



International EPI Cell Daily Evidence Digest – 24/07/2020

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
- Epidemiology and clinical - children and pregnancy
- Epidemiology and clinical - risk factors
- Epidemiology and clinical - other
- Infection control
- 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Please note that we are including preprints (**highlighted in red**), which are preliminary reports of work that have NOT been peer-reviewed.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
24.07.2020	Population Point Prevalence of SARS-CoV-2 Infection Based on a Statewide Random Sample - Indiana, April 25-29, 2020	MMWR Morb Mortal Wkly Rep / Article	<ul style="list-style-type: none">• In a random sample of Indiana residents aged ≥ 12 years ($n=3,658$), the estimated prevalence of current or previous SARS-CoV-2 infection in late April 2020 was 2.79%. Among persons with active infection, 44% reported no symptoms.

Epidemiology and clinical - children and pregnancy

Publication Date	Title / URL	Journal / Article type	Digest
23.07.2020	Neonatal management and outcomes during the COVID-19 pandemic: an observation cohort study	The Lancet Child & Adolescent Health / Article	<ul style="list-style-type: none"> • An observational cohort study (n=1481) aimed to discover best practices regarding SARS-CoV-2 infection control in mother–new-born dyads, and identify potential risk factors for transmission. • Data suggests perinatal transmission of COVID-19 is unlikely if precautions such as hand hygiene before skin-to-skin contact or wearing surgical masks near the neonate are undertaken. • Direct breastfeeding and allowing neonates to room in with their mothers are safe when paired with effective parental education of protective strategies.
17.07.2020	A national consensus management pathway for Paediatric Inflammatory Multisystem Syndrome - Temporally associated with SARS-CoV-2 (PIMS-TS): The results of a national Delphi process	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • A three-phase Delphi process was used to develop a consensus management pathway for children with Paediatric Inflammatory Multisystem Syndrome - Temporally associated with SARS-CoV-2 (PIMS-TS). • Future evidence will inform updates to this guidance, which in the interim provides a framework to support clinicians caring for children with PIMS-TS.

Epidemiology and clinical - risk factors

Publication Date	Title / URL	Journal / Article type	Digest
22.07.2020	Risk Factors Associated With Mortality Among Residents With Coronavirus Disease 2019 (COVID-19) in Long-term Care Facilities in Ontario, Canada	JAMA Netw Open / Original investigation	<ul style="list-style-type: none"> • In this cohort study of 627 LTC facilities, the incidence rate ratio for COVID-19–related death among LTC residents was 13 times higher than that among community-living adults older than 69 years. • Highlights the need for improved infection control, widespread testing, access to personal protective equipment, and other supports to protect this vulnerable population.
20.07.2020	Comparison of Reported Deaths From COVID-19 and Increase in Total Mortality in Italy	JAMA Intern Med / Editorial	<ul style="list-style-type: none"> • Compared the number of reported deaths from COVID-19 in Italy and the increase in total mortality. • Total annual mortality for Mar and early Apr was similar for 2015 through 2019 (average 20 214 deaths per year). For Mar 1 to Apr 4, 2020, however, there were 41 329 reported deaths, a 104.5% increase compared with the average number of deaths for the prior 5

			<p>years.</p> <ul style="list-style-type: none"> • Findings show that the official count of COVID-19 deaths in Italy has substantially understated the actual increase in mortality related to the pandemic, as is the case in other countries.
24.07.2020	Estimated County-Level Prevalence of Selected Underlying Medical Conditions Associated with Increased Risk for Severe COVID-19 Illness - United States, 2018	MMWR Morb Mortal Wkly Rep / Article	<ul style="list-style-type: none"> • Older adults and those with chronic obstructive pulmonary disease, heart disease, diabetes, chronic kidney disease, and obesity are at higher risk for severe COVID-19–associated illness. • The median model-based estimate of the prevalence of any of five underlying medical conditions associated with increased risk for severe COVID-19–associated illness among U.S. adults was 47.2% among 3,142 U.S. counties. The estimated number of persons with these conditions followed population distributions, but prevalence was higher in more rural counties.
01.07.2020	THYROTOXICOSIS IN PATIENTS WITH COVID-19: THE THYRCOV STUDY	Eur J Endocrinol / Article	<ul style="list-style-type: none"> • Assessed thyroid function in patients affected by COVID-19, based on the hypothesis that the cytokine storm associated with COVID-19 may influence thyroid function and/or SARS-CoV-2 may directly act on thyroid cells, such as previously demonstrated for SARS-CoV-1 infection. • Fifty-eight patients (20.2%) were found with thyrotoxicosis (overt in 31 cases), 15 (5.2%) with hypothyroidism (overt in only 2 cases), 214 (74.6%) with normal thyroid function. Serum thyrotropin values were inversely correlated with age of patients (rho -0.27; p<0.001) and IL-6 (rho -0.41; p<0.001). • This study provides a first evidence that COVID-19 may be associated with high risk of thyrotoxicosis in relationship with systemic immune activation induced by the SARS-CoV-2 infection.

