



COVID-19 Literature Digest – 17/09/2021

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 The reports include both preprints, which should be treated with caution as they are NOT peer-reviewed and may be subject to change, and also research that has been subject to peer review and wider scrutiny.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,

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On behalf of the PHE COVID-19 Literature Digest Team

Report for 17.09.2021 (please note that papers that have **NOT been peer-reviewed** are highlighted in red).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
10.09.2021	Differential antibody dynamics to SARS-CoV-2 infection and vaccination	bioRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none">• 62 COVID-19 convalescents were recruited between March and June 2020, before the emergence of the Alpha, Beta, Gamma, and Delta variants, and blood taken over approx. 6-9 months. 28 convalescents continued to provide blood donations after mRNA vaccination. 18 naïve vaccinees donated up to 8 repeated blood draws after mRNA vaccination until ~195 days after dose 2• Vaccination delivered robust initial virus-specific antibodies with some cross-variant coverage.• Antibodies induced by wildtype (pre-variant) infection showed highly stable long-term antibody dynamics but was more modest in magnitude• Vaccination after infection induced maximal antibody magnitudes with enhanced longitudinal stability while infection-naïve vaccinee antibodies fell with time to post-infection-alone levels.• Infection-induced antibodies demonstrated greater relative breadth in neutralising activity against variants and durability was greater in COVID-19-recovered subjects with dual memory B cell features of greater early antibody somatic mutation and cross-coronavirus reactivity.
16.09.2021	T cell immune responses to SARS-CoV-2 and variants of concern (Alpha and Delta) in infected and vaccinated individuals	Cellular & Molecular Immunology / Article	<ul style="list-style-type: none">• Authors present data identifying memory T cells with specificity and accuracy for the detection of CD4+/CD8+ T cell responses to SARS-CoV-2 peptides that differentiate infected and vaccinated individuals from those not exposed to SARS-CoV-2. In addition, analysis of T cell responses to VOCs (Alpha and Delta) showed that SARS-CoV-2 infection and vaccination with BNT162b2 elicited equivalent T cell responses.• Results demonstrate that T cells in infected or vaccinated individuals can elicit robust and cross-reactive immune responses against VOCs.

			<ul style="list-style-type: none"> • T cell immunity requires an infection to reactivate memory responses, which may result in mild or asymptomatic infections that would be considered “breakthrough” infection. Thus, the level and robustness of T cell memory responses would likely affect the clinical manifestations of the disease.
12.09.2021	Exposures to different SARS-CoV-2 spike variants elicit neutralizing antibody responses with differential specificity towards established and emerging strains	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Convalescent serum samples were collected based on prior infection with the following variants: B.1 (D614G mutation only; n=10 donors), B.1.429 (Epsilon; n=15), B.1.1.519 (n=6), P.2 (Zeta; n=1), B.1.526 (Iota; n=1), D614G infection followed by BNT162b2 vaccination (n=8), B.1.429 infection followed by BNT162b2 vaccination (n=17). Serum was also collected from healthy recipients of BNT162b2 (n=5) and mRNA-1273 (n=6) vaccines (vaccines based on the Wuhan spike sequence), with no prior infection • Delta variant is neutralized more effectively by serum elicited by prior exposure to two different variants — B.1.429 and B.1.1.519 — which have separate subsets of spike mutations overlapping with mutations in B.1.617.2 • Findings demonstrate the effect of serial exposure to two different versions of spike on neutralizing antibody response. Infection with B.1.429 (Epsilon) followed by vaccination led to greater cross-neutralization of B.1.429 and B.1.617.2 (Delta) compared to vaccination alone or D614G infection plus vaccination, supporting the notion that exposure to multiple spike variants expands neutralization specificity.
14.09.2021	Antibody responses to BNT162b2 mRNA vaccine: infection-naïve individuals with abdominal obesity warrant attention	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Study comparing antibody responses after 1st / 2nd dose of BNT162b2 [Pfizer] vaccine in individuals with / without abdominal obesity (AO), discerning between infection-naïve individuals / prior infection. • Infection-naïve, with AO (n=79) / without AO (n=102) • Between first and third month after 2nd dose, drop in IgG-TrimericS levels more remarkable in individuals with AO compared to those without (2.44 fold vs 1.82 fold). Confirmed even when adjusting for possible confounders. • Highlights the need to extend the duration of serological monitoring of antibody levels in infection-naïve individuals with abdominal obesity, a higher-risk population category in terms of possible weaker antibody response.

