-value=0.021). • Infected children were significantly more likely to have low viral load while adults were more likely to have moderate viral load (40.7% and 18.5% versus 13.8% and 51.7%, respectively; p-value=0.016). |

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| 07.08.2020 | Role of children in household transmission of COVID-19 | Arch Dis Child / Short Report | <ul style="list-style-type: none"> • All paediatric COVID-19 index cases and their household members reported from 20 Jan to 6 Apr 2020 in South Korea were reviewed. The secondary attack rate (SAR) from child index case to household secondary case was calculated. • 107 paediatric COVID-19 index cases and 248 of their household members were identified. One pair of paediatric index-secondary household case was identified, giving a household SAR of 0.5% (95% CI 0.0% to 2.6%). • The authors concluded that the SAR from children to household members was low in the setting of social distancing, underscoring the importance of rigorous contact tracing and early isolation in limiting transmission within households. |
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Epidemiology and clinical - risk factors

| Publication Date | Title / URL | Journal / Article type | Digest |
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| 10.08.2020 | Rapid Risk Assessment: Coronavirus disease 2019 (COVID-19) in the EU/EEA and the UK – eleventh update: resurgence of cases | European Centre for Disease Prevention and Control / Risk assessment | <ul style="list-style-type: none"> • In this update, they analyse the risk of further escalation of COVID-19 in the countries that have reported a recent increase in COVID-19 cases and the risk of further escalation of COVID-19 across all EU/EEA countries and the UK. |
| 07.08.2020 | COVID-19 Outbreak Among Employees at a Meat Processing Facility - South Dakota, March-April 2020 | MMWR Morb Mortal Wkly Rep / Report | <ul style="list-style-type: none"> • Between 16 Mar and 25 Apr 2020, 25.6% (n=929) of employees at a meat processing facility in South Dakota and 8.7% (n=210) of their contacts were diagnosed with COVID-19; two employees died. • The highest attack rates occurred among employees who worked <6 feet (2 metres) from one another on the production line. • Suggests implementing control measures before, or soon after, COVID-19 introduction into meat processing facilities, especially in areas where employees have prolonged, close contact with others, might substantially reduce the risk for COVID-19 spread within facilities. |
| 04.08.2020 | Increased risk of COVID-19 in haemodialysis healthcare workers in a tertiary centre in the North West of England | J Hosp Infect / Letter | <ul style="list-style-type: none"> • In an audit of occupational exposure in the authors haemodialysis (HD) services at a tertiary centre in the North West of England, they noticed increased risk of COVID-19 in HCWs in direct contact with COVID-19-infected patients. |
| 04.08.2020 | Characteristics and predictors of death among 4,035 consecutively hospitalized patients with COVID-19 in Spain | Clin Microbiol Infect / Article | <ul style="list-style-type: none"> • The authors analyse the characteristics and predictors of death in the first consecutive patients hospitalised with COVID-19 (n=4035; male=61%; median age=70) in 127 Spanish centres up to 17 Mar 2020. • The most common symptoms were a history of fever, cough, malaise, and dyspnoea. • Overall 1,131/4,035 (28%) patients died. Mortality increased with age (85.6% |

