



UK Health
Security
Agency

COVID-19 Literature Digest – 07/01/2022

Dear all,

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

UKHSA'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 The reports include both preprints, which should be treated with caution as they are NOT peer-reviewed and may be subject to change, and also research that has been subject to peer review and wider scrutiny.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 UKHSA. We do not accept responsibility for the availability, reliability or content of the items included in this resource.

To join our email distribution list, or to be removed, 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 Behavioural Sciences Weekly Report.

Best wishes,

Emma Farrow, James Robinson

On behalf of the UKHSA COVID-19 Literature Digest Team

Report for 07.01.2022 (please note that papers that have **NOT been peer-reviewed** are highlighted in red).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
22.12.2021	Children develop robust and sustained cross-reactive spike-specific immune responses to SARS-CoV-2 infection	Nat Immunol / Article	<ul style="list-style-type: none">• Authors compare antibody and cellular immunity in 91 children (aged 3–11 years) and 154 adults in England.• Children displayed high antibody responses against spike protein, and seroconversion boosted responses against seasonal Beta-coronaviruses via cross-recognition of S2 domain.• Neutralisation of viral variants comparable between children and adults.• Spike-specific T cell responses two-fold higher in children and detected in many seronegative children, suggesting pre-existing cross-reactive responses to seasonal coronaviruses.• Children retained antibody and cellular responses 6 months after infection, compared to relative waning in adults. Spike-specific responses were broadly stable beyond 12 months.• Associated comment: https://www.nature.com/articles/s41590-021-01094-x
03.01.2022	The hyper-transmissible SARS-CoV-2 Omicron variant exhibits significant antigenic change, vaccine escape and a switch in cell entry mechanism	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none">• UK authors demonstrate substantial immune escape of Omicron, with clear evidence of vaccine failure in dual vaccinated individuals and partial restoration of immunity following a third booster dose of mRNA vaccine.• Immunity from natural infection (without vaccination) is more protective than two vaccine doses, but inferior to three doses.
05.01.2022	Protection afforded by prior infection against SARS-CoV-2 reinfection with the Omicron variant	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none">• Authors estimated effectiveness of prior infection in preventing reinfection (PES) with Omicron and other variants in Qatar, using a test-negative, case-control study design.• PES against symptomatic reinfection estimated at 90.2% for Alpha, 84.8% Beta, 92.0% Delta, and 56.0% Omicron.• Protection afforded by prior infection in preventing symptomatic reinfection with Alpha, Beta, or Delta is robust, at about 90%. Lower with Omicron, at nearly 60%.
21.12.2021	Elevated temperature inhibits SARS-CoV-2 replication in respiratory epithelium independently of IFN-mediated innate immune defenses	PLoS Biol / Article	<ul style="list-style-type: none">• 3D modelling found that respiratory tissue incubated at 40°C remained permissive to SARS-CoV-2 entry but refractory to viral transcription, significantly reducing levels of viral RNA replication and apical shedding of infectious virus.

			<ul style="list-style-type: none"> • Presents the first evidence that febrile temperatures (38 to 41°C) associated with COVID-19 inhibit SARS-CoV-2 replication in respiratory epithelia.
23.12.2021	Humoral and cellular immune responses to two and three doses of SARS-CoV-2 vaccines in rituximab-treated patients with rheumatoid arthritis: a prospective, cohort study	Lancet Rheumatol / Article	<ul style="list-style-type: none"> • Norwegian prospective, cohort study: humoral/cellular immunity after 2-3 vaccine doses in 87 rituximab-treated patients with rheumatoid arthritis / 1114 healthy controls. • 19/87 (21·8%) had a serological response after two doses, compared to 1096 (98·4%) of control group. • 10/19 (53%) had CD4+ T-cell responses, 14 (74%) had CD8+ T-cell responses. • Time since last rituximab infusion / vaccine type were significantly associated with serological response. • 3rd dose induced serological responses in 8/49 (16·3%), but induced CD4+ and CD8+ T-cell responses in all patients assessed (n=12), including responses to Delta [B.1.617.2]. • Third dose 6–9 months after a rituximab infusion may not induce a serological response, but could boost cellular immune response. • Linked comment: https://doi.org/10.1016/S2665-9913(21)00418-5
27.12.2021	Omicron infection enhances neutralizing immunity against the Delta variant	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • South African study: 15 previously vaccinated and unvaccinated people infected with Omicron. • Ability to neutralize Omicron and Delta virus at enrolment versus a median of 14 days after enrolment measured. • Neutralization of Omicron increased 14-fold; Delta virus neutralization also increased 4·4-fold. • Vaccinated participants had better neutralizing response against Delta; more variable in unvaccinated. • Unclear if effective cross-neutralization of Delta by Omicron elicited antibodies, or activation of antibody immunity from previous infection and/or vaccination.
04.01.2022	T cell reactivity to the SARS-CoV-2 Omicron variant is preserved in most but not all prior infected and vaccinated individuals	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • US authors assessed cross-reactivity of T cell responses to Omicron in 76 adults. • Distinct proportion with prior infection and/or vaccination had substantially reduced T cell reactivity to Omicron (but not Delta). • 21·2% (10/47) had a >50% reduction in T cell response to Omicron spike. • Booster did not completely mitigate reduced T cell reactivity to Omicron.
30.12.2021	Preferential expansion upon boosting of cross-reactive “pre-existing” switched memory B cells that recognize the SARS-CoV-2 Omicron variant Spike protein	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Authors show that pre-existing memory B cell compartments are main source of cross-reactive Omicron variant RBD-recognizing B cells • After a booster, these give rise to (i) induced, activated, durable, switched memory B cell populations; (ii) non-durable, transiently activated, antigen-specific B cells; induced by vaccination and/or infection.

