



COVID-19 Literature Digest – 03/09/2021

Dear all,

Please find [today's report](#) below.

PHE's COVID-19 Literature Digest has been produced since February 2020. A selection of our previous Digests [can be found here](#). This resource aims to highlight a small selection of recent COVID-19 papers that are relevant to UK settings, contain new data, insights or emerging trends. The Digest Team generate a report once per week (Fri). The reports include both preprints, which should be treated with caution as they are NOT peer-reviewed and may be subject to change, and also research that has been subject to peer review and wider scrutiny. The Digest is very rapidly produced and does not claim to be a perfect product; the inclusion or omission of a publication should not be viewed as an endorsement or rejection by PHE. We do not accept responsibility for the availability, reliability or content of the items included in this resource.

To join our email distribution list please send a request to COVID.LitDigest@phe.gov.uk. If you are interested in papers relating to behaviour and social science please contact COVID19.behaviouralscience@phe.gov.uk to sign up to receive the PHE Behavioural Sciences Weekly Report.

Best wishes,

Emma Farrow, James Robinson, Kester Savage, Michael Cook
On behalf of the PHE COVID-19 Literature Digest Team

Report for 03.09.2021 (please note that papers that have **NOT been peer-reviewed** are highlighted in red).

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Serology and immunology

| Publication Date | Title/URL | Journal / Article type | Digest |
|------------------|--|---------------------------------------|--|
| 19.08.2021 | Autoantibodies neutralizing type I IFNs are present in ~4% of uninfected individuals over 70 years old and account for ~20% of COVID-19 deaths | Sci Immunol / Article | <ul style="list-style-type: none">• Authors detected auto-Abs neutralising 100-fold lower, more physiological, concentrations of IFN-α and/or -ω (100 pg/mL, in 1/10 dilutions of plasma) in 13.6% of 3,595 patients with critical COVID-19, including 21% of 374 patients aged >80 years, and 6.5% of 522 patients with severe COVID-19.• These antibodies are also detected in 18% of the 1,124 deceased patients.• Additionally, 1.3% of patients with critical COVID-19 and 0.9% of the deceased patients have auto-Abs neutralising high concentrations of IFN-β.• In a sample of 34,159 uninfected subjects from the general population, auto-Abs neutralising high concentrations of IFN-α and/or -ω are present in 0.18% of individuals between 18-69 years, 1.1% between 70-79 years, and 3.4% >80 years. Proportion of subjects carrying auto-Abs neutralising lower concentrations is greater in a subsample of 10,778 uninfected individuals. By contrast, auto-Abs neutralising IFN-β do not become more frequent with age.• Associated commentary: https://www.nature.com/articles/d41586-021-02337-5 |
| 25.08.2021 | Comparing SARS-CoV-2 natural immunity to vaccine-induced immunity: reinfections versus breakthrough infections | medRxiv (non-peer reviewed) / Article | <ul style="list-style-type: none">• Retrospective observational study in Israel compared three groups: 1) SARS-CoV-2-naive individuals who received two doses of Pfizer-BioNTech vaccine, 2) previously infected individuals who have not been vaccinated, and; 3) previously infected and single dose vaccinated individuals. Follow-up period was 1 June to 14 August 2021, when the Delta variant was dominant.• Naive vaccinees had 13.06-fold increased risk for breakthrough infection with Delta compared to those previously infected, when infection/vaccination occurred in January or February 2021. Increased risk was also significant for symptomatic disease. |

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| | | | <ul style="list-style-type: none"> • When allowing the infection to occur at any time before vaccination (from March 2020 to February 2021), evidence of waning natural immunity was demonstrated, though naive vaccinees had increased risk for breakthrough infection (5.96-fold) and symptomatic disease (7.13-fold). • Naive vaccinees were at greater risk for COVID-19-related-hospitalisations compared to previously infected people. |
| 01.09.2021 | Distinct systemic and mucosal immune responses during acute SARS-CoV-2 infection | Nat Immunol / Article | <ul style="list-style-type: none"> • An integrated systems approach to compare systemic and local immune responses during active SARS-CoV-2 infection in a well-characterized cohort of 49 patients with varying clinical severity and 12 healthy controls • This research identifies new host–viral–microbiome interactions during infection with SARS-CoV-2, which may help to uncover new strategies for identifying at-risk individuals. |