14.09.2021	Identification of resident memory CD8(+) T cells with functional specificity for SARS-CoV-2 in unexposed oropharyngeal lymphoid tissue	Sci Immunol / Report	<ul style="list-style-type: none"> • Authors show that SARS-CoV-2-unexposed children and adults commonly harbour tonsillar CD8+ TRM cells that react with SARS-CoV-2. • Detected in 26 / 81 (32%) tonsil samples from children (n=40) and adults (n=41) a year before COVID-19. • Pre-existing tissue-resident memory CD8+ T cells could potentially enable rapid sentinel immune responses against SARS-CoV-2.
14.09.2021	SARS-COV2 mutant-specific T cells and neutralizing antibodies after vaccination and up to 1 year after infection	medRxiv (non peer reviewed) / Article	<ul style="list-style-type: none"> • In 23 vaccinated subjects, high anti-SARS-CoV2 spike protein receptor binding domain (RBD) antibody titers were found. Average virus neutralization by antibodies, assessed as inhibition of ACE2 binding to RBD, was 2.2-fold reduced for delta mutant vs. wildtype RBD. • Strong T cell responses occurred for wildtype and mutant SARS-CoV2 variants, including delta (B.1.617.2), in fully vaccinated individuals, whereas they were partly reduced 1 year after natural infection. Antibody neutralisation of delta mutant was reduced compared to wt, as assessed in a novel inhibition assay with a finger stick drop of blood. • Authors conclude that immune responses after vaccination are stronger compared to those after naturally occurring infection, pointing out the need of the vaccine to overcome the pandemic.
16.09.2021	Single-cell immune profiling reveals distinct immune response in asymptomatic COVID-19 patients	Signal transduction and targeted therapy / Article	<ul style="list-style-type: none"> • Findings from 37 longitudinal collected peripheral blood mononuclear cell samples from asymptomatic, moderate, and severe patients with healthy controls demonstrate distinct immune profiles in asymptomatic COVID-19 patients and highlight the difference of immune response toward disease progression. • Asymptomatic patients displayed increased CD56⁺CD16⁻ natural killer (NK) cells and upregulation of interferon-gamma in effector CD4⁺ and CD8⁺ T cells and NK cells. They showed more robust TCR clonal expansion, especially in effector CD4⁺ T cells, but lack strong BCR clonal expansion compared to moderate patients.

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Vaccines

Publication Date	Title/URL	Journal / Article type	Digest
10.09.2021	Localising Vaccination Services: Qualitative Insights on an Orthodox Jewish Collaboration with Public health during the UK coronavirus Vaccine Programme	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Case study of coronavirus vaccination programme (CVP) co-delivered by public health services / Orthodox Jewish health organisation. • 28 semi-structured interviews, themes shared. • Localised approach to delivering immunisation programmes, involving trusted community organisations, creates opportunity for ethnic and religious minorities to collaborate in safeguarding community health.
14.09.2021	PHE: Duration of protection of COVID-19 vaccines against clinical disease, 9 September 2021	Gov.uk (non peer reviewed) / Research and analysis	<ul style="list-style-type: none"> • Results indicate waning VE against symptomatic disease with both the Pfizer and AstraZeneca vaccines from approximately 10 weeks after the second dose. This is most evident in older adults. • Some indication of waning VE against hospitalisation from 15 weeks after the second dose, in particular among recipients of the AstraZeneca vaccine, though largely in clinical risk groups, including those who are immunosuppressed, where faster waning may be predicted. • VE against hospitalisation, even within clinical risk groups, at 15-20 weeks is 75-90% with the AstraZeneca vaccine and over 90% with the Pfizer vaccine.
13.09.2021	SARS-CoV-2 anti-spike IgG antibody responses after second dose of ChAdOx1 or BNT162b2 in the UK general population	medRxiv (non peer reviewed) / Article	<ul style="list-style-type: none"> • UK study: 2nd ChAdOx1 [AstraZeneca] / BNT162b2 [Pfizer] dose significantly boosts anti-spike IgG levels; dosing interval has limited impact on antibody response. • Protection estimated at 0.5-1 year for ChAdOx1 / >1 year after BNT162b2, could reduce with variants. • Older individuals, males, those with long-term health conditions have substantially faster antibody declines with BNT162b2 but not ChAdOX1. • Reducing dosing interval to 8 weeks for both / further to 3 weeks for BNT162b2 may help increase short-term protection against Delta. • Support 3rd booster, prioritised to more vulnerable.
13.09.2021	Efficacy of two doses of COVID-19 vaccine against severe COVID-19 in those with risk conditions and residual risk to the clinically extremely vulnerable: the REACT-SCOT case-control study	medRxiv (non peer reviewed) / Article	<ul style="list-style-type: none"> • Scottish national study: does COVID-19 efficacy vary with clinical risk category / severe COVID-19 (critical care or fatal outcome) risk factors in double vaccinated. • Efficacy against severe COVID-19 of two doses: 93% without designated risk conditions; 89% with moderate risk conditions; 66%

