Public Health England

International EPI Cell Evidence Digest – 22/07/2020

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- Serology and immunology
- Diagnostics and genomics
- Epidemiology and clinical - risk factors
- Epidemiology and clinical - other
- 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Please note that we are including preprints (highlighted in red), which are preliminary reports of work that have NOT been peer-reviewed.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
21.07.2020	Seroprevalence of Antibodies to SARS-CoV-2 in 10 Sites in the United States, March 23-May 12, 2020	JAMA Intern Med / Article	• In this cross-sectional study of 16,025 residual clinical specimens, estimates of the proportion of persons with detectable SARS-CoV-2 antibodies ranged from 1.0% in the San Francisco Bay area (collected April 23-27) to 6.9% of persons in New York City (collected March 23-April 1). Six to 24 times more infections were estimated per site with seroprevalence than with COVID-19 case report data. • For most sites, it is likely that greater than 10 times more SARS-CoV-2 infections occurred than the number of reported COVID-19

			cases; most persons in each site, however, likely had no detectable SARS-CoV-2 antibodies.
20.07.2020	Detection of IgG antibody during the follow-up in patients with COVID-19 infection	Crit Care / Article	• Studied 484 patients with positive IgG, the minimum period from onset to IgG detection was 10 days, and the maximum period was 100 days. Meanwhile, 18% of these patients had negative IgG results, and this was confirmed by more than two IgG tests in 37 patients. The mean duration from onset to IgG test was close between positive and negative IgG groups (50.5 ± 14.8 vs. 43.3 ± 15.0, days). • Inferred that compared to patients with positive IgG, those with negative IgG might have relatively mild COVID-19 infection, and the slight impact on their immune system leads to the higher lymphocyte and negative IgG during the follow-up period. This hypothesis was also supported by the CT finding that the residual infection on chest CT disappears more quickly in patients with negative IgG. If this is the case, the risk of re-infection of COVID-19 in these patients should be carefully assessed in the later stage of epidemic prevention.
16.07.2020	Humoral Response Dynamics Following Infection with SARS-CoV-2	medRxiv (non-peer reviewed) / Article	• A prospective cohort study of 67 adult healthcare workers sought to understand humoral dynamics following SARS-CoV-2 infection using monthly serial serological samples from 29.04.2020 until 30.06.2020. • After SARS-CoV-2 infection, the predicted half-life of nucleoprotein antibody was 52 days with 50% of seropositives becoming seronegative to this antibody at 195 days. • Widely used serological tests that depend on the N-antibody will therefore significantly underestimate the prevalence of infection following the majority of infections.

Diagnostics and genomics

Publication Date	Title / URL	Journal / Article type	Digest
20.07.2020	Lessons from Mass-Testing for COVID-19 in Long Term Care Facilities for the Elderly in San Francisco	Clin Infect Dis / Article	• Describe four LTCF outbreaks where mass testing identified a high proportion of asymptomatic infections (4-41% in health care workers and 20-75% in residents), indicating that symptom-based

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			screening alone is insufficient for monitoring for COVID-19 transmission.
20.07.2020	A recurrent mutation at position 26,340 of SARS-CoV-2 is associated with failure of the E-gene qRT-PCR utilized in a commercial dual-target diagnostic assay	J Clin Microbiol / Article	• Reports the identification of a C-to-U transition at position 26,340 of the SARS-CoV-2 genome which is associated with failure of the cobas® SARS-CoV-2 E-gene qRT-PCR in eight patients. • This work highlights the necessity of monitoring SARS-CoV-2 for the emergence of SNPs which might adversely affect RT-PCRs used in diagnostics. Additionally, it argues that two regions in SARS-CoV-2 should be targeted to avoid false negatives.
21.07.2020	Phylogenetic and phylodynamic analyses of SARS-CoV-2	Virus Res / Article	• To investigate evolutionary and epidemiological dynamics of the COVID-19 outbreak, 112 genomes of SARS-CoV-2 strains sampled from China and 12 other countries between 24 Dec 2019 and 9 Feb 2020 were analysed. • Estimates the time to the most recent common ancestor (TMRCA) and evolutionary rate of SARS-CoV-2 to be 12 Nov 2019 (95% BCI: 11 October 2019 and 09 Dec 2019) and 9.90×10^{-4} substitutions per site per year (95% BCI: 6.29×10^{-4}-1.35×10^{-3}), respectively. • The very low R(e) estimates of SARS-CoV-2 during the recent sampling period may be the result of extreme societal lockdown efforts in China.
19.07.2020	The short and long-range RNA-RNA Interactome of SARS-CoV-2	bioRxiv (non-peer reviewed) / Article	• Coronaviruses are dependent on long-distance RNA-RNA interactions to regulate viral transcription and replication pathways. • Study experimentally mapped the in vivo RNA-RNA interactome of the full-length SARS-CoV-2 genome and its subgenomic mRNAs. • Findings illuminate RNA-based mechanisms governing replication, discontinuous transcription, and translation of coronaviruses.