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Vaccines

| Publication Date | Title/URL | Journal / Article type | Digest |
|------------------|--|-----------------------------|--|
| 27.08.2021 | Hospital admission and emergency care attendance risk for SARS-CoV-2 delta (B.1.617.2) compared with alpha (B.1.1.7) variants of concern: a cohort study | Lancet Infect Dis / Article | <ul style="list-style-type: none"> • National study: all patients in England with COVID-19 between 29.03.21 and 23.05.21 • 43,338 COVID-19-positive patients (8682 with delta / 34 656 with alpha; median age 31 years) • Hospital admission or emergency care attendance within 14 days: 498 (5.7%)with delta / 1448 (4.2%) with alpha variant • Most patients unvaccinated (32,078 [74.0%] across both groups) • Results suggest patients with delta variant had more than two times the risk of hospital admission compared with patients with alpha. • Associated comment: https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00474-6/fulltext |
| 01.09.2021 | Risk factors and disease profile of post-vaccination SARS-CoV-2 infection in UK users of the COVID Symptom Study app: a prospective, community-based, nested, case-control study | Lancet Infect Dis / Article | <ul style="list-style-type: none"> • Self-reported data from UK-based, adult (≥18 years) users of COVID Symptom Study mobile phone app. • 1,240,009 app users reported 1st vaccine, 6030 (0.5%) subsequently tested positive. Risk factors: frailty in older adults (≥60 years), individuals living in highly deprived areas, obesity. |

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| | | | <ul style="list-style-type: none"> • 971,504 reported 2nd dose, 2370 (0.2%) subsequently tested positive. • Vaccination (versus no vaccination) associated with (i) reduced odds of hospitalisation or having more than five symptoms in first week of illness following 1st or 2nd dose; (ii) long-duration (≥ 28 days) symptoms following 2nd dose. |
| 29.08.2021 | COVID-19-associated hospitalizations among vaccinated and unvaccinated adults ≥ 18 years - COVID-NET, 13 states, January 1 - July 24, 2021 | medRxiv (non-peer reviewed) / Article | <ul style="list-style-type: none"> • From 1 January - 30 June 2021, adults (≥ 18 years) with confirmed SARS-CoV-2 infection were identified from >250 acute care hospitals in the US population-based network COVID-NET. • During the whole study period fully vaccinated cases increased from 1 (0.01%) to 321 (16.1%) per month • Among 4,732 sampled cases, fully vaccinated persons admitted with COVID-19 were older compared with unvaccinated (median age 73 years v. 59 years), more likely to have 3+ underlying medical conditions (201 (70.8%) v. 2,305 (56.1%)) and be residents of long-term care facilities (37 (14.5%) v. 146 (5.5%)). • From 24 Jan. - 24 Jul. 2021, cumulative hospitalisation rates were 17 times higher in unvaccinated persons compared with vaccinated (423 v. 26 per 100,000 population, respectively); rate ratios were 23, 22 and 13 for those aged 18-49, 50-64, and ≥ 65 years respectively. • For 27 Jun. - 24 Jul. 2021, hospitalisation rates were ≥ 10 times higher in unvaccinated persons compared with vaccinated persons for all age groups across all weeks. |
| 01.09.2021 | Resurgence of SARS-CoV-2 Infection in a Highly Vaccinated Health System Workforce | N Engl J Med / Correspondence | <ul style="list-style-type: none"> • Uni. of California San Diego Health workforce 83% vaccinated by July 2021. • Vaccine effectiveness exceeded 90% March - June, fell to 65.5% in July • July COVID-19 cases by month vaccinations completed: Jan/Feb, attack rate 6.7 per 1000 persons; Mar-May, 3.7 per 1000; unvaccinated, 16.4 per 1000. • Coincident with California's mask mandate ending on June 15, rapid dominance of B.1.617.2 (delta). |
| 02.09.2021 | Vaccine effectiveness against infection with the Delta (B.1.617.2) variant, Norway, April to August 2021 | Euro Surveill / Article | <ul style="list-style-type: none"> • Population-based cohort study in Norway ($n = 4,204,859$) investigated vaccine effectiveness (VE). Vaccines included Pfizer-BioNTech, Moderna, and Oxford-AstraZeneca, including some mixed dosing schedules. • Delta variant was identified in 5,430 (0.13%) individuals, of whom 84 were admitted to hospital. |