Epidemiology and clinical – other

Publication Date	Title / URL	Journal / Article type	Digest
22.07.2020	The Contribution of the Age Distribution of Cases to COVID-19 Case Fatality Across Countries: A 9-Country Demographic Study	Ann Intern Med / Article	<ul style="list-style-type: none"> • A cross-sectional demographic study (n=1,223,261) measured the contribution of distortions from the age distributions of confirmed COVID-19 cases to CFRs within and across populations. • Selective testing and identifying of older cases considerably warped estimates of lethality of COVID-19 within populations, and comparisons across countries.

			<ul style="list-style-type: none"> • Suggests removing age distortions and focusing on differences in age-adjusted case fatality will be essential for accurately comparing countries' performance.
23.07.2020	A large COVID-19 outbreak in a high school 10 days after schools' reopening, Israel, May 2020	Eurosurveillance / Rapid communication	<ul style="list-style-type: none"> • On 13 March 2020, Israel's government declared closure of all schools. Schools fully reopened on 17 May 2020. • Ten days later, a major outbreak of COVID-19 occurred in a high school. The first case was registered on 26 May, the second on 27 May. They were not epidemiologically linked. Testing of the complete school community revealed 153 students (attack rate: 13.2%) and 25 staff members (attack rate: 16.6%) who were COVID-19 positive.
23.07.2020	SARS-CoV-2 Virus Isolated From the Mastoid and Middle Ear: Implications for COVID-19 Precautions During Ear Surgery	JAMA Otolaryngol Head Neck Surg / Research letter	<ul style="list-style-type: none"> • Present confirmation of SARS-CoV-2 colonization of the middle ear and mastoid in 2 of 3 patients.
23.07.2020	Association of Social Distancing, Population Density, and Temperature With the Instantaneous Reproduction Number of SARS-CoV-2 in Counties Across the United States	JAMA Netw Open / Original investigation	<ul style="list-style-type: none"> • In this cohort study of 211 counties in 46 states, social distancing, temperate weather, and lower population density were associated with a decrease in the instantaneous reproduction number of SARS-CoV-2. • Of these county-specific factors, social distancing appeared to have the most substantial association with a reduction in SARS-CoV-2 transmission.
21.07.2020	SARS-CoV-2 Titers in Wastewater Are Higher than Expected from Clinically Confirmed Cases	mSystems / Article	<ul style="list-style-type: none"> • Tested wastewater collected at a major urban treatment facility in Massachusetts and detected SARS-CoV-2 RNA from the N gene at significant titres (57 to 303 copies per ml of sewage) in the period from 18 to 25 March 2020 using RT-qPCR. • Validated detection of SARS-CoV-2 by Sanger sequencing the PCR product from the S gene. • Viral titres observed were significantly higher than expected based on clinically confirmed cases in Massachusetts as of 25 March. • Approach is scalable and may be useful in modelling the SARS-CoV-2 pandemic and future outbreaks.
20.07.2020	Age-Dependent Progression of SARS-CoV-2 Infection in Syrian Hamsters	Viruses / Article	<ul style="list-style-type: none"> • Compared the course of SARS-CoV-2 infection in young and aged Syrian hamsters. • Show that virus replication in the upper and lower respiratory tract was independent of the age of the animals. However, older hamsters exhibited more pronounced and consistent weight loss. In situ hybridization in the lungs identified viral RNA in bronchial epithelium, alveolar epithelial cells type I and II, and macrophages. • Histopathology revealed clear age-dependent differences, with