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| | | | <p>occurring in older than 65 years).</p> <ul style="list-style-type: none"> • 17 factors were independently associated with increased hazard of death, the strongest among them including advanced age, liver cirrhosis, low age-adjusted oxygen saturation, higher concentrations of C-reactive protein, and lower estimated glomerular filtration rate. |
| 07.08.2020 | Clinical characteristics and predictors of outcomes of hospitalized patients with COVID-19 in a multi-ethnic London NHS Trust: a retrospective cohort study | Clin Infect Dis / Article | <ul style="list-style-type: none"> • The authors evaluate factors associated with mortality in patients (n=614 patients; median age=69 years; male=62%) admitted for COVID-19 in three large London hospitals between 25 Feb and 5 Apr, censored as of 1 May 2020. • A total of 381 (62%) had been discharged alive, 178 (29%) died and 55 (9%) remained hospitalized at censoring. • Severe hypoxemia, leukocytosis, thrombocytopenia, severe renal impairment, and low albumin were associated with death. • Forty percent (244) were from BAME groups, 38% (235) white and for 22% (135) ethnicity was unknown. BAME patients were younger and had fewer comorbidities. • Whilst the unadjusted odds of death did not differ by ethnicity, when adjusting for age, sex and comorbidities, black patients were at higher odds of death compared to white. This association was stronger when further adjusting for admission severity. |
| 04.08.2020 | Age-specific SARS-CoV-2 infection fatality ratio and associated risk factors, Italy, February to April 2020 | Eurosurveillance / Rapid Communication | <ul style="list-style-type: none"> • The authors analysed 5,484 close contacts of COVID-19 cases in Italy, all tested for SARS-CoV-2. • Infection fatality ratio was 0.43% (95% confidence interval (CI): 0.21–0.79) for individuals younger than 70 years and 10.5% (95% CI: 8.0–13.6) for older individuals. • Risk of death after infection was 62% lower (95% CI: 31–80) in clusters identified after 16 March 2020 and 1.8-fold higher for males (95% CI: 1.03–3.16). |
| 07.08.2020 | Case Rates, Treatment Approaches, and Outcomes in Acute Myocardial Infarction During the Coronavirus Disease 2019 Pandemic | JAMA Cardiol / Brief report | <ul style="list-style-type: none"> • Cross-sectional study analysed acute myocardial infarction (AMI) hospitalisations (n=15,244; male = 66%) in 6 US States to define changes in AMI case rates, patient demographics, cardiovascular comorbidities, treatment approaches, and in-hospital outcomes during the pandemic. • Although no statistically significant difference in treatment approaches was found, the risk-adjusted mortality rate among patients with ST-segment elevation myocardial infarction increased substantially. • The findings of this study show that changes in AMI hospitalizations and in-hospital outcomes occurred during the COVID-19 pandemic periods analysed; additional research is warranted to explain the higher mortality rate among patients with ST-segment elevation myocardial infarction. |

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| 07.08.2020 | HIV infection and COVID-19 death: population-based cohort analysis of UK primary care data and linked national death registrations within the OpenSAFELY platform | medRxiv (non-peer reviewed) / Article | <ul style="list-style-type: none"> • A large-scale English population-based study investigated whether HIV infection was associated with risk of COVID-19 death. • There were 14,882 COVID-19 deaths during the study period, with 25 among people with HIV. • People living with HIV had nearly three-fold higher risk of COVID-19 death than those without HIV after adjusting for age and sex (HR=2.90, 95% CI 1.96-4.30). • The association was attenuated but risk remained substantially raised, after adjustment for deprivation and ethnicity (adjusted HR=2.52, 1.70-3.73) and further adjustment for comorbidities (HR=2.30, 1.55-3.41). • There was some evidence that the association was larger among people of black ethnicity (HR = 3.80, 2.15-6.74, compared to 1.64, 0.92-2.90 in non-black individuals, p-interaction=0.045). |
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Epidemiology and clinical – other

| Publication Date | Title / URL | Journal / Article type | Digest |
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| 07.08.2020 | SARS-CoV-2 Transmission and Infection Among Attendees of an Overnight Camp - Georgia, June 2020 | MMWR Morb Mortal Wkly Rep / Report | <ul style="list-style-type: none"> • A total of 597 Georgia residents attended a camp in Georgia. Median camper age was 12 years (range = 6–19 years), and 53% (182 of 346) were female. The median age of staff members and trainees was 17 years (range = 14–59 years), and 59% (148 of 251) were female. • Test results were available for 344 (58%) attendees; among these, 260 (76%) were positive. The overall attack rate was 44% (260 of 597), 51% among those aged 6–10 years, 44% among those aged 11–17 years, and 33% among those aged 18–21 years (Table). Attack rates increased with increasing length of time spent at the camp, with staff members having the highest attack rate (56%). • These findings demonstrate that SARS-CoV-2 spread efficiently in a youth-centric overnight setting, resulting in high attack rates among persons in all age groups, despite efforts by camp officials to implement most recommended strategies to prevent transmission. |
| 06.08.2020 | Epidemiology of measles during the COVID-19 pandemic, a description of the surveillance data, 29 EU/EEA countries and the United Kingdom, January to May 2020 | Eurosurveillance / Rapid communication | <ul style="list-style-type: none"> • The number of measles cases declined in EU/EEA countries and the UK in 2020. • Reported cases to the ECDC decreased from 710 to 54 between Jan and May. Epidemic intelligence screening observed a similar trend. • Under-diagnoses and under-reporting during the COVID-19 pandemic should be ruled out before concluding reduced measles circulation is because of social distancing and any community control measures taken to control COVID-19. |