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| | | | <ul style="list-style-type: none"> • VE against laboratory confirmed infection with Delta was 22.4% among partly vaccinated and 64.6% among fully vaccinated individuals, compared with 54.5% and 84.4% against the Alpha variant. |
| 30.08.2021 | Comparison of SARS-CoV-2 Antibody Response Following Vaccination With BNT162b2 and mRNA-1273 | JAMA / Research Letter | <ul style="list-style-type: none"> • 1647 double vaccinated Belgium health care workers: (i) 688 (mean age 43.2; 21.8% previously infected) with mRNA-1273 [Moderna]; (ii) 959 (mean age 44.7; 13.2% previously infected) with BNT162b2 [Pfizer]. • Significantly higher humoral immunogenicity of Moderna compared with Pfizer in infected and uninfected participants, and across age categories. • Moderna's higher mRNA content and longer interval between shots (4 weeks vs 3 weeks) may explain this. |
| 01.09.2021 | Reactogenicity and immunogenicity after a late second dose or a third dose of ChAdOx1 nCoV-19 in the UK: a substudy of two randomised controlled trials (COV001 and COV002) | Lancet / Article | <ul style="list-style-type: none"> • Persistence of immunogenicity after (i) single dose ChAdOx1 [AstraZeneca]; (ii) extended interval (44–45 weeks) between 1st and 2nd dose; (iii) after 3rd, booster dose 28–38 weeks later. • Extended interval before 2nd dose leads to increased antibody titres. (median total IgG titre: 923 EUs with 8-12 week interval; 1860 EUs/15-25 week; 3738 EUs/44–45 week). • After 3rd dose, antibodies induced to level correlating with high efficacy after 2nd dose, boosts T-cell responses. (In 73 [81%] participants, median total IgG titre: 3746 EUs; versus median 1792 EUs after 2nd dose). • Linked comment: https://doi.org/10.1016/S0140-6736(21)01817-1 |
| 27.08.2021 | Pfizer and BioNTech Initiate Rolling Submission of Supplemental Biologics License Application to U.S. FDA for Booster Dose of COMIRNATY® in Individuals 16 and Older | Pfizer (non-peer reviewed) / News | <ul style="list-style-type: none"> • New Phase 3 data suggests booster (third) dose of Comirnaty (Pfizer–BioNTech) COVID-19 vaccine induces significant SARS-CoV-2 neutralising antibody titers and demonstrated a favourable safety and tolerability profile • SARS-CoV-2 neutralising titers against the wild-type strain one month after booster dose were 3.3 times the titers one month after the second dose • Pfizer and BioNTech intend to file these data with the European Medicines Agency (EMA) and other regulatory authorities around the world in coming weeks |
| 31.08.2021 | BNT162b2 vaccine booster dose protection: A nationwide study from Israel | medRxiv (non-peer reviewed) / Article | <ul style="list-style-type: none"> • Between 30 July and 22 August 2021 this study followed 1,144,690 individuals aged 60 years and older who were eligible for a third (booster) dose of the Pfizer BNT162b2 vaccine • Twelve days or more after the booster dose an 11.4-fold decrease in the relative risk of confirmed infection and a >10-fold decrease in the relative risk of severe illness was observed. |

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| | | | <ul style="list-style-type: none"> • Sensitivity analysis found ≈5-fold protection against confirmed infection. |
| 30.08.2021 | Waning immunity of the BNT162b2 vaccine: A nationwide study from Israel | medRxiv (non-peer reviewed) / Article | <ul style="list-style-type: none"> • Analyses data on all PCR positive SARS-CoV-2 test results between 11-31 July 2021 (n=12,927) for Israeli residents fully vaccinated with BNT162b2 (Pfizer) vaccine before June 2021 • The rates of both documented SARS-CoV-2 infections and severe COVID-19 exhibit a statistically significant increase as time from second vaccine dose elapsed • Elderly individuals (60+) who received their second dose in March 2021 were 1.6 times more protected against infection and 1.7 times more protected against severe COVID-19 compared to those who received their second dose in January 2021. Similar results were found for different age groups. |
| 26.08.2021 | Initial experience of the safety and tolerability of the BNT162b2 (Pfizer-Bio-N-Tech) vaccine in extremely vulnerable children aged 12-15 years | Arch Dis Child / Research letter | <ul style="list-style-type: none"> • Parental reporting of the reactogenicity of the Pfizer vaccine in 27 children found all adverse reactions mild/moderate except for one child with severe fatigue and severe discomfort combined with increased agitation until day 7. • Adverse effects included changes to seizure type, mild rash, headache, diarrhoea, presumed sore throat, neck pain, difficulty sleeping, low blood sugars. • Paracetamol use with dose 1 was high and fever (temperature ≥38°C) was more common than in adults. |
| 01.09.2021 | Viral loads of Delta-variant SARS-CoV2 breakthrough infections following vaccination and booster with the BNT162b2 vaccine | medRxiv (non-peer reviewed) / Article | <ul style="list-style-type: none"> • Analysis of 11,889 infections during the current wave in Israel (28 June to 24 August 2021), dominated by the Delta-variant, suggests that breakthrough infections in recently vaccinated patients (within 2 months of second dose) have lower viral loads compared to unvaccinated patients, with the extent of viral load reduction similar to pre-Delta breakthrough observations. • Protection starts diminishing for patients two months post vaccination and ultimately vanishes for patients 6 months or longer post vaccination; however, diminishing vaccine effectiveness on breakthrough infection viral loads is restored following the booster vaccine. |
| 23.08.2021 | Vaccine Effectiveness against Referral to Hospital and Severe Lung Injury Associated with COVID-19: A Population-based Case-control Study in St. Petersburg, Russia | medRxiv (non-peer reviewed) / Article | <ul style="list-style-type: none"> • Case-control study in St. Petersburg, Russia assessed vaccine effectiveness (VE) of Gam-COVID-Vac (Sputnik vaccine) against lung injury and referral to hospital:13,894 patients included, 1,291 (9.3%) met the criteria for complete vaccination status, and 495 (3.6%) were referred to hospital. |

