



International EPI Cell Daily Evidence Digest – 19/06/2020

This Daily 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
- Guidance, consensus statements and hospital resources (no digest)
- 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Please note that we are including preprints (**highlighted in red**), which are preliminary reports of work that have NOT been peer-reviewed.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 |
|------------------|--|--|--|
| 18.06.2020 | Prevalence of SARS-CoV-2 specific neutralising antibodies in blood donors from the Lodi Red Zone in Lombardy, Italy, as at 06 April 2020 | Eurosurveillance / Rapid communication | <ul style="list-style-type: none">• Evaluated SARS-CoV-2 RNA and neutralising antibodies in blood donors (BD) residing in the Lodi Red Zone, Italy.• Of 390 BDs recruited after 20 Feb 2020 – when the first COVID-19 case in Lombardy was identified, 91 (23%) aged 19–70 years were antibody positive.• Viral RNA was detected in an additional 17 (4.3%) BDs, yielding ca |

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| | | | 28% (108/390) with evidence of virus exposure. <ul style="list-style-type: none"> • Five stored samples collected as early as 12 Feb were seropositive. |
| 16.06.2020 | Detection of antibodies to the SARS-CoV-2 spike glycoprotein in both serum and saliva enhances detection of infection | medRxiv (non-peer reviewed) / Article | <ul style="list-style-type: none"> • UK study to test whether suboptimal sensitivity of antibody assays and the compartmentalization of the antibody response may contribute to difficulties in detection of antibody during and after SARS-CoV-2 infection in subjects with mild disease and asymptomatic infections. • Anti-spike, but not nucleocapsid, IgG, IgA and IgM antibody responses were readily detectable in saliva from non-hospitalized symptomatic and asymptomatic individuals. Antibody responses in saliva and serum were largely independent of each other and symptom reporting. |
| 15.06.2020 | A thermostable, closed, SARS-CoV-2 spike protein trimer | bioRxiv (non-peer reviewed) / Article | <ul style="list-style-type: none"> • The authors have designed mutations in the spike (S) protein of SARS-CoV-2 which allow production of thermostable, crosslinked, S protein trimers that are trapped in the closed, pre-fusion, state. • They have determined the structures of crosslinked and non-crosslinked proteins, identifying two distinct closed conformations of the S trimer. • They demonstrate that the designed, thermostable, closed S trimer can be used in serological assays. This protein has potential applications as a reagent for serology, virology and as an immunogen. |

Diagnostics

| Publication Date | Title/URL | Journal/ Article type | Digest |
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| 18.06.2020 | Multicentre comparison of quantitative PCR-based assays to detect SARS-CoV-2, Germany, March 2020 | Eurosurveillance / Rapid communication | <ul style="list-style-type: none"> • Compared 11 different RT-PCR test systems used in seven diagnostic laboratories in Germany in Mar 2020. • While most assays performed well, they identified detection problems in a commonly used assay that may have resulted in false-negative test results during the first weeks of the pandemic. |
| 16.06.2020 | Combined point of care nucleic acid and antibody testing for SARS-CoV-2: a prospective cohort study in suspected moderate to severe COVID-19 disease | medRxiv (non-peer reviewed) / Article | <ul style="list-style-type: none"> • To assess the diagnostic accuracy of combined rapid antibody point of care (POC) and nucleic acid assays for suspected COVID-19 disease in the emergency department, 45 participants had specimens tested for nucleic acid in nose/throat swabs as well as stored sera for antibodies. • The overall sensitivity of rapid NAAT diagnosis was 79.2% (95CI 57.8-92.9%) and 50.0% (11.8-88.2) at days 8-28. |