Infection control

| Publication Date | Title / URL | Journal / Article type | Digest |
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| 06.08.2020 | How to set up government-led national hygiene communication campaigns to combat COVID-19: a strategic blueprint | BMJ Glob Health / Article | <ul style="list-style-type: none"> • Large-scale changes in population behaviour are required to reduce the transmission of COVID-19, however the emergency context is not conducive to the sort of careful communications planning that would normally be required to meet such a task. • In this short guide, the authors argue that a minimum of strategic planning can be undertaken rapidly, and that good use can be made of simple principles of behaviour change, even during pandemics. • The aim is to provide a blueprint that governments and their partners, especially in low-income settings, can follow to design, coordinate and resource national communications efforts to combat the COVID-19 pandemic immediately and for the longer term. |
| 07.08.2020 | Characteristics and Outcomes of Contacts of COVID-19 Patients Monitored Using an Automated Symptom Monitoring Tool - Maine, May-June 2020 | MMWR Morb Mortal Wkly Rep / Report | <ul style="list-style-type: none"> • Using automated symptom monitoring as a part of the US State of Maine's contact tracing program was well received, with the majority of the 1,622 monitored contacts (96.4%) agreeing to automated symptom monitoring. • Automated symptom monitoring promptly identified COVID-19 diagnoses among monitored contacts. A total of 190 contacts (11.7%) developed COVID-19. • Suggests automated tools, available in multiple languages and formats, might improve contact tracing programs and reduce resource needs, including staffing. |
| 04.08.2020 | Bioaerosol Sampling of a Ventilated Patient with COVID-19 | Am J Infect Control / Brief Report | <ul style="list-style-type: none"> • This study sought to determine whether SARS-CoV-2 was present in the patient room of a COVID-19 positive patient on a ventilator. • Bioaerosol samples were collected in an airborne infection isolation room, bathroom and anteroom of a ventilated patient with COVID-19. 28 samples were negative for SARS-CoV-2 nucleic acid, possibly due to the patient being on a closed-circuit ventilator or the efficiency of the air exchanges in the room. • This study found that the level of SARS-CoV-2 in the air of the patient room was lower than a detectable level. |
| 04.08.2020 | Is there an adequate alternative for commercially manufactured face masks? A comparison of various materials and forms | J Hosp Infect / Article | <ul style="list-style-type: none"> • Dutch study analysed effectiveness of combinations of readily available materials and models for making a face mask, and compared with N95/FFP2/KN95 masks that entered the Netherlands in April-May 2020. • Suggests it would be possible to reduce the reproduction rate of COVID-19 from 2.4 to below one if 39% of the population wear a mask made from ePM₁, 85% commercially manufactured filter fabric and in a duckbill form. This mask performs better than 80% of imported N95/FFP2/KN95 masks and provides a better fit than a surgical mask. |

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| | | | <ul style="list-style-type: none"> • Two layers of quilt fabric with a household paper towel as filter is also a viable choice for protecting the user and the environment. |
| 04.08.2020 | Face masks prevent transmission of respiratory diseases: a meta-analysis of randomized controlled trials | medRxiv (non-peer reviewed) / Article | <ul style="list-style-type: none"> • Meta-analysis of RCTs of non-surgical face masks in preventing viral respiratory infections in non-hospital and non-household settings at cumulative and maximum follow-up as primary endpoints, yielding five studies published before 29 May 2020. • Face masks decreased infections across all studies at maximum follow-up ($p=0.0318$, $RR=0.608$ [0.387 - 0.956]), and particularly in studies without non-compliance bias. • Significant between-study heterogeneity in studies with bias was found ($I^2=71.2\%$, $p=0.0077$). Adjusted meta-regression was used to account for heterogeneity. • Results support a significant protective effect of masking ($p=0.0006$, $\beta=0.0214$, $SE=0.0062$). No severe adverse effects were detected. |