			<ul style="list-style-type: none"> • Two pre-existing, cross-reactive, resting switched memory B cell compartments (CD27- and CD27+) in unvaccinated and uninfected individuals already contain memory B cells against non-RBD portions of wild type and Omicron spike proteins.
22.12.2021	Prolonged activation of nasal immune cell populations and development of tissue-resident SARS-CoV-2-specific CD8(+) T cell responses following COVID-19	Nat Immunol / Letter	<ul style="list-style-type: none"> • Authors characterise nasal and systemic immune cells using samples from 29 individuals with COVID-19 and 12 healthy donors • During acute COVID-19 increased nasal granulocytes, monocytes, CD11c(+) natural killer (NK) cells and CD4(+) T effector cells were observed. • Mucosal proinflammatory populations positively associated with peripheral blood human leukocyte antigen-DR(low) monocytes, CD38+PD1+CD4+T effector cells and plasmablasts. • Nasal immune cells mostly normalised following convalescence, except for CD127+ granulocytes and CD38+CD8+ tissue-resident memory T cells. • SARS-CoV-2-specific CD8+ T cells persisted at least 2 months after viral clearance in the nasal mucosa.
28.12.2021	Evidence for increased SARS-CoV-2 susceptibility and COVID-19 severity related to pre-existing immunity to seasonal coronaviruses	Cell Rep / Report	<ul style="list-style-type: none"> • Study using pre-pandemic sera from 888 healthy adults and sera longitudinally collected from 96 COVID-19 patients. • Authors monitored IgG-type antibody levels against nucleocapsid and spike S1 domain of SARS-CoV-2 and all four seasonal coronaviruses, and against full-length spike protein of SARS-CoV-2, HCoV-NL63, and HCoV-OC43. • Findings suggest pre-existing, anti-nucleocapsid antibodies against endemic α-coronaviruses and S2 domain-specific anti-spike antibodies against β-coronavirus HCoV-OC43 are elevated in patients with COVID-19 compared to pre-pandemic donors (particularly pronounced in males and critically ill patients). • Suggests pre-existing immunity to seasonal coronaviruses may increase susceptibility to SARS-CoV-2 and predispose individuals to adverse COVID-19 outcome.

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Vaccines

Publication Date	Title/URL	Journal / Article type	Digest
04.01.2022	Real-world Effectiveness of the Pfizer-BioNTech BNT162b2 and Oxford-AstraZeneca ChAdOx1-S Vaccines Against SARS-CoV-2 in Solid	Transplantation / Article	<ul style="list-style-type: none"> • Retrospective study of SARS-CoV-2 infections/deaths among solid organ and islet transplant (SOT) recipients in England (01.09.2020 to 31.08.2021) • In this cohort 39,260 (90.3%) had 2 vaccine doses, 1141 (2.6%) had 1 vaccine dose, and 3080 (7.1%) were unvaccinated.

	Organ and Islet Transplant Recipients		<ul style="list-style-type: none"> • Vaccination was not associated with reduction in risk of testing positive for SARS-CoV-2 (risk-adjusted infection incidence rate ratio=1.29) • Overall hazard ratio for death within 28 days of SARS-CoV-2 infection was 0.80, suggesting 20% risk reduction for death in vaccinated patients. • Two doses of Oxford-AstraZeneca were associated with significantly reduced risk of death (hazard ratio, 0.69), while vaccination with Pfizer-BioNTech was not (0.97).
20.12.2021	Reduced neutralisation of SARS-CoV-2 omicron B.1.1.529 variant by post-immunisation serum	Lancet / Correspondence	<ul style="list-style-type: none"> • UK authors report substantial decrease in neutralisation titre in recipients of both homologous ChAd and BNT primary courses, with evidence of some recipients not neutralising at all. • Given Omicron's antigenic distance from ancestral strains, tailored vaccines may be needed, but are unlikely to give protection against previous strains • Current monovalent vaccine strategy may switch towards multivalent formulations currently used in seasonal influenza vaccines.
22.12.2021	Severity of Omicron variant of concern and vaccine effectiveness against symptomatic disease: national cohort with nested test negative design study in Scotland	University of Edinburgh (not peer reviewed) / Preprint	<ul style="list-style-type: none"> • By 19.12.2021 there were 23,840 S gene negative cases in Scotland, UK [SGN; indicative of Omicron variant], predominantly in 20-39 year-old group (11,732; 49.2%). • Proportion of possible reinfections among SGN cases was 10-fold greater than that of S gene positive [SGP; indicative of Delta variant]. • Total of 15 hospital admissions among SGN (adjusted observed/expected ratio=0.32). • Third/booster vaccine dose associated with 57% reduction in risk of SGN symptomatic infection relative to ≥25 weeks post second dose.
20.12.2021	Moderna Announces Preliminary Booster Data and Updates Strategy to Address Omicron Variant	Moderna (non-peer reviewed) / News	<ul style="list-style-type: none"> • Study of sera from 40 Moderna COVID-19 booster recipients suggests 50 µg or 100 µg booster increases Omicron neutralising antibody levels approximately 37-fold and 83-fold, respectively. • Moderna will continue to advance an Omicron-specific booster (mRNA-1273.529) to clinical trials.
30.12.2021	Johnson & Johnson COVID-19 Vaccine Demonstrates 85 Percent Effectiveness against Hospitalization in South Africa when Omicron was Dominant	Johnson & Johnson (non-peer reviewed) / Press Release	<ul style="list-style-type: none"> • Johnson & Johnson preliminary results from two studies: (i) South African Phase 3b Sisonke study: homologous Ad26.COVID.S (Janssen) booster demonstrated 85% effectiveness against COVID-19-related hospitalization, among healthcare workers after Omicron became dominant. (ii) Separate analysis of immune response, conducted by Beth Israel Deaconess Medical Center: a heterologous Ad26.COVID.S booster in individuals who initially received BNT162b2 (Pfizer) vaccine generated a 41-fold increase in neutralizing antibody responses by four weeks following the boost and a 5-fold increase in CD8+ T-cells to Omicron by two weeks.
06.01.2022	Serological responses to COVID-19 Comirnaty booster vaccine, London,	Euro Surveill / Rapid Communication	<ul style="list-style-type: none"> • Serum samples were collected pre- and post-booster vaccination with Comirnaty [Pfizer-BioNTech] in 626 participants (aged ≥ 50 years) who had received two