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| | | | <ul style="list-style-type: none"> • Adjusted VE against referral to hospital was 81% for complete vaccination; effect of the partial vaccination was not statistically significant. VE against referral to hospital was more pronounced in women (84%) compared to men (76%). • Vaccine protective effect increased with increasing lung injury categories, from 54% against any sign of lung injury to 76% against more than 50% lung involvement. • Sharp increase was observed in the probability of hospital admission with age for non-vaccinated patients compared with an almost flat relationship for the completely vaccinated group. |
| 30.08.2021 | Exploring Vaccine Hesitancy in Care Home Employees in North West England: A Qualitative Study | medRxiv (non-peer reviewed) / Article | <ul style="list-style-type: none"> • Semi-structured interviews with 10 currently unvaccinated care home employees (aged 25 to 61 years old) in North West England explored vaccine hesitancy. • Analysis identified eight themes: 1) perceived [low] risk of COVID-19; 2) efficacy of the vaccine; 3) concerns about the vaccine; 4) mistrust in authorities; 5) facilitators to getting the vaccine [wanting to protect others, perceived severity of COVID-19, and workplace norms]; 6) [negative] views on potential mandatory COVID-19 vaccination policies; 7) negative experiences of care work during the COVID-19 pandemic, and: 8) communication challenges. |
| 31.08.2021 | Prevalence of Allergic Reactions After Pfizer-BioNTech COVID-19 Vaccination Among Adults With High Allergy Risk | JAMA Netw Open / Original investigation | <ul style="list-style-type: none"> • Cohort study of 8102 individuals with an allergy history, of whom 429 (5%) were identified as “highly allergic” using an algorithm; this group was referred to receive BNT162b2 (Pfizer-BioNTech) vaccination under medical supervision. • In total 98% of highly allergic individuals had no allergic reaction, 6 (1%) had mild allergic responses, and 3 (0.7%) had anaphylactic reactions. This suggests most patients with a history of allergic diseases and, particularly, highly allergic patients can be safely immunised by using a simple algorithm. • Invited commentary: https://dx.doi.org/10.1001/jamanetworkopen.2021.22326 |

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Diagnostics and genomics

| Publication Date | Title/URL | Journal / Article type | Digest |
|------------------|--|---|--|
| 28.08.2021 | Feasibility and acceptability of SARS-CoV-2 testing and surveillance in primary school children in England: Prospective, cross-sectional study | PLoS One / Article | <ul style="list-style-type: none"> • Staff and students in 131 primary schools asked to complete a questionnaire at recruitment and provide weekly nasal swabs for SARS-CoV-2 RT-PCR testing (n = 86) or swabs with blood samples for antibody testing (n = 45) at beginning and end of summer half-term. • Staff were willing to have more frequent testing than parents of primary school children. Nose swabs and oral fluids were more acceptable for children than throat swabs or blood sampling. |
| 31.08.2021 | Pooled RT-qPCR testing for SARS-CoV-2 surveillance in schools - a cluster randomised trial | EClinicalMedicine / Research Paper | <ul style="list-style-type: none"> • 3970 students / school staff in 14 German educational facilities tested 2-3 times per week, for at least 3 consecutive weeks. • Saliva samples collected using 'lolly method', students suck on swab for 15 seconds. • In secondary schools, no difference in number of positive students identified from pooled oropharyngeal swabs compared to pooled saliva samples. • Substantial number of asymptomatic cases in children and adolescents. • Screening by RT-qPCR-based pooled testing with easily obtainable saliva samples is feasible method to detect incident cases and observe transmission dynamics. |
| 21.08.2021 | Repeat positive SARS-CoV-2 RNA testing in nursing home residents during the initial 9 months of the COVID-19 pandemic: an observational retrospective analysis | Lancet Reg Health Am / Research Article | <ul style="list-style-type: none"> • Analysis of State-wide RT-PCR data from residents living in Connecticut's 212 nursing homes, 5.03.2020 - 15.12.2020. • 156 residents with positive RNA-based PCR tests occurring ≥90 days after an initial positive test. • Deaths reported in 12.8% (20/156), with 80% (16/20) having one or more negative tests prior to repeat positive test. • High frequency of repeat positive tests, compared to younger populations / community dwelling elderly, suggest immunity may wane more quickly following natural infection in this demographic. |
| 11.08.2021 | Detection of SARS-CoV-2 antibodies formed in response to the BNT162b2 and mRNA-1237 mRNA vaccine by commercial antibody tests | Vaccine / Article | <ul style="list-style-type: none"> • Cohort study of 225 healthcare workers and residents of long-term care facilities (177 receiving BNT162b2 and 48 receiving mRNA-1273). • Nucleocapsid IgG was found in 4.1% and 21.9% of the BNT162b2 (baseline) and mRNA-1273 (2-weeks post first dose). • All anti-spike assays included in the study (Abbott SARS-CoV-2 IgG, Abbott SARS-CoV-2 IgG II Quant, DiaSorin Trimeric S IgG, and GenScript cPASS) detected antibodies post-vaccination; average increase of 87.2% |