Treatment

| Publication Date | Title / URL | Journal / Article type | Digest |
|------------------|--|----------------------------------|--|
| 07.08.2020 | Antibiotic use in patients with COVID-19: a 'snapshot' Infectious Diseases International Research Initiative (ID-IRI) survey | J Antimicrob Chemother / Article | <ul style="list-style-type: none"> • An investigation of antibiotic prescribing practices in patients with COVID-19 using a survey of 166 hospital staff from 23 countries and 82 different hospitals. • The study revealed widespread broad-spectrum antibiotic use in patients with COVID-19. Implementation of antimicrobial stewardship principles is warranted to mitigate the negative consequences of antibiotic therapy. |

Modelling

| Publication Date | Title / URL | Journal / Article type | Digest |
|------------------|---|------------------------|--|
| 07.08.2020 | Using a real-world network to model localized COVID-19 control strategies | Nat Med / Letter | <ul style="list-style-type: none"> • The authors simulated control strategies for COVID-19 transmission in a real-world social network generated from high-resolution GPS data gathered in the course of a citizen-science experiment. • Tracing contacts of contacts reduced the size of simulated outbreaks more than tracing of only contacts, but this strategy also resulted in almost half of the local population being quarantined at a single point in time. • Testing and releasing non-infectious individuals from quarantine led to increases |

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| | | | <p>in outbreak size, suggesting contact tracing and quarantine might be most effective as a 'local lockdown' strategy when contact rates are high.</p> <ul style="list-style-type: none"> • Suggests combining physical distancing with contact tracing could enable epidemic control while reducing the number of quarantined individuals. |
| 03.08.2020 | Determining the optimal strategy for reopening schools, the impact of test and trace interventions, and the risk of occurrence of a second COVID-19 epidemic wave in the UK: a modelling study | Lancet Child Adolesc Health / Article | <ul style="list-style-type: none"> • The authors present a modelling study using Covasim, a stochastic individual-based model for transmission of COVID-19, calibrated to the UK epidemic. • Assuming 68% of contacts could be traced, they estimate 75% of individuals with symptomatic infection would need to be tested and positive cases isolated if schools return full-time in September, or 65% if a part-time rota system were used. If only 40% of contacts could be traced, these figures would increase to 87% and 75%, respectively. • Without these levels of testing and contact tracing, reopening of schools together with gradual relaxing of lockdown measures is likely to induce a second wave peaking in Dec2020 if schools open full-time in September, and in February 2021, if a part-time rota system were adopted. |
| 07.08.2020 | Wrong person, place and time: viral load and contact network structure predict SARS-CoV-2 transmission and super-spreading events | medRxiv (non-peer reviewed) / Article | <ul style="list-style-type: none"> • Authors designed mathematical models of COVID-19 and influenza linking observed viral shedding patterns with key epidemiologic features of each virus, including distribution of secondary cases attributed to each infected person (individual R0) and duration between symptom onset in the transmitter and secondarily infected person (serial interval). • Suggests people with COVID-19 or influenza are usually contagious for fewer than two days congruent with peak viral load several days after infection, and transmission is unlikely below a certain viral load. • COVID-19 super-spreader events with over 10 secondary infections occur when infected person briefly sheds at a very high viral load and has a high concurrent number of exposed contacts. |

Overviews, comments and editorials

| Publication Date | Title / URL | Journal / Article type |
|------------------|--|-------------------------------------|
| 07.08.2020 | Notes from the Field: Characteristics of Meat Processing Facility Workers with Confirmed SARS-CoV-2 Infection - Nebraska, April-May 2020 | MMWR Morb Mortal Wkly Rep / Comment |
| 07.08.2020 | Digital technologies in the public-health response to COVID-19 | Nat Med / Article |
| 07.08.2020 | Covid-19: Was the decision to delay the UK's lockdown over fears of "behavioural fatigue" based on evidence? | BMJ / News |

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| 05.08.2020 | Covid-19: Where are we on immunity and vaccines? | Bmj / News |
| 04.08.2020 | COVID-19 and preschool wheeze care: lessons learned | Lancet Respir Med / Spotlight |
| 07.08.2020 | Obesity and COVID-19: Blame isn't a strategy | The Lancet Diabetes & Endocrinology / Editorial |
| 07.08.2020 | Successful Elimination of Covid-19 Transmission in New Zealand | New England Journal of Medicine / Correspondence |

Produced by the PHE COVID-19 Literature Digest Team

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