	United Kingdom, September to December 2021		<p>Comirnaty doses (< 30 days or ≥30 days apart), or two Vaxzevria [Oxford-Astrazeneca] doses (≥ 30 days apart).</p> <ul style="list-style-type: none"> • Spike antibody GMTs peaked 2–4 weeks after second dose, fell significantly ≤ 38 weeks later and rose above primary immunisation GMTs 2–4 weeks post-booster, regardless of primary vaccine type/schedule. • Higher post-booster responses observed with a longer interval between primary immunisation and boosting.
15.12.2021	Efficacy and Safety of NVX-CoV2373 in Adults in the United States and Mexico	N Engl J Med / Article	<ul style="list-style-type: none"> • US Phase 3 trial: participants randomised to receive two doses of NVX-CoV2373 (Novavax; n=19,714) protein-based vaccine or placebo (n=9868) 21 days apart. • 77 Covid-19 cases (14 among vaccine / 63 among placebo groups); vaccine efficacy (VE) was 90.4%. • All moderate-to-severe cases occurred in placebo recipients (VE 100%). • Most sequenced viral genomes (48/61, 78.7%) were variants of concern/interest (VOC/VOI), mainly represented by Alpha; VE against any VOC/VOI was 92.6%. • Reactogenicity was mostly mild-to-moderate and transient; more frequent in NVX-CoV2373 recipients and after second dose. • Preprint previously included.
22.12.2021	Rapid increase in Omicron infections in England during December 2021: REACT-1 study	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • In December 2021, highest-ever recorded numbers of daily SARS-CoV-2 infections in England. • First Omicron infection detected in London on 3.12.2021; rapid increase (vs Delta, Delta sub-lineages) with daily increase of 66.0% in the odds of Omicron infection. • Large fall in swab positivity among mostly vaccinated older children (12-17 years) compared with unvaccinated younger children (5-11 years), and in adults who received a third vs. two doses of vaccine. • Associated press release: https://www.gov.uk/government/news/latest-react-1-findings-show-omicron-infections-rising-fast-while-highlighting-success-of-vaccination-programmes
29.12.2021	Vaccine effectiveness against hospital admission in South African health care workers who received a homologous booster of Ad26.COVID during an Omicron COVID19 wave: Preliminary Results of the Sisonke 2 Study	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • The Sisonke 2 study estimated vaccine effectiveness (VE) of a Janssen vaccine booster in 69,092 South African healthcare workers (HCW) during a period of omicron variant circulation [08.11.2021 to 17.12.2021], compared to unvaccinated individuals. • After adjusting for confounders, findings suggest that VE for hospitalisation increased over time since booster dose (63% at 0-13 days; 84% at 14-27 days; and 85% at 1-2 months).
23.12.2021	Final efficacy analysis, interim safety analysis, and immunogenicity of a single dose of recombinant novel coronavirus vaccine (adenovirus type	Lancet / Article	<ul style="list-style-type: none"> • Authors report results on final efficacy and interim safety analyses of this phase 3 trial of Ad5-nCoV, a single-dose adenovirus type 5 (Ad5) vectored vaccine.

	5 vector) in adults 18 years and older: an international, multicentre, randomised, double-blinded, placebo-controlled phase 3 trial		<ul style="list-style-type: none"> • One dose of Ad5-nCoV showed a 57.5% efficacy against symptomatic COVID-19 infection at 28 days or more postvaccination (21 250 participants; 45 days median duration of follow-up). • Associated comment: https://doi.org/10.1016/S0140-6736(21)02834-8
20.12.2021	Cellular and humoral functional responses after BNT162b2 mRNA vaccination differ longitudinally between naive and subjects recovered from COVID-19	Cell Rep / Report	<ul style="list-style-type: none"> • Examines vaccine-induced [Pfizer-BioNTech] immune responses in 16 naive participants and 11 participants recovered from Covid-19 ('recovered group'). • Blood samples taken before vaccination, after first dose, 14 days, and approximately 8 months after vaccination. • Plasma spike (S)-specific immunoglobulins peak after one vaccine dose in recovered group, while a second dose is needed in naive group. • Comparable neutralising antibodies and S-specific B cell levels late post-vaccination in both groups. • Naive group exhibit higher SARS-CoV-2-specific cytokine production, CD4+ T cell activation, and proliferation than recovered group; however, approximately 8 months post-vaccination, SARS-CoV-2-specific responses were comparable between the groups.
23.12.2021	Immunogenicity and Safety Following a Homologous Booster Dose of a SARS-CoV-2 recombinant spike protein vaccine (NVX-CoV2373): A Phase 2 Randomized Placebo-Controlled Trial	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Novavax reports phase 2 trial results. • Single booster dose of NVX-CoV2373 administered approximately 6 months after primary series induced a substantial increase in humoral antibodies that was >4-fold higher than antibody titers associated with high levels of efficacy in two phase 3 studies. • For prototype strain and select variants (Alpha, Beta, Delta and Omicron), post-booster immune responses were notably higher than those associated with high levels of efficacy in phase 3 NVX-CoV2373 studies. • Press release: https://ir.novavax.com/2021-12-22-Novavax-Announces-Initial-Omicron-Cross-Reactivity-Data-from-COVID-19-Vaccine-Booster-and-Adolescent-Studies

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Diagnosics and genomics

Publication Date	Title/URL	Journal / Article type	Digest
05.01.2022	SARS Antibody Testing in Children: Development of Oral Fluid Assays for IgG Measurements	Microbiol Spectr / Article	<ul style="list-style-type: none"> • Reports first large-scale assessment of the suitability of oral fluids for detection of SARS-CoV-2 antibody obtained from healthy children attending school, as well as adults. • The sample type (gingiva-crevicular fluid) can be self-collected.