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| | | | <p>for BNT162b2 and 25.2% for mRNA-1273 between the first and last sampling time points.</p> <ul style="list-style-type: none"> • Neutralising antibodies detected at all post-vaccine timepoints for both vaccine arms, with increasing titers over time. |
| 02.09.2021 | Whole genome sequencing identifies multiple loci for critical illness caused by COVID-19 | medRxiv (non-peer reviewed) / Article | <ul style="list-style-type: none"> • GenOMICC (Genetics of Mortality in Critical Care) study: whole genome sequencing and statistical mapping in 7,491 critically-ill cases compared with 48,400 population controls to discover and replicate 22 independent variants that significantly predispose to life-threatening COVID-19. • Identified 15 new independent associations with severe COVID-19, including variants within genes involved in interferon signalling (IL10RB, PLSCR1), leucocyte differentiation (BCL11A), and blood type secretor status (FUT2). • Evidence implicating expression of multiple genes was found, including reduced expression of a membrane flippase (ATP11A), and increased mucin expression (MUC1), in severe disease. • Demonstrates that comparison between critically-ill cases and population controls is highly efficient for genetic association analysis and enables detection of therapeutically-relevant mechanisms of disease. |
| 31.08.2021 | Lectins enhance SARS-CoV-2 infection and influence neutralizing antibodies | Nature / Article | <ul style="list-style-type: none"> • Authors show that C-type lectin receptors, DC-SIGN, L-SIGN and the sialic acid-binding Ig-like lectin 1 (SIGLEC1) function as attachment receptors by enhancing ACE2-mediated infection and modulating the neutralising activity of different classes of spike-specific antibodies. • Collectively, the findings of this study identify a lectin-dependent pathway that enhances ACE2-dependent infection by SARS-CoV-2 and reveal distinct mechanisms of neutralisation by different classes of spike-specific antibodies. |

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Epidemiology and clinical - children and pregnancy

| Publication Date | Title/URL | Journal / Article type | Digest |
|------------------|---|--------------------------------|---|
| 30.08.2021 | One-Year Outcomes of Critical Care Patients Post-COVID-19 Multisystem Inflammatory Syndrome in Children | JAMA Pediatr / Research Letter | <ul style="list-style-type: none"> • Small UK study, 12 month follow up of 68 of 76 patients (89%) of initial surviving cohort with PIMS-TS or MIS-C . |

- Data identify a group of patients with a risk of significant long-term morbidity, the majority had good outcomes with no significant medium- or long-term sequelae.

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Epidemiology and clinical - long-term complications / sequelae

| Publication Date | Title/URL | Journal / Article type | Digest |
|------------------|--|---|--|
| 31.08.2021 | Increasing incidence of parosmia and phantosmia in patients recovering from COVID-19 smell loss | medRxiv (non-peer reviewed) / Article | <ul style="list-style-type: none"> • Longitudinal survey of individuals suffering COVID-19-related smell loss assessed disease symptoms and gustatory and olfactory function: 12,313 completed an initial survey (S1) between April and September 2020, and 27.5% (n=3,386) completed a follow-up survey (S2) between September 2020 and February 2021 • On follow-up (median ~200 days since COVID-19 onset), ~60% of women and ~48% of men reported less than 80% of their pre-illness smell ability. • Taste typically recovered faster than smell, and taste loss rarely persisted if smell recovered. • Prevalence of parosmia and phantosmia was ~10% of participants in S1 and increased substantially in S2: ~47% for parosmia and ~25% for phantosmia. • Persistent smell impairment was associated with more symptoms overall, suggesting it may be a key marker of long-COVID. • During COVID-19 illness, ability to smell was slightly lower among those who did not recover their pre-illness ability to smell at S2. |
| 02.09.2021 | Long COVID - the physical and mental health of children and non-hospitalised young people 3 months after SARS-CoV-2 infection; a national matched cohort study (The CLoCk) Study | Research Square (non-peer reviewed) / Article | <ul style="list-style-type: none"> • Describes post-COVID symptomatology after three months in a national sample of 3,065 children and young people (CYP; 11-17 years old) with PCR-confirmed SARS-CoV-2 infection compared to 3,739 test-negative controls. • At PCR-testing, 35.4% of test-positives and 8.3% of test-negatives had any symptoms whilst 30.6% and 6.2%, respectively, had 3+ symptoms. • At 3 months post-testing, 66.5% of test-positives and 53.3% of test-negatives had any symptoms, whilst 30.3% and 16.2%, respectively, had 3+ symptoms. • Latent class analysis identified two classes, characterised by “few” or “multiple” symptoms; this latter class was more frequent among test- |

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| | | | positives, females, older CYP and those with worse pre-test physical and mental health. |
| 02.09.2021 | Evolution of COVID-19 symptoms during the first 12 months after illness onset | Clin Infect Dis / Article | <ul style="list-style-type: none"> • Findings from the RECoVERED Study, a prospective cohort study with 342 adult participants show that post-COVID syndrome is common, even after mild disease • 12 months after symptom onset, 40% of participants continued to report ≥1 symptom. This proportion rose to 86.7% in those with severe/critical disease • The recovery of female participants was 35% slower than the males, and obese participants recovered 38% slower than those of normal weight, making female sex and obesity the strongest predictors of a slow recovery |