			<p>young hamsters launching earlier and stronger immune cell influx than aged hamsters. The latter developed conspicuous alveolar and perivascular edema, indicating vascular leakage. In contrast, they observed rapid lung recovery at day 14 after infection only in young hamsters.</p> <ul style="list-style-type: none"> Propose that comparative assessment in young versus aged hamsters of SARS-CoV-2 vaccines and treatments may yield valuable information, as this small-animal model appears to mirror age-dependent differences in human patients.
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Infection control

Publication Date	Title / URL	Journal / Article type	Digest
21.07.2020	Feasibility of Separate Rooms for Home Isolation and Quarantine for COVID-19 in the United States	Ann Intern Med / Article	<ul style="list-style-type: none"> A study to determine feasibility of separate rooms for isolation and quarantine for housing units in the United States, using data from the 2017 American Housing Survey. Data suggests 1 in 5 U.S. homes lack sufficient space and plumbing facilities to comply with recommendations to isolate or quarantine to limit household spread of COVID-19. This proportion is particularly high among homes occupied by minority and poor individuals, and among apartments. Several limitations to the findings and potential policy recommendations are discussed.
13.07.2020	The Infectious Nature of Patient-Generated SARS-CoV-2 Aerosol	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> Collected aerosol samples around six patients admitted into mixed acuity wards in April 2020. Measurements were made to characterize the size distribution of aerosol particles, and size-fractionated, aerosol samples were collected to assess the presence of infectious virus in particles sizes of >4.1 μm, 1-4 μm, and <1 μm in the patient environment. SARS-CoV-2 RNA was detected in all six rooms in all particle size fractions. Increases in viral RNA during cell culture of the virus from recovered aerosol samples demonstrated the presence of infectious, replicating virions in three <1 μm aerosol samples ($P < 0.05$). The infectious nature of aerosol collected in this study further suggests that airborne transmission of COVID-19 is possible, and that

			aerosol prevention measures are necessary to effectively stem the spread of SARS-CoV-2.
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Treatment

Publication Date	Title / URL	Journal / Article type	Digest
23.07.2020	Hydroxychloroquine with or without Azithromycin in Mild-to-Moderate Covid-19	NEJM / Article	<ul style="list-style-type: none"> • A randomized controlled trial of 504 patients hospitalized with mild-to-moderate Covid-19 found the use of hydroxychloroquine, alone or with azithromycin, did not improve clinical status at 15 days as compared with standard care.
22.07.2020	Chloroquine does not inhibit infection of human lung cells with SARS-CoV-2	Nature / Article	<ul style="list-style-type: none"> • Show that engineered expression of TMPRSS2, a cellular protease that activates SARS-CoV-2 for entry into lung cells, renders SARS-CoV-2 infection of Vero cells insensitive to chloroquine. • Moreover, the authors report that chloroquine does not block SARS-CoV-2 infection of the TMPRSS2-positive lung cell line Calu-3. • These results indicate that chloroquine targets a pathway for viral activation that is not operative in lung cells and is unlikely to protect against SARS-CoV-2 spread in and between patients.

Modelling

Publication Date	Title / URL	Journal / Article type	Digest
20.07.2020	The impact of the COVID-19 pandemic on cancer deaths due to delays in diagnosis in	Lancet Oncol / Article	<ul style="list-style-type: none"> • Estimated the impact of delays in diagnosis on cancer survival outcomes in four major tumour types. • Substantial increases in the number of avoidable cancer deaths in

[England, UK: a national, population-based, modelling study](#)

England are to be expected as a result of diagnostic delays due to the COVID-19 pandemic in the UK. Urgent policy interventions are necessary, particularly the need to manage the backlog within routine diagnostic services to mitigate the expected impact of the COVID-19 pandemic on patients with cancer.

Overviews, comments and editorials

Publication Date	Title / URL	Journal / Article type
23.07.2020	Masking lack of evidence with politics	CEBM / Viewpoint
30.06.2020	A metabolic handbook for the COVID-19 pandemic	Nat Metab / Perspective
22.07.2020	Rapid Scaling Up of Covid-19 Diagnostic Testing in the United States — The NIH RADx Initiative	NEJM / Special report
23.07.2020	Monitoring approaches for health-care workers during the COVID-19 pandemic	The Lancet Infectious Diseases / Comment

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