			<ul style="list-style-type: none"> • Anti-NP IgG capture assay performed best: overall sensitivity/specificity of 75% and 99% compared with paired serum antibodies. • Sensitivity observed in children (80%) was higher than in adults (67%). • Overall, data indicates oral fluid assays are suitable for population-based sero-epidemiology studies in children and highly acceptable in children/adults.
29.12.2021	Omicron and S-Gene Target Failure Cases in the Highest COVID-19 Case Rate Region in Canada - December 2021	J Med Virol / Letter	<ul style="list-style-type: none"> • Omicron first detected in Kingston, Frontenac, Lennox & Addington region of Canada on 03.12.2021. As of 21.12.2021, 1574 active cases. • 59% were 18-24 year olds, 27% 25-39 years olds. Main outbreaks in post-secondary education (N=64), food & beverage settings (N=106). • Main reported symptoms were nasal congestion (73%), cough (65%); only 10% reported shortness of breath. 9.6% were asymptomatic. • There were 12 re-infections with Omicron, all were symptomatic and double-vaccinated.
17.12.2021	SARS-CoV-2 Omicron spike mediated immune escape, infectivity and cell-cell fusion	bioRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Compared to Delta, Omicron BA.1 confers very significant evasion of therapeutic monoclonal and vaccine-elicited polyclonal neutralising antibodies after two doses. • Longitudinal serum samples from double vaccinated individuals: (i) BNT162b2 [Pfizer] >10-fold loss of neutralisation against Omicron compared to Delta; (ii) mRNA 1273 [Moderna] similar; (iii) ChAdOx-1 [AstraZeneca] no neutralisation detectable for the majority; (iv) Coronavac 0/9 had detectable neutralisation. • mRNA booster rescues and broadens neutralisation in short term. • Antiviral drugs remdesevir and molnupiravir retain efficacy against Omicron BA.1. • Omicron spike is relatively poorly cleaved, shows impaired entry and replication in lung cells expressing TMPRSS2.
31.12.2021	The SARS-CoV-2 variant, Omicron, shows rapid replication in human primary nasal epithelial cultures and efficiently uses the endosomal route of entry	bioRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Authors show Omicron replicates rapidly in human primary airway cultures, more so even than Delta. • Spike still uses human ACE2 as primary receptor (+ other species ACE2), binds more strongly than other variants. • Appears less reliant on TMPRSS2 for cell entry; can enter some cell types more efficiently using endosomal route. • May replicate more at transmission site, not deeper lung, so shift to efficient transmission / away from severe disease.
28.12.2021	Comparison of infectious SARS-CoV-2 from the nasopharynx of vaccinated and unvaccinated individuals	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • US study: levels of infectious virus in 125 patients, 72 vaccinated / 53 unvaccinated, with no significant differences in titers of virus. • Proportion of nasopharyngeal samples with culturable virus 21% in vaccinated patients Vs. 40% in unvaccinated. • Sampling July to August 2021, when Delta dominant and pre-Omicron

Epidemiology and clinical - children and pregnancy

Publication Date	Title/URL	Journal / Article type	Digest
20.12.2021	Risk factors for PICU admission and death among children and young people hospitalized with COVID-19 and PIMS-TS in England during the first pandemic year	Nat Med / Article	<ul style="list-style-type: none"> Examines data for all hospitalisations among children and young people (CYP; 0–17 years) in England from 01.02.2019 to 31.01.2021. There were 6,338 hospitalisations with COVID-19, of which 259 were admitted to a paediatric intensive care unit (PICU) and eight died. There were 712 hospitalisations with paediatric inflammatory multi-system syndrome temporally associated with SARS-CoV-2 (PIMS-TS), of which 312 were admitted to a PICU and fewer than five died. Hospitalisations with COVID-19 and PIMS-TS were more common among males, older CYP, those from socioeconomically deprived neighbourhoods, and those of non-White ethnicity (Black, Asian, Mixed or Other).
17.12.2021	Risk of SARS-CoV-2 testing, PCR-confirmed infections and COVID-19-related hospital admissions in children and young people: birth cohort study	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> Epidemiology of SARS-CoV-2 in children and young people (CYP) aged <23 years; cohort of all Scottish births since 1997 (1,226,855 CYP). Infants had highest COVID-19-related admission rates. Chronic conditions, particularly multiple types, strongly associated with admissions across all ages. 89% of admitted children had no chronic conditions recorded. CYP COVID-19-related hospital admissions 2% - 1/3rd of rates in adults >45 years (depending on age group)
21.12.2021	Rapid rise in paediatric COVID-19 hospitalisations during the early stages of the Omicron wave, Tshwane District, South Africa	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> 6,287 paediatric (≤ 19 years) COVID-19 cases recorded in Tshwane District, South Africa, 31.10.2021 - 11.12.2021. 462 (7.2%) were hospitalized in 42 hospitals (18% of overall admissions); of 75 viral specimens sequenced, 99% were Omicron. Young children (0-4 years) were most affected. Length of hospital stay was short (mean 3.2 days). Seven children were ventilated; four children died, all related to complex underlying co-pathologies.
31.12.2021	COVID-19 Vaccine Safety in Children Aged 5-11 Years - United States, November 3-December 19, 2021	MMWR Morb Mortal Wkly Rep / Article	<ul style="list-style-type: none"> US CDC preliminary safety findings following administration of approximately 8 million doses of Pfizer vaccine to children aged 5-11 years. Myocarditis among age group appears rare; 11 verified reports have been received. Local and systemic reactions after vaccination were commonly reported. Serious adverse events were rarely reported.
20.12.2021	Multisystem Inflammatory Syndrome in Children by COVID-19 Vaccination Status of Adolescents in France	JAMA / Research Letter	<ul style="list-style-type: none"> French cohort study to estimate risk of Multisystem Inflammatory Syndrome in Children (MIS-C) among adolescents by COVID-19 vaccination status. During study period (01.09 - 31.10.2021) 107 children with MIS-C were hospitalized.