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Epidemiology and clinical – risk factors

| Publication Date | Title/URL | Journal / Article type | Digest |
|------------------|--|---------------------------|---|
| 01.09.2021 | Penetration and impact of COVID-19 in long term care facilities in England: population surveillance study | Int J Epidemiol / Article | <ul style="list-style-type: none"> • Lab-confirmed SARS-CoV-2 cases in England, notified to Public Health England 01.01.20 - 25.12.20 matched to residential property classifications. • Cases identified in 69.5% of all long-term care facilities (LTCF); 33.1% experiencing multiple outbreaks. • 67% increased odds of death in residents compared with those not residing in LTCFs. • 20,544 associated deaths in residents; 31.3% of all COVID-19 deaths occurred in this setting in spite of early policies. |
| 01.09.2021 | Risk of hospital admission with covid-19 among teachers compared with healthcare workers and other adults of working age in Scotland, March 2020 to July 2021: population based case-control study | BMJ / Research | <ul style="list-style-type: none"> • All COVID-19 cases in adults aged 21 to 65 (n=132 420) in Scotland, March 2020 - July 2021. • Comparator groups to active teachers were healthcare workers and their household members / remaining general population of working age. • Compared with adults of working age who are otherwise similar, teachers and their household members: (i) not at increased risk of hospital admission with covid-19; (ii) at lower risk of severe covid-19. |

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| 27.08.2021 | Pre-existing health conditions and severe COVID-19 outcomes: an umbrella review approach and meta-analysis of global evidence | BMC Med / Research article | <ul style="list-style-type: none"> • Umbrella review, summarising global evidence on risk of severe COVID-19 outcomes in patients with pre-existing health conditions. Includes 160 primary studies from 120 systematic reviews until 11 Dec 2020. • Diabetes, obesity, heart failure, COPD and dementia associated with fatal COVID-19 in different regions, although the estimates varied. • Evidence from Europe and North America showed liver cirrhosis and active cancer also associated with increased risk of death. |
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Epidemiology and clinical – other

| Publication Date | Title/URL | Journal / Article type | Digest |
|------------------|--|-------------------------------------|--|
| 31.08.2021 | Association Between COVID-19 and Myocarditis Using Hospital-Based Administrative Data — United States, March 2020–January 2021 | MMWR Morb Mortal Wkly Rep / Article | <ul style="list-style-type: none"> • Cohort study used data from a large hospital-based US database; monthly number of myocarditis and COVID-19 inpatient encounters was assessed before and during the COVID-19 pandemic (January 2019 through May 2021); patients receiving vaccination during December 2020–February 2021 were excluded, as were those for whom information on sex was missing. • During March 2020–January 2021, patients with COVID-19 had nearly 16 times the risk for myocarditis compared with patients who did not have COVID-19, and risk varied by sex and age. |
| 27.08.2021 | Outbreak Associated with SARS-CoV-2 B.1.617.2 (Delta) Variant in an Elementary School — Marin County, California, May–June 2021. | MMWR Morb Mortal Wkly Rep / Article | <ul style="list-style-type: none"> • 26 COVID-19 cases among Marin County elementary school students and their contacts 23.05.21–12.06.21 following exposure to an unvaccinated infected teacher. • 50% attack rate in one affected classroom; risk correlated with seating proximity to the teacher. |

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Infection control / non-pharmaceutical interventions

| Publication Date | Title/URL | Journal / Article type | Digest |
|------------------|---|--|---|
| 01.09.2021 | The Impact of Community Masking on COVID-19: A Cluster-Randomized Trial in Bangladesh | Innovations for Poverty Action (non-peer reviewed) / Working Paper | <ul style="list-style-type: none"> Cluster-randomized trial of community-level mask promotion in rural Bangladesh, Nov 2020 to April 2021 (N=600 villages, N=342,126 adults). Authors cross-randomized mask promotion strategies at village and household level, including cloth vs. surgical masks. Intervention led to a 9.3% reduction in symptomatic SARS-CoV-2 seroprevalence (corresponds to 103 fewer symptomatic seropositives) / 11.9% reduction in prevalence of COVID-like symptoms, corresponding to 1,587 fewer people reporting these symptoms. Effects substantially larger in villages randomized to receive surgical masks (n = 200). Relative reduction in symptomatic seroprevalence 11% overall, 23% among individuals aged 50-60, and 35% among those over 60. |
| 03.09.2021 | Screening Programs for SARS-CoV-2 Infections on a University Campus - Austin, Texas, September 30-November 30, 2020 | MMWR Morb Mortal Wkly Rep / Article | <ul style="list-style-type: none"> A targeted screening program at a university in Texas, USA focussed on Big Ticket holders (students with season tickets to athletic events). In total 48 cases of COVID-19 were identified in this group during September–November 2020, 18 (38%) of which were in asymptomatic persons. This population of infected students was demographically different from those identified through clinical or community testing programs, more risk-tolerant, and less willing to participate in public health prevention activities. |