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| | | | <ul style="list-style-type: none"> • Sensitivity and specificity of the combined rapid POC diagnostic tests reached 100% (95CI 85.8-100) and 94.7% (95CI 74.0-99.0) overall. Dual point of care SARS-CoV-2 testing can significantly improve diagnostic sensitivity, whilst maintaining high specificity. |
| 12.06.2020 | Overhauling a faulty control in the CDC-recommended SARS-CoV-2 RT-PCR test panel | bioRxiv (non-peer reviewed) / Article | <ul style="list-style-type: none"> • The authors report that the CDC-recommended h-RP primer/probe set has a faulty design, because both PCR primers are located in the same exon, which allows for unwanted PCR-amplification of background genomic DNA (gDNA). • Presence of gDNA in samples resulted in false-positive signals for the h-RP test control. This could lead to false-negative test outcomes, since the CDC interpretation of an absent SARS-CoV-2 rRT-PCR signal plus a positive h-RP rRT-PCR signal is interpreted as '2019-nCoV not detected', whereas a false-positive h-RP rRT-PCR signal resulting from amplification of gDNA should be interpreted as 'Invalid Result' and the procedure should be repeated. • Replacement of the CDC-recommended PCR reverse primer with their selected exon-exon junction reverse primer corrected the problem of false-positive results with this important SARS-CoV-2 RT-PCR test control and thus eliminated the problem of potential false-negative COVID-19 diagnoses. |

Genomics

| Publication Date | Title/URL | Journal/ Article type | Digest |
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| 17.06.2020 | Genomewide Association Study of Severe Covid-19 with Respiratory Failure | NEJM / Article | <ul style="list-style-type: none"> • Conducted a genomewide association study involving 1980 patients with Covid-19 and severe disease (defined as respiratory failure) at seven hospitals in the Italian and Spanish epicentres of the SARS-CoV-2 pandemic in Europe. • Identified a 3p21.31 gene cluster as a genetic susceptibility locus in patients with Covid-19 with respiratory failure and confirmed a potential involvement of the ABO blood-group system. |
| 17.06.2020 | Deep mutational scanning of SARS-CoV-2 receptor binding domain reveals constraints on folding and ACE2 binding | bioRxiv (non-peer reviewed) / Article | <ul style="list-style-type: none"> • The authors experimentally measure how all amino-acid mutations to the receptor binding domain (RBD) of the SARS-CoV-2 spike glycoprotein affect expression of folded protein and its affinity for ACE2. • Most mutations are deleterious for RBD expression and ACE2 |

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| | | | <p>binding, but a substantial number of mutations are well tolerated or even enhance ACE2 binding, including at ACE2 interface residues that vary across SARS-related coronaviruses.</p> <ul style="list-style-type: none"> • However, they find no evidence that these ACE2-affinity enhancing mutations have been selected in current SARS-CoV-2 pandemic isolates. |
| 16.06.2020 | Genome-wide CRISPR screen reveals host genes that regulate SARS-CoV-2 infection | bioRxiv (non-peer reviewed) / Article | <ul style="list-style-type: none"> • The authors performed a genome-wide CRISPR screen with SARS-CoV-2 to inform our understanding of COVID-19 pathogenesis. • Identified known SARS-CoV-2 host factors including the receptor ACE2 and protease Cathepsin L. • They additionally discovered novel pro-viral genes and pathways including the SWI/SNF chromatin remodelling complex and key components of the TGF-β signalling pathway. Small molecule inhibitors of these pathways prevented SARS-CoV-2-induced cell death. • They revealed that the alarmin HMGB1 is critical for SARS-CoV-2 replication. In contrast, loss of the histone H3.3 chaperone complex sensitized cells to virus-induced death. |

Epidemiology and clinical - risk factors

| Publication Date | Title/URL | Journal/ Article type | Digest |
|------------------|---|------------------------------------|--|
| 17.06.2020 | Ethnicity and Outcomes from COVID-19: The ISARIC CCP-UK Prospective Observational Cohort Study of Hospitalised Patients | SSRN (not peer-reviewed) / Article | <ul style="list-style-type: none"> • Investigated ethnic inequalities in critical care admission patterns, the need for invasive mechanical ventilation (IMV), and in-hospital mortality, among hospitalised patients with COVID-19. • Of 34,986 patients enrolled (from 260 hospitals across the UK), 30,693 (88%) had ethnicity recorded: South Asian (1,388, 5%), East Asian (266, 1%), Black (1,094, 4%), Other Ethnic Minority (2,398, 8%) (collectively Ethnic Minorities), and White groups (25,547, 83%). • Ethnic Minorities were younger and more likely to have diabetes (type 1/type 2) but had fewer other comorbidities such as chronic heart disease or dementia than the White group. • Ethnic Minorities in hospital with COVID-19 were more likely to be admitted to critical care and receive IMV than Whites, despite similar disease severity on admission, similar duration of symptoms, and being younger with fewer comorbidities. South Asians are at greater risk of |