			<p>in those designated as clinically extremely vulnerable (CEV) and eligible for shielding.</p> <ul style="list-style-type: none"> • 330 severe COVID-19 cases in double-vaccinated: 47% had moderate risk conditions; 41% were CEV. • Among CEV, highest in solid organ transplants at 98 but absolute risk of severe COVID-19 still low (14 cases in 16079 person-months of follow-up). • Two doses protect against severe COVID-19 in CEV individuals but residual risk remains far higher in those who are CEV than in those who are not.
12.09.2021	Efficacy of vaccination against severe COVID-19 in relation to Delta variant and time since second dose: the REACT-SCOT case-control study	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Scottish matched case-control study, 1.12.2020 - 19.08.2021: (i) has vaccine efficacy (VE) against severe COVID-19 (critical care or fatal outcome) decreased since Delta; (ii) has efficacy waned since 2nd dose. • May 2021 decrease in VE against severe COVID-19, coinciding with B.1.1.7 (Alpha) replacement by B.1.617.2 (Delta). Reversed over next month. • In most recent time window, efficacy of two doses against severe COVID-19 was 91% for AstraZeneca / 92% for mRNA (Pfizer or Moderna). • Efficacy against COVID-19 declined rapidly in first two months since second dose but more slowly thereafter.
14.09.2021	VEEP: Vaccine effectiveness table, 7 September 2021	Gov.uk (non peer reviewed) / Expert Panel	<ul style="list-style-type: none"> • Graphic summary of current data regarding vaccine effectiveness against infection, symptomatic infection and severe disease with Alpha and Delta variants with one or two doses of AstraZeneca, Pfizer and Moderna vaccines • Highlights gaps in current knowledge and provides sources of the data
15.09.2021	Protection of BNT162b2 Vaccine Booster against Covid-19 in Israel	N Engl J Med / Article	<ul style="list-style-type: none"> • Israel approved 3rd (booster) BNT162b2 [Pfizer] dose approved on 30.07.2021 for persons ≥ 60 years old who had received 2nd dose at least 5 months earlier. • Compared rate of confirmed Covid-19 / severe illness between those who had received a booster injection (booster group) and the non-booster group. • ≥ 12 days after booster, rate of confirmed infection lower in booster group by a factor of 11.3; rate of severe illness lower by a factor of 19.5.

			<ul style="list-style-type: none"> • Rate of confirmed infection at least 12 days after vaccination lower than rate after 4-6 days by a factor of 5.4.
12.09.2021	Safety and efficacy of the mRNA BNT162b2 vaccine against SARS-CoV-2 in five groups of immunocompromised patients and healthy controls in a prospective open-label clinical trial	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Clinical trial with 449 adult patients in five groups: Primary (n=90) or secondary immunodeficiency disorders due to HIV (n=90), allogeneic hematopoietic stem cell transplantation/chimeric antigen receptor T cell therapy (n=90), solid organ transplantation (SOT) (n=89), or chronic lymphocytic leukaemia (CLL) (n=90) • Severe adverse events (SAEs) were more common in the SOT group and lowest in the HIV group. • 5 of 28 SAEs were assessed as being possibly linked to the vaccination, including vasovagal reaction in a HIV patient, febrile neutropenia in a HSCT patient, rejection in a liver transplant patient, and syncope in another liver transplant patient. One patient died of lung failure two months after the first vaccination. No SAE was observed in the healthy control group • The highest seroconversion-failure rate was found in the SOT group, with only 43.4% responding, followed by the CLL group, PID group, HSCT group and the HIV group
15.09.2021	Antibody response to a fourth mRNA Covid-19 vaccine boost in weak responder kidney transplant recipients	medRxiv (non peer reviewed) / Article	<ul style="list-style-type: none"> • Approximately 50% of patients who failed to respond after the second dose, seroconverted after a third booster dose; however it can still be argued that patients with low titres of anti-spike IgGs remain insufficiently protected against severe Covid-19 because they usually lack neutralizing antibodies • A total of 92 kidney transplant recipients (KTR) whose anti-spike IgG titre was between 1 and 143 BAU/mL (27 women, 65 men) received a fourth booster dose (BNT162b2 n=34, mRNA-1273 n=58) and had their anti-spike IgG titres measured 2 to 6 weeks thereafter. • There were no safety concerns with the fourth vaccine dose and the authors conclude that a fourth booster vaccine dose aiming at raising the titre of anti-spike IgGs should be offered to KTR who failed to respond adequately after three doses.
15.09.2021	Safety and immunogenicity of SARS-CoV-2 variant mRNA vaccine boosters in healthy adults: an interim analysis	Nature Medicine / Article	<ul style="list-style-type: none"> • 20 participants were randomly selected for inclusion in this interim analysis based on visit assessments completed and sample availability of pre-booster sera • All boosters, including mRNA-1273, numerically increased neutralization titres against the wild-type D614G virus compared to peak titres against wild-type D614G measured 1 month after the