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Transmission

| Publication Date | Title/URL | Journal / Article type | Digest |
|------------------|--|------------------------|--|
| 30.08.2021 | Healthcare-associated COVID-19 in England: a national data linkage study | J Infect / Article | <ul style="list-style-type: none"> Analysed admission records for all hospitals in England and SARS-CoV-2 national test data for the period 1 March to 31 August 2020 Findings suggest up to 1 in 6 SARS-CoV-2 infections among hospitalised patients with COVID-19 during the study period could be attributed to nosocomial transmission, but these represent less than 1% of an estimated 3 million COVID-19 cases. Preprint previously included |

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| 02.08.2021 | Factors Associated With Household Transmission of SARS-CoV-2: An Updated Systematic Review and Meta-analysis | JAMA Netw Open / Systematic review | <ul style="list-style-type: none"> • Updated systematic review (20.10.2020 - 17.06.2021) and meta-analysis of 87 studies representing 1 249 163 household contacts from 30 countries • Estimated household secondary attack rate was 19%. • Recent studies have generated higher household secondary attack rate estimates; potential explanations include improved diagnostic procedures and tools, more contagious variants, and different study locations. |
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Treatment

| Publication Date | Title/URL | Journal / Article type | Digest |
|------------------|---|---------------------------------------|---|
| 02.09.2021 | Ivermectin for Prevention and Treatment of COVID-19 Infection: A Systematic Review, Meta-analysis, and Trial Sequential Analysis to Inform Clinical Guidelines. | Am J Ther / Systematic review | <ul style="list-style-type: none"> • Systematic review of 24 randomized controlled trials with 3406 participants. Meta-analysis of 15 trials found that ivermectin reduced the risk of death compared with no ivermectin • Evidence of moderate certainty finds that large reductions in COVID-19 deaths are possible using ivermectin; used early in the clinical course it may reduce progression to severe disease. • The safety profile and low cost of ivermectin suggest that it is likely to have a significant impact on the SARS-CoV-2 pandemic globally. |
| 28.08.2021 | Association between tocilizumab, sarilumab and all-cause mortality at 28 days in hospitalized patients with COVID-19: A network meta-analysis | medRxiv (non-peer reviewed) / Article | <ul style="list-style-type: none"> • Meta-analysis based on 898 eligible patients (278 deaths) from REMAP-CAP and 3710 eligible patients from 18 trials (1278 deaths) from the prospective meta-analysis. • Summary ORs for 28-day mortality were similar for tocilizumab (0.82) and sarilumab (0.80) compared with usual care or placebo. The summary OR for 28-day mortality comparing tocilizumab with sarilumab was 1.03. The association is not dependent on the choice of interleukin-6 receptor antagonist. |
| 01.09.2021 | Efficacy and safety of baricitinib for the treatment of hospitalised adults with COVID-19 (COV-BARRIER): a randomised, double-blind, parallel-group, placebo-controlled phase 3 trial | Lancet Respir Med / Article | <ul style="list-style-type: none"> • International Phase 3, double-blind, placebo-controlled trial: 1525 hospitalised adults with COVID-19 randomly assigned to baricitinib (n=764) or placebo group (n=761). • Results suggest baricitinib reduces 28-day and 60-day mortality when used in addition to current standard of care (including systemic corticosteroids, e.g. dexamethasone, and antivirals, e.g. remdesivir). • Baricitinib and placebo groups had similar safety profiles. |

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| | | | <ul style="list-style-type: none"> • Associated comment: https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00358-1/fulltext |
| 28.08.2021 | Effect of losartan on hospitalized patients with COVID-19-induced lung injury: A randomized clinical trial | medRxiv (non-peer reviewed) / Article | <ul style="list-style-type: none"> • Randomised trial of hospitalised COVID-19 patients with respiratory sequential organ failure assessment score of at least 1 and not already taking a renin-angiotensin-aldosterone system (RAAS) inhibitor: 101 were assigned to losartan (50 mg PO twice daily for 10 days) and 104 to placebo. • Compared to placebo, losartan did not significantly affect the ratio of imputed partial pressure of oxygen to fraction of inspired oxygen (PaO₂/FiO₂) at 7 days [difference of -24.8]. • Losartan did not improve any secondary clinical outcome, but worsened vasopressor-free days. |
| 01.09.2021 | Fostamatinib for the treatment of hospitalized adults with COVID-19 A randomized trial | Clin Infect Dis / Article | <ul style="list-style-type: none"> • 30 patients were treated with fostamatinib and 29 with placebo in trial to test hypothesis that this novel spleen tyrosine kinase inhibitor, will ameliorate Fc activation and attenuate harmful effects of the immune response to SARS-CoV-2 • Serious adverse events occurred in 10.5% of patients in the fostamatinib group compared to 22% in the placebo group. Three deaths occurred by day 29, all in the placebo group • The addition of fostamatinib to standard of care was well tolerated and associated with improved clinical outcomes compared to placebo |