			<ul style="list-style-type: none"> • 33 (31%) were adolescents eligible for vaccination: 0 fully vaccinated, 7 received 1 dose (median 25 days before MIS-C onset), 26 unvaccinated. • Results suggest that COVID-19 mRNA vaccination was associated with a lower incidence of MIS-C in adolescents.
22.12.2021	Local and systemic responses to SARS-CoV-2 infection in children and adults	Nature / Article	<ul style="list-style-type: none"> • Authors analysed paediatric and adult COVID-19 patients and healthy controls (total n=93) using single-cell multi-omic profiling of matched nasal, tracheal, bronchial and blood samples. • In healthy paediatric airways, cells observed already in an interferon-activated state, that upon SARS-CoV-2 infection was further induced especially in airway immune cells. • Systemic response in children characterised by increases in naive lymphocytes and a depletion of natural killer cells; in adults, cytotoxic T cells and interferon-stimulated subpopulations were significantly increased.
07.01.2022	Receipt of COVID-19 Vaccine During Pregnancy and Preterm or Small-for-Gestational-Age at Birth — Eight Integrated Health Care Organizations, United States, December 15, 2020–July 22, 2021	MMWR Morb Mortal Wkly Rep / Article	<ul style="list-style-type: none"> • Retrospective cohort study of >40,000 pregnant US women found COVID-19 vaccination during pregnancy was not associated with increased risk for preterm birth (adjusted hazard ratio [aHR] = 0.91) or small-for-gestational-age at birth (aHR = 0.95), compared with unvaccinated pregnant women. • Additionally, no increased risk found when stratified by mRNA COVID-19 vaccine dose, or by second or third trimester vaccination, compared to unvaccinated pregnant women.
04.01.2022	Clinical characteristics and risk factors for maternal deaths due to COVID-19 in Brazil: A nationwide population-based cohort study	J Travel Med / Article	<ul style="list-style-type: none"> • Population-based cohort of all pregnant/postpartum women hospitalised with COVID-19 notified to a Brazilian surveillance system (SIVEP-Gripe) from February 2020 to September 2021. • Total of 1858 deaths (12.3%), a maternal mortality rate of 7.5 per 1000 patients-days. • Factors independently associated with death: postpartum status on admission (adjusted HR 1.4); hypoxemia on admission (aHR 1.2); pre-existing clinical conditions (aHRs 1.2 for one and 1.3 for two comorbidities); and requiring non-invasive (aHR 2.6) or invasive ventilatory support (aHR 7.1).
20.12.2021	Diabetes mellitus, maternal adiposity, and insulin-dependent gestational diabetes are associated with Covid-19 in pregnancy: The INTERCOVID Study	Am J Obstet Gynecol / Article	<ul style="list-style-type: none"> • Multinational study, March 2020-February 2021 with 2071 pregnant women ≥18 years. • Covid-19 associated with pre-existing diabetes mellitus (DM), overweight/obesity, gestational diabetes mellitus (GDM). • GDM association specifically among women requiring insulin, whether normal-weight or overweight/obese. • Somewhat stronger association between Covid-19 diagnosis and women with pre-existing DM, whether of normal weight or overweight/obese.

- DM and overweight/obesity are risk factors for Covid-19 diagnosis in pregnancy, and insulin-dependent GDM is also associated with the disease.

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Epidemiology and clinical – risk factors

Publication Date	Title/URL	Journal / Article type	Digest
28.12.2021	Impact of Coinfection With SARS-CoV-2 and Influenza on Disease Severity: A Systematic Review and Meta-Analysis	Front Public Health / Systematic Review	<ul style="list-style-type: none"> • Systematic review: impact of SARS-CoV-2 and influenza coinfection on disease severity; search to 09.07.2021. • 12 studies included with 9,498 patients. Coinfection not significantly associated with mortality. • Subgroup analysis: in 5 Chinese studies, mortality significantly lower in coinfection patients versus significantly increased mortality found in 4 studies outside of China. • Limitations include high level of heterogeneity, limited data on influenza subtypes and other confounders.
18.12.2021	A comprehensive systematic review and meta-analysis of the global data involving 61,532 cancer patients with SARS-CoV-2 infection	medRxiv (non-peer reviewed) / Systematic Review	<ul style="list-style-type: none"> • Systematic review to determine the risk by age, tumour type, treatment of SARS-CoV-2 infection in cancer patients. • Search to 14.06.2021; 81 studies included (61,532 cancer patients). • Meta-analysis of 19 studies comparing cancer patients with COVID-19 to cohorts without cancer and COVID-19. • Cancer patients, particularly younger cancer patients, appear at increased risk of mortality from COVID-19 compared to non-cancer patients. • Differences in outcomes were seen based on tumour types and treatment.
23.12.2021	Inequalities in excess premature mortality in England during the COVID-19 pandemic: a cross-sectional analysis of cumulative excess mortality by area deprivation and ethnicity	BMJ Open / Original research	<ul style="list-style-type: none"> • Statistical model estimates increased mortality in population subgroups, compared to previous 5 year trends. • Indirect effect of pandemic on premature mortality has disproportionately affected (i) people in ethnic minority groups (regardless of area-based deprivation); (ii) the White group in most deprived areas.
05.01.2022	The impact of vaccination on incidence and outcomes of SARS-CoV-2 infection in patients with kidney failure in Scotland	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Authors investigated effects of vaccination on incidence of infection, hospitalization and death in patients with kidney failure requiring kidney replacement therapy (KRT). • As of 19.09.2021: 93% (n=5281) of KRT population in Scotland had received two vaccine doses / 814 cases of SARS-CoV-2 infection (15.1% of KRT population). • Vaccine effectiveness vs infection 33% / hospitalization 38% .