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| | | | dying, due at least in part to a higher prevalence of pre-existing diabetes. |
| 15.06.2020 | Global, regional, and national estimates of the population at increased risk of severe COVID-19 due to underlying health conditions in 2020: a modelling study | The Lancet Global Health / Article | <ul style="list-style-type: none"> • Estimated the number of individuals at increased risk of severe disease (defined as those with at least one condition listed as “at increased risk of severe COVID-19” in current guidelines) by age , sex, and country for 188 countries using prevalence data from the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2017 and UN population estimates for 2020. • About one in five individuals worldwide could be at increased risk of severe COVID-19, should they become infected, due to underlying health conditions, but this risk varies considerably by age. Estimates are uncertain, and focus on underlying conditions rather than other risk factors such as ethnicity, socioeconomic deprivation, and obesity, but provide a starting point for considering the number of individuals that might need to be shielded or vaccinated as the global pandemic unfolds. |
| 18.06.2020 | Association between high serum total cortisol concentrations and mortality from COVID-19 | The Lancet Diabetes & Endocrinology / Correspondence | <ul style="list-style-type: none"> • Patients admitted to three large teaching hospitals (Charing Cross, Hammersmith, and St Mary’s) in London, UK, with a clinical suspicion of COVID-19 were included in this series. • Analyses showed for the first time that patients with COVID-19 mount a marked and appropriate acute cortisol stress response and that this response is significantly higher in this patient cohort than in individuals without COVID-19. • Found that high cortisol concentrations were associated with increased mortality and a reduced median survival, probably because this is a marker of the severity of illness. |
| 18.06.2020 | COVID-19 in patients with rheumatic diseases in northern Italy: a single-centre observational and case-control study | The Lancet Rheumatology / Article | <ul style="list-style-type: none"> • Aimed to analyse the course of SARS-CoV-2 infection in patients with rheumatic and musculoskeletal diseases living in a district of Lombardy with a high prevalence of COVID-19. • Of 1525 patients, 117 (8%) presented with symptoms that were compatible with COVID-19. 65 patients had a swab confirmation of SARS-CoV-2 infection, whereas 52 presented with a spectrum of symptoms indicative of COVID-19 but were not swab tested. • A poor outcome from COVID-19 seems to be associated with older age and the presence of comorbidities rather than the type of rheumatic disease or the degree of pharmacological immunosuppression. |