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Modelling

| Publication Date | Title/URL | Journal / Article type | Digest |
|------------------|--|---------------------------------|--|
| 31.08.2021 | The association of community mobility with the time-varying reproduction number (R) of SARS-CoV-2: a modelling study across 330 local UK authorities | Lancet Digital Health / Article | <ul style="list-style-type: none"> • UK study linking data on community mobility from Google with data on R from 330 UK local authorities, 01.06.2020 - 13.02.2021. • Increasing trend for first 6 weeks of 2021 in effect of visits to retail and recreation places and workplaces on R. • Increased visits to retail and recreation places, workplaces, transit stations in cities are important drivers of transmission, new variants may further amplify these. |

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| 30.08.2021 | Analysis of alternative Covid-19 mitigation measures in school classrooms: an agent-based model of SARS-CoV-2 transmission | medRxiv (non-peer reviewed) / Article | <ul style="list-style-type: none"> • Model is applied to re-examine Covid-19 in schools in the UK in autumn 2020, and to forecast infection levels in autumn 2021 when Delta variant is likely to dominate. • Results suggest that testing-based surveillance of infections with isolation of positive cases is more effective than bubble quarantine both for reducing transmission in schools and for avoiding pupil absence, even accounting for insensitivity of self-administered tests. |
| 01.09.2021 | Augmenting contact matrices with time-use data for fine-grained intervention modelling of disease dynamics: A modelling analysis | Stat Methods Med Res / Article | <ul style="list-style-type: none"> • Combining data of two large-scale population-wide surveys allowed for more fine-grained intervention modelling; the derived contact matrices were applied in a dynamic-transmission model to explore the impact on the COVID-19 pandemic • Findings indicated that most physical contacts in those aged 0–24 years were associated with schools or institutes of higher learning. For adults aged 25–64 years, closing workplaces has the highest effect on reducing physical contact. For those aged 65+ years, reducing the number of social visits has the highest impact on reduced contacts, with a comparable reduction also in adolescents and young adults (aged 16–24 years). • Whilst the predicted impact of fewer contacts in parks, bars/cafes/restaurants, and non-essential shopping is small, changes in mixing patterns and time use particularly immediately after permitting social activities again may pose increased short-term transmission risks. |
| 27.08.2021 | A pre-registered short-term forecasting study of COVID-19 in Germany and Poland during the second wave | Nat Commun / Article | <ul style="list-style-type: none"> • Thirteen modelling teams from Germany, Poland, Switzerland, the United Kingdom and the United States contributed forecasts of weekly confirmed cases and deaths, from 12.10.2020 – 19.12.2020, the second pandemic wave in Germany and Poland • Over the course of 10 weeks, some models achieved better average scores than others, while relative performance has been fluctuating; considerable heterogeneity was found between forecasts from different models and a tendency to overconfident forecasting • This evaluation finds different models may be best suited to different phases of an epidemic and highlights the importance of considering several independently run models rather than focusing attention on a single one, as is sometimes the case in public discussions. |

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Guidance and consensus statements

| Publication Date | Title/URL | Journal / Article type |
|------------------|--|--|
| 01.09.2021 | Joint Committee on Vaccination and Immunisation (JCVI) advice on third primary dose vaccination [for severely immunosuppressed people] | Gov.uk / Independent report |
| 27.08.2021 | SPI-M-O: Consensus statement on COVID-19, 11 August 2021 NOTE: Includes return to schools | Gov.uk (non-peer reviewed) / Research and analysis |

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Overviews, comments and editorials

| Publication Date | Title/URL | Journal / Article type |
|------------------|--|---|
| 02.09.2021 | Covid-19: 80% of young adults in UK are likely to have antibodies, data suggest | BMJ / News |
| 01.09.2021 | Cellular host factors for SARS-CoV-2 infection | Nat Microbiol / Review Article |
| 30.08.2021 | SARS-CoV-2 variants with shortened incubation periods necessitate new definitions for nosocomial acquisition | J Infect / Correspondence |
| 27.08.2021 | US COVID origins report: researchers pleased with scientific approach | Nature / News |
| 24.08.2021 | Testing indicators to monitor the COVID-19 pandemic | Lancet Infect Dis / Comment |
| 06.07.2021 | Unequal pandemic, fairer recovery: the COVID-19 impact inquiry report | Health Foundation / Report |
| 02.09.2021 | Review Article: Vaccination for patients with inflammatory bowel disease during the COVID-19 pandemic | Aliment Pharmacol Ther / Review Article |
| 24.08.2021 | Making COVID-19 vaccinations accessible for people with disabilities | Vaccine / Commentary |
| 02.09.2021 | Ronapreve for prophylaxis and treatment of covid-19 | BMJ / Editorial |

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