			<ul style="list-style-type: none"> • 9.2% of fully vaccinated individuals died within 28 days of a positive PCR test (7% dialysis patients, 10% kidney transplant recipients), Vs. <0.1% of vaccinated Scottish population admitted to hospital or dying due to COVID-19. • Note, pre-booster programme / Omicron
16.12.2021	Predictors of SARS-CoV-2 infection in a multi-ethnic cohort of United Kingdom healthcare workers: a prospective nationwide cohort study (UK-REACH)	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Analysis of over 12,000 UK Healthcare workers (HCWs); nearly a quarter reported infection in first year of pandemic. • Occupational risk factors include nursing/midwifery role (versus doctor), cohabiting with another key worker, working in hospital inpatient or ambulance settings. • Lower risk include: (i) HCWs in South West England / Scotland versus West Midlands; (ii) HCWs working in ICU. • Sociodemographic risk factors include younger age, higher religiosity (interrelated to a person's ethnicity) . • Black HCWs more likely to contract COVID-19 than White colleagues; some factors interrelated to ethnicity identified.
27.12.2021	Occupation and COVID-19 mortality in England: a national linked data study of 14.3 million adults	Occup Environ Med / Article	<ul style="list-style-type: none"> • Retrospective cohort study (24.01.2020-28.12.2020) of over 14 million people aged 40–64 years living in England. • Authors estimated age-standardised mortality rates (ASMRs) per 100 000 person-years at risk stratified by sex and occupation. • For most occupations, confounding factors and mediators other than workplace exposure to SARS-CoV-2 explained 70%–80% of the excess age-adjusted occupational differences. Those included geography, ethnicity or education, living conditions. • People in occupations involving contacts with patients (eg, health and social care workers) or the public (eg, bus drivers, retail workers) remained at elevated risk of death involving COVID-19, even after accounting for other factors. • In men, ASMRs highest among taxi and cab drivers or chauffeurs at 119.7 deaths per 100 000. • Preprint previously included.
03.01.2022	Diminished antibody response against SARS-CoV-2 Omicron variant after third dose of mRNA vaccine in kidney transplant recipients	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • US prospective, multi-center cohort study: 51 adult kidney transplant recipients (KTRs) who received three doses of BNT162b2 [Pfizer] or mRNA-1273 [Moderna]. • No KTRs had neutralizing responses to Omicron before third vaccine dose. • After third dose, 12% KTRs had neutralizing responses to Omicron Vs. wild-type (61%) and Delta (59%). • Three patients (6%) developed breakthrough SARS-CoV-2 infection at a median of 89 days.
29.12.2021	Immune responses following third COVID-19 vaccination are reduced in patients with hematological	Cancer Cell / Letter	<ul style="list-style-type: none"> • Authors evaluated 199 cancer patients (n = 115 [58%] with solid cancer) who received a third vaccine dose.

	malignancies compared to patients with solid cancer		<ul style="list-style-type: none"> • Third dose can generate NAb in patients who are non-responders following two doses, especially heterologous BNT162b2 [Pfizer] booster in individuals who initially received ChAdOx1 [AstraZenca]. • High proportion of patients with solid cancer had detectable responses after third vaccination, comparable to individuals without cancer. • Significant number of patients with hematological malignancies still had undetectable neutralizing responses following a third vaccine dose, especially against variants. • Pre-Omicron
27.12.2021	Factors for severe outcomes following SARS-CoV-2 infection in people with cystic fibrosis in Europe	ERJ Open Res / Article	<ul style="list-style-type: none"> • Up to 31.12.2020, a total of 828 people with cystic fibrosis (pwCF) and SARS-CoV-2 infection were reported in 26 European countries [incidence was 17.2 per 1000 pwCF]; 23.7% were hospitalised and 1.4% died • Incidence higher in lung-transplanted (28.6) versus non-lung-transplanted pwCF (16.6). • Factors associated with symptomatic SARS-CoV-2 infection (75.7% of cases) were age >40 years, at least one F508del mutation and pancreatic insufficiency. • Hospitalisation, oxygen therapy, intensive care, respiratory support and death were 2- to 6-fold more frequent in lung-transplanted versus non-lung-transplanted pwCF. • Lung transplantation, CF-related diabetes (CFRD), moderate/severe lung disease, and azithromycin use were associated with hospitalisation and oxygen therapy.
22.12.2021	Characteristics and outcomes of patients with COVID-19 with and without prevalent hypertension: a multinational cohort study	BMJ Open / Article	<ul style="list-style-type: none"> • Retrospective international cohort study using 15 healthcare databases [from USA, Europe and South Korea]. • Identified 2,851,035 patients diagnosed with COVID-19 (diagnosed cohort) and 563,708 hospitalised patients with COVID-19 (hospitalised cohort). • Hypertension more prevalent in hospitalised cohort. • Hypertensive patients in diagnosed cohort had more hospitalisations and increased mortality compared to non-hypertensive. • Hypertensive patients in hospitalised cohort were more likely to have acute respiratory distress syndrome, arrhythmia and increased mortality than non-hypertensive patients.
07.01.2022	Risk Factors for Severe COVID-19 Outcomes Among Persons Aged ≥18 Years Who Completed a Primary COVID-19 Vaccination Series - 465 Health Care Facilities, United States, December 2020-October 2021	MMWR Morb Mortal Wkly Rep / Article	<ul style="list-style-type: none"> • Among 1,228,664 people completing primary Covid-19 vaccination in the US [December 2020 to October 2021], severe Covid-19 outcomes (0.015%) or death (0.0033%) were rare. • Risk of severe COVID-19 outcomes higher among persons aged ≥65 years (adjusted odds ratios [aOR]=3.22), with immunosuppression (aOR = 1.91), pulmonary disease (aOR = 1.69), liver disease (aOR=1.68), chronic kidney disease (aOR=1.61), neurologic disease (aOR=1.54), diabetes (aOR=1.47), or cardiac disease (aOR=1.44).