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| 18.06.2020 | Prognosis of patients with sickle cell disease and COVID-19: a French experience | The Lancet Haematology / Comment | <ul style="list-style-type: none"> • 83 inpatients with sickle cell disease infected by SARS-CoV-2 from 24 centres were enrolled. • Results suggest that COVID-19, even if potentially severe, does not seem to carry an increased risk of morbidity or mortality in patients with sickle cell disease, as most patients worldwide have the SS/Sβ⁰ genotype and are younger than 45 years. • Findings also suggest that vaso-occlusive crisis can complicate COVID-19 infection, occurring in around half of inpatients with sickle cell disease. |
| 16.06.2020 | Incidence of acute kidney injury in COVID-19 infection: a systematic review and meta-analysis | Crit Care / Research letter | <ul style="list-style-type: none"> • Performed a systematic review and meta-analysis of published articles to quantify the incidence of acute kidney injury (AKI) in COVID-19 patients. • Final analysis included 20 articles comprising 6945 patients from China, Italy, the UK, and the USA. • Several mechanisms are possible for AKI in COVID-19 patients, including multi-organ dysfunction syndrome, SARS-CoV-2 direct kidney infection, AKI following ARDS, infection-related generalized mitochondrial failure, and cytokine storm syndrome. • Early recognition and treatment of AKI may limit associated complications such as long-term chronic kidney disease or end-stage kidney disease. |
| 17.06.2020 | Associations of Global Country Profiles and Modifiable Risk Factors with COVID-19 Cases and Deaths | medRxiv (non-peer reviewed) / Article | <ul style="list-style-type: none"> • Oxford University-led analysis of global data to determine associations of modifiable risk factors with total cases and excess deaths. Wealthier countries had the greatest caseload. • Obesity was the primary modifiable risk factor for infection and greater age, male sex, physical inactivity and low salt consumption were associated with excess deaths. • Obesity was less influential on mortality than physical inactivity. Globally, obesity confers vulnerability to SARS-CoV-2 infection and physical inactivity likely explains the greater mortality in the obese. • High salt consumption may induce reductions in tissue ACE2 expression and subsequently reduce mortality rates. |
| 16.06.2020 | COVID-19 outcomes, risk factors and associations by race: a comprehensive analysis using electronic health records data in Michigan Medicine | medRxiv (non-peer reviewed) / Article | <ul style="list-style-type: none"> • Retrospective cohort study with comparative control groups, to systematically determine patient characteristics associated with racial/ethnic disparities in COVID-19 outcomes. • Of 5,698 patients, (median age, 47 years; 38% male; mean BMI, 30.1), the majority were non-Hispanic Whites (NHW, 59.2%) and non-Hispanic Black/African-Americans (NHAA, 17.2%). |

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| | | <ul style="list-style-type: none"> • Adjusting for age, sex, and SES, NHAA were 1.66 times more likely to be hospitalized, 1.52 times more likely to enter ICU. • In addition to older age, male sex and obesity, pre-existing type II diabetes/kidney diseases and living in high population density areas were associated with high risk for COVID-19 susceptibility and poor prognosis. Association of risk factors with COVID-19 outcomes differed by race. NHAA patients were disproportionately affected by obesity and kidney disease. |
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Epidemiology and clinical – other

| Publication Date | Title/URL | Journal/ Article type | Digest |
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| 18.06.2020 | ISS study on waste water, in Milan and Turin Sars-Cov-2 already present in December - press release [Original title: Studio ISS su acque di scarico, a Milano e Torino Sars-Cov-2 presente già a dicembre] | Istituto Superiore di Sanità / Higher Institute of Health, Italy / Press release | <ul style="list-style-type: none"> • Press release in Italian, announcing that traces of the SARS-CoV-2 virus already existed in the waste waters of Milan and Turin in Dec 2019. • The study examined 40 wastewater samples collected from Oct 2019 to Feb 2020, and 24 control samples for which the sampling date (Sept 2018 - June 2019). • The results, confirmed in two different laboratories with two different methods, showed the presence of SARS-Cov-2 RNA in the samples taken in Milan and Turin on 12/18/2019 and in Bologna on 01/29/2020. In the same cities, positive samples were also found in the following months of Jan and Feb 2020, while samples from Oct and Nov 2019, as well as all the control samples, gave negative results. • These results are consistent with other results obtained from the retrospective analysis on samples of patients hospitalized in France, which identified a SARS-CoV-2 positive in a respiratory sample , therefore clinical, dating back to the end of Dec 2019, and to a recent Spanish work that found SARS-CoV-2 RNA in waste water samples collected in mid-January in Barcelona, about 40 days before the notification of the first autochthonous case. |
| 18.06.2020 | Report 28 - Excess non-COVID-19 deaths in England and Wales between 29th February and 5th June 2020 | Imperial College / Report | <ul style="list-style-type: none"> • Estimates the excess deaths that were not recorded as associated with COVID-19 in the death certificate (excess non-COVID-19 deaths) as the deaths for which COVID-19 was not reported as the cause, compared to those we would have expected to occur had the pandemic not happened. |