Epidemiology and clinical - risk factors

Publication Date	Title / URL	Journal / Article type	Digest
20.07.2020	Outcomes of COVID-19 in Patients with CLL: A Multicenter, International Experience	Blood / Article	• CLL patients diagnosed with symptomatic COVID-19 across 43 international centres (n=198) were included. • Hospital admission occurred in 90%. Median age at COVID-19 diagnosis was 70.5 years. At a median follow-up of 16 days, the overall case fatality rate (CFR) was 33%, though 25% remain admitted.

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			• These data suggest that the subgroup of CLL patients admitted with COVID-19, regardless of disease phase or treatment status, are at high risk of death.
20.07.2020	Thrombosis in Hospitalized Patients With COVID-19 in a New York City Health System	JAMA / Research letter	• Assessed the incidence of, and risk factors for, venous and arterial thrombotic events in all hospitalized patients with COVID-19 at a large health system consisting of 4 hospitals in New York City. • Among 3334 consecutive hospitalized COVID-19 patients, the median age was 64 (interquartile range, 51-75) years; 39.6% were female. • A thrombotic event occurred in 16.0%. D-dimer level at presentation was independently associated with thrombotic events, consistent with an early coagulopathy.
19.07.2020	Clinical Characteristics and Outcomes for 7,995 Patients with SARS-CoV-2 Infection	medRxiv (non-peer reviewed) / Article	• An observational study of people testing positive for SARS-CoV-2 infection (n=7,995) found older age and male sex were the most strongly associated risks for admission and in-hospital mortality. • While minority racial and ethnic groups had increased burden of disease and risk of admission, age-adjusted in-hospital mortality for discharged patients was not significantly different among racial and ethnic groups.

Epidemiology and clinical – other

Publication Date	Title / URL	Journal / Article type	Digest
17.07.2020	Contact Tracing during Coronavirus Disease Outbreak, South Korea, 2020	Emerg Infect Dis / Article	• The authors analysed reports for 59,073 contacts of 5,706 COVID-19 index patients reported in South Korea from 20 January- 27 March 2020. • Of 10,592 household contacts, 11.8% had COVID-19. • Of 48,481 non-household contacts, 1.9% had COVID-19. • With index patients 30–39 years of age as reference, detection of COVID-19 contacts was significantly higher for index patients >40 years of age in non-household settings. For most age groups, COVID-19 was detected in significantly more household than non-household contacts.
20.07.2020	Basic epidemiological parameter values from data of real-world in mega-cities:	BMC Infect Dis / Article	• To investigate the epidemiological parameters in SARS-CoV-2 infected cases in Beijing, the authors studied all confirmed cases and close contacts in Beijing from Jan 1st to Apr 3rd 2020. The