- All persons with severe outcomes had at least one risk factors; 77.8% (n=28) who died had at least four, as did 56.9% (n=87) of survivors who had respiratory failure or ICU admission.

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Epidemiology and clinical – other

Publication Date	Title/URL	Journal / Article type	Digest
23.12.2021	SARS-CoV-2 variants of concern and variants under investigation in England: Technical briefing 33	UKHSA (non-peer reviewed) / Briefing	<ul style="list-style-type: none"> • Provides an update on previous briefings to 17 December 2021 • Little diversity within Omicron BA.1 clade; two acquired mutations in spike noted in UK data set (A701V and R346K). • Preliminary analysis suggests risk of hospital admission for Omicron is reduced compared to Delta [excluding known reinfections]; hazard ratio of 0.62 for emergency department attendance or admission, and 0.38 for admission alone. • Evidence of waning of vaccine effectiveness against symptomatic disease (15 to 25% reduction in VE after 10 weeks); waning faster for Omicron vs Delta infections. • Approximately 9.5% of Omicron infections have been identified as reinfections [likely to be a substantial underestimate]. • Iterated secondary attack rates continue to show higher secondary attack rates for Omicron vs Delta • Associated comment: https://doi.org/10.1136/bmj.n3151
31.12.2021	Technical briefing: Update on hospitalisation and vaccine effectiveness for Omicron VOC-21NOV-01 (B.1.1.529)	UKHSA (non-peer reviewed) / Research and analysis	<ul style="list-style-type: none"> • Provides an update on previous briefings up to 23 December 2021 • Up to 29 December 2021 there; 198,348 confirmed cases of Omicron identified in England; 451,194 probable cases identified through S-gene target failure (SGTF); and 815 individuals admitted to emergency departments • Two studies [relatively small numbers] found substantial reduction in risk of hospitalisation for Omicron cases after 3 doses of vaccine compared to unvaccinated; a previous finding of reduced hospitalisation for Omicron compared to Delta is confirmed by updated Study 1.
Feb 2022	Monitoring populations at increased risk for SARS-CoV-2 infection in the community using population-level demographic and behavioural surveillance	Lancet Reg Health Eur / Article	<ul style="list-style-type: none"> • UK large scale community ‘COVID Infection Survey’ estimated key predictors of SARS-CoV-2 positivity in UK, aiming to provide up-to-date information on changes in populations at increased risk. • Period covered 19.07.2020 - 17.07.2021 included 4,091,537 RT-PCR results from 482,677 individuals of which, 29,903 (0.73%) were positive • Findings by period include: (i) Sept-Nov 2020, rates higher in younger ages, those living in Northern England, major urban conurbations, more deprived areas, larger

households; (ii) Dec 2020-Jan 2021 (Alpha), high positivity shifted to southern geographical regions; (iii) June-July 2021 (Delta) independently higher in younger, male, and unvaccinated groups.

- Authors able to identify populations at increased risk of SARS-CoV-2 infection in real-time, and monitor important trends across UK.

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Infection control / non-pharmaceutical interventions

Publication Date	Title/URL	Journal / Article type	Digest
23.12.2021	The effectiveness of PPE in reducing the transmission of COVID-19 in health and social care settings: December 2021 update, 12 December 2021	Gov.uk (non-peer reviewed) / Research and analysis	<ul style="list-style-type: none"> • Updates previous rapid literature search to December 2021 • Highly likely that use of PPE (e.g. masks, gloves, gowns) together with behavioural infection control measures (e.g. hand washing), will result in decreased risk of Covid19 transmission in social care. • Procedures (e.g. donning, doffing, and disposal of used PPE) should be consistently followed to be effective; extra training is required. • N95 masks provide better protection than cloth or surgical masks if used correctly; face shields (visors) should not be used for respiratory protection. • Evidence suggests exposure to COVID-19 in household/private setting is a stronger risk factor than work exposure for infection in health care workers.
04.01.2022	Test to release from isolation after testing positive for SARS-CoV-2	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Using individual infectiousness and lateral flow tests (LFT) model, authors evaluate test-to-release policies against fixed-duration isolation policies. • Number of infectious days in community reduced to almost zero by requiring at least 2 consecutive days of negative tests, after initially testing positive. • Fewer days' wait until initiating testing (e.g 3 or 5 days) results in more days saved vs. a 10-day isolation period. • Limited data on omicron acknowledged.