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| | | | <ul style="list-style-type: none"> • There were 8,983 total excess non-COVID-19 deaths in England. For every 100 COVID-19 deaths during the period from 29th Feb to 5th June 2020 there were 19 cumulative excess non-COVID-19 deaths. • Excess non-COVID-19 deaths could be due to non-reporting of COVID-19 on the death certificate or an increase in mortality for non-COVID-19 conditions. • Severely ill patients may have been unable to access life-saving emergency treatment because of constraints in healthcare provision, or because they avoided seeking care due to concern over hospital-acquired infection, or to avoid burdening healthcare providers. |
| 18.06.2020 | Negative SARS-CoV-2 PCR in patients with chilblain-like lesions | The Lancet Infectious Diseases / Correspondence | <ul style="list-style-type: none"> • Prospective cohort study in patients with cutaneous manifestations who were referred to Centre Hospitalier Universitaire de Nice, France, between April 9 and 17, 2020, with suspected SARS-CoV-2 infection. 40 consecutive patients (21 [53%] female) with chilblain-like lesions were included. • Results suggest that chilblain-like lesions are associated with mild or asymptomatic SARS-CoV-2 infection. • Physicians should be aware that most patients presenting with chilblain-like lesions will probably have negative PCR results at the time of presentation. |
| 16.06.2020 | Early postmortem brain MRI findings in COVID-19 non-survivors | Neurology / Article | <ul style="list-style-type: none"> • This study investigates the occurrence of structural brain abnormalities in non-survivors of COVID-19 in a virtopsy framework. • Post-mortem brain MRI demonstrates haemorrhagic and PRES-related brain lesions in non-survivors of COVID-19. • SARS-CoV-2-related olfactory impairment seems to be limited to olfactory bulbs. • Brainstem MRI findings do not support a brain-related contribution to respiratory distress in COVID-19. |
| 16.06.2020 | Prevalence of COVID-19 Infection and Outcomes Among Symptomatic Healthcare Workers in Seattle, Washington | Clin Infect Dis / Article | <ul style="list-style-type: none"> • Established two high-throughput employee testing centres in Seattle, Washington with drive-through and walk-through options for symptomatic employees in the University of Washington Medicine system and its affiliated organizations. • Between Mar 12 and Apr 23, a total of 3,477 symptomatic employees were tested for COVID-19 at two employee testing centres; 185 (5.3%) employees tested positive for COVID-19. The prevalence of SARS-CoV-2 was similar when comparing frontline HCWs (5.2%) to non-frontline staff (5.5%). Among 174 positive employees reached for follow-up at |

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| | | | least 14 days after diagnosis, 6 reported COVID-related hospitalization; all recovered. |
| 17.06.2020 | Introduction to and spread of COVID-19 in care homes in Norfolk, UK | medRxiv (non-peer reviewed) / Article | <ul style="list-style-type: none"> • Secondary analysis of a dataset about 248 care homes in Norfolk, eastern England, undertaking two stage modelling, first for any detection of COVID-19 in the homes, and a second model to relate any increases in case counts after introduction to staffing or PPE levels. • The counts of non-care workers had strongest relationships (and only link significant at $p < 0.05$) to any introduction of SARS-CoV-2 to the homes. • After a home had at least one detected case, higher staff levels and more severe PPE shortages were most linked to higher case counts ($p < 0.05$) during the monitoring period. • Better managing aspects of staff interaction with residents and some working practices should help reduce ingress to and spread of COVID-19 within residential homes for the elderly. |
| 15.06.2020 | Delirium is a presenting symptom of COVID-19 in frail, older adults: a cohort study of 322 hospitalised and 535 community-based older adults | medRxiv (non-peer reviewed) / Article | <ul style="list-style-type: none"> • Observational cohort study (London) to assess how frailty affects presenting COVID-19 symptoms in older adults. • Findings in the hospital cohort (n=322) showed significantly higher prevalence of delirium in the frail sample, with no difference in fever or cough. • Findings in the community-based cohort (n=535) showed significantly higher prevalence of probable delirium in frailer, older adults, and fatigue and shortness of breath. |