	the characteristics of COVID-19 in Beijing, China		epidemiological and virological characteristics of SARS-CoV-2 were analysed. • A total of 602 cases were positive for SARS-CoV-2, including 585 confirmed patients and 17 asymptomatic infections. • The transmissibility of SARS-CoV-2 was relatively high, especially among households and from HCWs, which draws specific public health attention. So far, no evidence of widespread circulation of SARS-CoV-2 in communities in Beijing was found.
20.07.2020	Characteristics and Mortality of Hospitalized Patients With COVID-19 in Iran: A National Retrospective Cohort Study	Ann Intern Med / Letter	• Describes the characteristics and mortality among hospitalized patients with laboratory-confirmed COVID-19 in Iran (n=28,981). • The high case-fatality rate they saw is consistent with the hospitalized population; milder cases were likely excluded. Consistent with other studies, hypoxemia, fever, and cough were common presenting symptoms, as were comorbidities.
21.07.2020	Evidence of exposure to SARS-CoV-2 in cats and dogs from households in Italy	bioRxiv (non-peer reviewed) / Article	• Study assessed SARS-CoV-2 infection in over 500 companion animals living in northern Italy, sampled at a time of frequent human infection. • No animals tested PCR positive. • 3.4% of dogs and 3.9% of cats had measurable SARS-CoV-2 neutralizing antibody titres. • Dogs from COVID-19 positive households significantly more likely to test positive than those from COVID-19 negative households. • Recommends investigation of risk factors and potential to infect other species.
21.07.2020	Global seasonality of human seasonal coronaviruses: a clue for post-pandemic circulating season of SARS-CoV-2 virus?	J Infect Dis / Systematic review	• Systematic review to provide an overview of the global seasonality of seasonal coronaviruses. Findings offer clues to the possible post-pandemic circulating season of SARS-CoV-2 and add to the knowledge pool necessary for post-pandemic preparedness for SARS-CoV-2. • Human seasonal coronaviruses are found to be prevalent in winter months in most temperate sites, coinciding with influenza and respiratory syncytial virus season, but less seasonal in tropics and in temperate sites of China.

Treatment

Publication Date	Title / URL	Journal / Article type	Digest
15.07.2020	Observational Study of Haloperidol in Hospitalized Patients with Covid-19	medRxiv (non-peer reviewed) / Article	• In an observational study involving patients with Covid-19 (n=13,279) who had been admitted to the hospital, haloperidol use was not associated with risk of intubation or death, or with time to hospital discharge. • Authors suggest that haloperidol is unlikely to have a clinical efficacy for Covid-19.

Modelling

Publication Date	Title / URL	Journal / Article type	Digest
20.07.2020	Effect of delays in the 2-week-wait cancer referral pathway during the COVID-19 pandemic on cancer survival in the UK: a modelling study	The Lancet Oncology / Article	• Examined the impact of different scenarios of lockdown-accumulated backlog in cancer referrals on cancer survival, and the impact on survival per referred patient due to delayed referral versus risk of death from nosocomial infection with SAR-CoV-2. • Prompt provision of additional capacity to address the backlog of diagnostics will minimise deaths as a result of diagnostic delays that could add to those predicted due to expected presentational delays. Prioritisation of patient groups for whom delay would result in most life-years lost warrants consideration as an option for mitigating the aggregate burden of mortality in patients with cancer.

Guidance, consensus statements

Publication Date	Title / URL	Journal / Article type
21.07.2020	COVID-19 Rail Protocol: Recommendations for safe resumption of railway services in Europe	European Centre for Disease Prevention and Control / Protocol

Overviews, comments and editorials

Publication Date	Title / URL	Journal / Article type
21.07.2020	Communicating with children about COVID-19	The Lancet Infectious Diseases / Media watch
20.07.2020	Addendum to: Children are not COVID-19 super spreaders: time to go back to school	Arch Dis Child / PostScript
21.07.2020	The RECOVERY Platform	NEJM / Editorial
21.07.2020	Rapid Decay of Anti–SARS-CoV-2 Antibodies in Persons with Mild Covid-19	NEJM / Correspondence
17.07.2020	Non-invasive saliva specimens for the diagnosis of COVID-19: caution in mild outpatient cohorts with low prevalence	Clin Microbiol Infect / Letter
21.07.2020	Serosurveillance and the COVID-19 Epidemic in the US: Undetected, Uncertain, and Out of Control	Jama / Editorial
20.07.2020	Covid-19: Male disadvantage highlights the importance of sex disaggregated data	Bmj / Views and reviews
20.07.2020	COVID-19 and cardiovascular disease: from basic mechanisms to clinical perspectives	Nat Rev Cardiol / Review
21.07.2020	Using the right words to address racial disparities in COVID-19	The Lancet Public Health / Comment
17.07.2020	Health Policy and Leadership Models During the COVID-19 Pandemic- Review Article	Int J Surg / Review

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