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Treatment

Publication Date	Title/URL	Journal / Article type	Digest
30.12.2021	The effect of colchicine on mortality outcome and duration of hospital stay in patients with COVID-19: A meta-analysis of randomized trials	Immun Inflamm Dis / Systematic Review	<ul style="list-style-type: none"> • Systematic review (up to 17.11.2021) identified 10 RCTs which included 17,976 patients with COVID-19 (8427 randomised to colchicine group, and 9549 to control group). • No significant difference in odds of mortality (pooled OR = 0.76), but a significant reduction in the duration of hospital stay with the use of colchicine (pooled standardised mean difference (SMD) = -0.59). • Limitations include variety of dosing regimens, lack of high-quality trials, and relatively small sample sizes re. estimation of pooled SMD of the duration of hospital stay.
21.12.2021	Fluvoxamine for Outpatient COVID-19 to Prevent Hospitalization: A Systematic Review and Meta-Analysis	medRxiv (non-peer reviewed) / Systematic review	<ul style="list-style-type: none"> • Systematic review up to 12.11.2021 included 2196 participants from 3 trials. • Findings suggest fluvoxamine [an SSRI-type antidepressant] has high probability of preventing hospitalisation in outpatients with COVID-19 under various assumptions. • Risk ratios for hospitalisation: 0.75 for frequentist analysis; 0.78 for Bayesian weakly neutral prior; and 0.73 for Bayesian moderately optimistic prior. • Probability of any effect on hospitalisation was 94.1% to 98.3%, and of moderate effect was 81.6% to 91.1%. • Limitations: variability in healthcare practices, resource availability, and circulating variants between trials.
16.12.2021	Namilumab or infliximab compared with standard of care in hospitalised patients with COVID-19 (CATALYST): a randomised, multicentre, multi-arm, multistage, open-label, adaptive, phase 2, proof-of-concept trial	Lancet Respir Med / Article	<ul style="list-style-type: none"> • UK study, set in 9 hospitals in England and Wales between 15.06.2020 and 18.02.2021, of reduction in inflammation (measured by CRP concentration) in hospitalised patients with COVID-19 pneumonia. • 146 patients included in study and randomly assigned usual care (54), namilumab (57), or infliximab (35). • Probabilities that interventions superior to usual care alone in reducing C-reactive protein concentration over time: 97% for namilumab; 15% for infliximab.
23.12.2021	A Phase 2a clinical trial of Molnupiravir in patients with COVID-19 shows accelerated SARS-CoV-2 RNA clearance and elimination of infectious virus	Sci Transl Med / Report	<ul style="list-style-type: none"> • US Phase 2a, randomized clinical trial to evaluate safety, tolerability, and antiviral activity of molnupiravir dosed twice daily (BID) for 5 days in 202 unvaccinated patients with mild to moderate COVID-19. • Time to viral RNA clearance decreased in 800 mg molnupiravir group (median 14 days) Vs. placebo group (median 15 days). • Infectious virus detected in swabs from 1.9% of 800 mg molnupiravir group Vs 16.7% of placebo group at day 3 of treatment. • Treatment Day 5: no infectious virus isolated from participants receiving 400 or 800 mg molnupiravir Vs. 11.1% of placebo recipients.

15.12.2021	Rivaroxaban versus no anticoagulation for post-discharge thromboprophylaxis after hospitalisation for COVID-19 (MICHELLE): an open-label, multicentre, randomised, controlled trial	Lancet / Article	<ul style="list-style-type: none"> • Brazilian multicentre, randomised trial focused on 320 hospitalised COVID-19 patients at increased risk for venous thromboembolism who were randomly assigned (1:1) to receive, at hospital discharge, rivaroxaban 10 mg/day or no anticoagulation for 35 days (160 in each group). • Study covers 08.10.2020 - 29.06.2021. All patients received thromboprophylaxis with standard doses of heparin during hospitalisation. • Findings that in high risk patients discharged after COVID-19 hospitalisation, thromboprophylaxis with rivaroxaban 10 mg/day for up to 35 days improved clinical outcomes, reducing thrombotic events compared with no post-discharge anticoagulation. • Associated comment: https://doi.org/10.1016/S0140-6736(21)02503-4
21.12.2021	Randomized Controlled Trial of Early Outpatient COVID-19 Treatment with High-Titer Convalescent Plasma	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • In a multicentre, double-blind RCT, 1225 non-hospitalised US adults with Covid-19 were randomised and 1181 transfused (convalescent plasma n=592, or placebo n=589) within 8 days. • In modified intention-to-treat analysis, the primary endpoint [hospitalisation within 28 days] occurred in 37/589 (6.3%) placebo and 17/592 (2.9%) convalescent plasma participants (relative risk, 0.46); adjusting for covariates related to the outcome did not change conclusions. • Note: plasma was collected before widespread vaccine availability and ended prior to arrival of Omicron.

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Modelling

Publication Date	Title/URL	Journal / Article type	Digest
22.12.2021	Report 50 - Hospitalisation risk for Omicron cases in England	Imperial College London (non-peer reviewed) / Report	<ul style="list-style-type: none"> • Analyses data from all PCR-confirmed SARS-CoV-2 cases in England between 01.12.2021 and 14.12.2021. • Findings suggest overall reduction in hospitalisation risk for Omicron relative to Delta infections, although reduction varies by chosen endpoint. • Previous infection reduces hospitalisation risk approximately 50% and risk of a hospital stay of 1+ days by 61% [before adjustment]. • Model adjustments for historical infection and observed reinfection are moderate, but significant for evaluating severity overall. • Using hospital stay of 1+ days as endpoint, adjusted relative risk of reinfections versus primary cases is 0.31 (a 69% reduction in hospitalisation risk)

- Among those receiving two doses of Pfizer or Moderna, hazard ratios for hospital attendance with Omicron are similar to Delta, while Omicron hazard ratios are generally lower than Delta among Oxford-AstraZeneca recipients [Authors emphasise limited sample sizes to date].

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Overviews, comments and editorials

Publication Date	Title/URL	Journal / Article type
22.12.2021	JCVI statement on COVID-19 vaccination of children and young people: 22 December 2021	JCVI / Independent Report
24.12.2021	COVID-19 vaccine breakthrough infections	Science / Perspective
25.12.2021	Addressing Vaccine Hesitancy to Reduce Racial and Ethnic Disparities in COVID-19 Vaccination Uptake Across the UK and US	Front Public Health / Opinion
31.12.2021	What is the impact of microvascular complications of diabetes on severe COVID-19?	Microvasc Res / Article
24.12.2021	COVID-19 and stillbirth: direct vs indirect effect of the pandemic	Ultrasound Obstet Gynecol / Opinion
05.01.2022	Omicron's feeble attack on the lungs could make it less dangerous	Nature / News
16.12.2021	Covid-19: Runny nose, headache, and fatigue are commonest symptoms of omicron, early data show	BMJ / News

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