Infection control

| Publication Date | Title/URL | Journal/ Article type | Digest |
|------------------|---|---------------------------------------|--|
| 16.06.2020 | Towards intervention development to increase the uptake of COVID-19 vaccination among those at high risk: outlining evidence-based and theoretically informed future intervention content | medRxiv (non-peer reviewed) / Article | <ul style="list-style-type: none"> • Cross-sectional survey of 527 high-risk individuals (older adults aged 65+ and patients with chronic respiratory disease) to understand the barriers and facilitators to receiving a future COVID-19 vaccine. • 86% of respondents want to receive a COVID-19 vaccine. This was positively correlated with the perception that COVID-19 will continue for a long time, and negatively associated with the perception that the media has over-exaggerated the risk. • The majority of barriers and facilitators could be mapped onto the beliefs about consequences Theoretical Domains Framework (TDF) |

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| | | | domain, with themes relating to personal health, health consequences to others, concerns of vaccine safety, and severity of COVID-19. |
| 15.06.2020 | Transmission of SARS-CoV-2 by inhalation of respiratory aerosol in the Skagit Valley Chorale superspreading event | medRxiv (non-peer reviewed) / Article | <ul style="list-style-type: none"> • Using data from the Skagit Valley Chorale rehearsal COVID-19 outbreak, and based on a conditional assumption that transmission during this outbreak was by inhalation of respiratory aerosol, the authors infer the emission rate of airborne infectious quanta from the primary source. • They also explore how the risk of infection would vary with several influential factors: the rates of removal of respiratory aerosol by ventilation; deposition onto surfaces; and viral decay. • The results indicate an emission rate of the order of a thousand quanta per hour (mean [interquartile range] for this event = 970 [680-1190] quanta per hour) and demonstrate that the risk of infection is modulated by ventilation conditions, occupant density, and duration of shared presence with an infectious individual. |

Treatment

| Publication Date | Title/URL | Journal/ Article type | Digest |
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| 16.06.2020 | GM-CSF blockade with mavrilimumab in severe COVID-19 pneumonia and systemic hyperinflammation: a single-centre, prospective cohort study | The Lancet Rheumatology / Article | <ul style="list-style-type: none"> • Aimed to examine whether mavrilimumab, an anti-granulocyte-macrophage colony-stimulating factor receptor-α monoclonal antibody, added to standard management, improves clinical outcomes in patients with COVID-19 pneumonia and systemic hyperinflammation. • Single-centre prospective cohort study. Between Mar 17 and Apr 15, 2020, 13 non-mechanically ventilated patients (median age 57 years [IQR 52–58], 12 [92%] men) received mavrilimumab and 26 patients (median age 60 [IQR 53–67], 17 [65%] men) in the control group received standard care. • Mavrilimumab treatment was associated with improved clinical outcomes compared with standard care in non-mechanically ventilated patients with severe COVID-19 pneumonia and systemic hyperinflammation. Treatment was well tolerated. Confirmation of efficacy requires controlled testing. |

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| 16.06.2020 | Invasive mechanical ventilation in COVID-19 patient management: the experience with 469 patients in Wuhan | Crit Care / Research letter | <ul style="list-style-type: none"> • Collected and analysed the data of 469 ICU COVID-19 patients who were hospitalized from Feb 2020 to the end of Mar in 13 ICUs in Wuhan. • Data suggests that early intubation may not help patients but instead, make things head towards the wrong direction. We should try to avoid IV and utilize NIV at the early stage of respiratory failure until IV is inevitable. |
| 17.06.2020 | GLUCOCOVID: A controlled trial of methylprednisolone in adults hospitalized with COVID-19 pneumonia | medRxiv (non-peer reviewed) / Article | <ul style="list-style-type: none"> • Multicentric, partially randomized, preference, open-label trial on 85 patients, to determine whether a 6-day course of intravenous methylprednisolone (MP) improves outcome in patients with SARS CoV-2 infection at risk of developing ARDS. • The use of MP was associated with a reduced risk of the composite endpoint (death, admission to the intensive care unit (ICU) or requirement of non-invasive ventilation (NIV)) in the intention-to-treat, age-stratified analysis (combined risk ratio -RR- 0.55 [95% CI 0.33-0.91]; p=0.024). • The decrease in C-reactive protein levels was more pronounced in the MP group (p=0.0003). Hyperglycemia was more frequent in the MP group. • A short course of MP had a beneficial effect on the clinical outcome of severe COVID-19 pneumonia, decreasing the risk of the composite end point of admission to ICU, NIV or death. |

Modelling

| Publication Date | Title/URL | Journal/ Article type | Digest |
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| 16.06.2020 | Effectiveness of isolation, testing, contact tracing, and physical distancing on reducing transmission of SARS-CoV-2 in different settings: a mathematical modelling study | The Lancet Infectious Diseases / Article | <ul style="list-style-type: none"> • Aimed to estimate the reduction in transmission under different control measures across settings and how many contacts would be quarantined per day in different strategies for a given level of symptomatic case incidence. • Used a model of individual-level transmission stratified by setting (household, work, school, or other) based on BBC Pandemic data from 40 162 UK participants. • Analysis estimated that a high proportion of cases would need to self-isolate and a high proportion of their contacts to be successfully traced to ensure an effective reproduction number lower than 1 in the |

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| | | | absence of other measures. If combined with moderate physical distancing measures, self-isolation and contact tracing would be more likely to achieve control of SARS-CoV-2 transmission. |
| 16.06.2020 | Age-dependent effects in the transmission and control of COVID-19 epidemics | Nat Med / Letter | <ul style="list-style-type: none"> • The COVID-19 pandemic has shown a markedly low proportion of cases among children. Age disparities in observed cases could be explained by children having lower susceptibility to infection, lower propensity to show clinical symptoms or both. • Evaluated these possibilities by fitting an age-structured mathematical model to epidemic data from China, Italy, Japan, Singapore, Canada and South Korea. • Estimate that susceptibility to infection in individuals under 20 years of age is approximately half that of adults aged over 20 years, and that clinical symptoms manifest in 21% (95% credible interval: 12-31%) of infections in 10- to 19-year-olds, rising to 69% (57-82%) of infections in people aged over 70 years. • Accordingly, they find that interventions aimed at children might have a relatively small impact on reducing SARS-CoV-2 transmission, particularly if the transmissibility of subclinical infections is low. |
| 17.06.2020 | Household secondary attack rate of COVID-19 and associated determinants in Guangzhou, China: a retrospective cohort study | The Lancet Infectious Diseases / Article | <ul style="list-style-type: none"> • Used a comprehensive contact tracing dataset from the Guangzhou CDC to estimate the secondary attack rate of COVID-19 among household and non-household contacts, using a statistical transmission model. • Between Jan 7, 2020, and Feb 18, 2020, they traced 195 unrelated close contact groups (215 primary cases, 134 secondary or tertiary cases, and 1964 uninfected close contacts). • Concluded that SARS-CoV-2 is more transmissible in households than SARS-CoV and MERS coronavirus. Older individuals (aged ≥ 60 years) are the most susceptible to household transmission of SARS-CoV-2. In addition to case finding and isolation, timely tracing and quarantine of close contacts should be implemented to prevent onward transmission during the viral incubation period. |

Guidelines, consensus statements

| Publication Date | Title/URL | Journal/ Article type |
|------------------|---|---|
| 17.06.2020 | Monitoring and evaluation framework for COVID-19 response activities in the EU/EEA and the UK | European Centre for Disease Control and Prevention / Technical report |

Overviews, comments and editorials

| Publication Date | Title/URL | Journal/ Article type |
|------------------|---|---|
| 16.06.2020 | Understanding SARS-CoV-2-related multisystem inflammatory syndrome in children | Nat Rev Immunol / Comment |
| 18.06.2020 | Transmission Dynamics of COVID-19 | Oxford COVID-19 Evidence Service / Evidence synthesis |
| 16.06.2020 | Delivering evidence-based critical care for mechanically ventilated patients with COVID-19 | The Lancet Respiratory Medicine / Comment |
| 18.06.2020 | Host range of SARS-CoV-2 and implications for public health | The Lancet Microbe / Comment |
| 16.06.2020 | Case isolation, contact tracing, and physical distancing are pillars of COVID-19 pandemic control, not optional choices | The Lancet Infectious Diseases / Comment |

Produced by the PHE COVID-19 Literature Digest Team