			<p>primary series; significant increases were observed for mRNA-1273 and mRNA-1273.211</p> <ul style="list-style-type: none"> • All boosters increased neutralization titres against key VOCs and VOIs, including B.1.351, P.1. and B.1.617.2, that were statistically equivalent to peak titres measured after the primary vaccine series against wild-type D614G virus, with superior titres against some VOIs.
15.09.2021	SARS-CoV-2 Neutralization with BNT162b2 Vaccine Dose 3	N Engl J Med / Correspondence	<ul style="list-style-type: none"> • After phase 1–2–3 trial in which two BNT162b2 (Pfizer) doses administered 21 days apart, efficacy waned to 84% between 4-6 months after dose 2. • Third BNT162b2 dose 7.9 to 8.8 months after dose 2 to 11 participants 18-55 years old / 12 aged 65-85. • 1 month later, neutralization GMTs against wild-type virus increased to 5 times higher (age 18-55) / 7 times higher (age 65-85) as GMTs 1 month after dose 2. • Similar pattern seen in assays of neutralization GMTs against recombinant virus with delta variant spike. • A third dose could prolong protection and further increase the breadth of protection.
17.09.2021	Interim Estimates of COVID-19 Vaccine Effectiveness Against COVID-19–Associated Emergency Department or Urgent Care Clinic Encounters and Hospitalizations Among Adults During SARS-CoV-2 B.1.617.2 (Delta) Variant Predominance — Nine States, June–August 2021	MMWR Morb Mortal Wkly Rep / Article	<ul style="list-style-type: none"> • Data on vaccine effectiveness (VE) since B.1.617.2 (Delta) predominant. Medical encounters (32,867) from 187 hospitals / 221 emergency departments (EDs) and urgent care (UC) clinics across 9 US states. • Among fully vaccinated patients, proportion vaccinated among hospitalizations and ED/UC encounters, respectively: Pfizer, 55.3% and 53.6%; Moderna, 38.8% and 36.1%; Janssen, 6.0% and 10.3%. • Median interval from fully vaccinated to hospital admission or ED/UC encounter, respectively: 110 and 93 days (Pfizer-BioNTech); 106 and 96 days (Moderna); 94 and 94 days (Janssen).
14.09.2021	Reports of myocarditis and pericarditis following mRNA COVID-19 vaccines: A review of spontaneously reported data from the UK, Europe, and the US	medRxiv (non peer reviewed) / Article	<ul style="list-style-type: none"> • Using reporting data from the United Kingdom, United States, and European Economic Area this study provides evidence that younger people, and particularly males, more frequently report myocarditis and pericarditis than older people, following vaccination with mRNA COVID-19 vaccines. • While more frequent following the second dose, these are rare events with mild clinical course followed, in most cases, by full recovery. Reporting rates of myocarditis and pericarditis were consistent between the data sources.

			<ul style="list-style-type: none"> As vaccine programmes progress with the focus shifting to younger people, it is possible that more cases of myocarditis and pericarditis will be reported.
14.09.2021	BNT162b2-Elicited Neutralization of Delta Plus, Lambda, and Other Variants	bioRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> Authors report ability of 20 human sera, drawn 2 or 4 weeks after two doses of BNT162b2, to neutralize USA-WA1/2020 SARS-CoV-2 bearing variant spikes from Delta plus (Delta-AY.1, Delta-AY.2), Delta-Δ144 (Delta with the Y144 deletion of the Alpha variant), Lambda, and B.1.1.519 lineage viruses. All sera neutralize the variant viruses to titers of ≥80. Neutralization titers against Lambda and B.1.1.519 variants and against USA-WA1/2020 are equivalent. The susceptibility of Delta plus, Lambda, and other variants to neutralization by the sera indicates that antigenic change has not led to virus escape from vaccine-elicited neutralizing antibodies
15.09.2021	Safety, Immunogenicity, and Efficacy of COVID-19 Vaccine in Children and Adolescents: A Systematic Review	medRxiv (non peer reviewed) / Systematic Review	<ul style="list-style-type: none"> Systematic review including 8 published (2851 children or adolescents) and 28 ongoing clinical trials. Results showed that selected COVID-19 vaccines had a good safety profile in children and adolescents, with mostly mild and moderate adverse effects, including injection site pain, fatigue, headache, and chest pain. A few cases of myocarditis and pericarditis were also reported. Authors conclude that some COVID-19 vaccines have potential protective effects in children and adolescents, but awareness is needed to monitor their possible adverse effects after injection, especially myocarditis and pericarditis
12.09.2021	Effectiveness of the Single-Dose Ad26.COV2.S COVID Vaccine	medRxiv (non peer reviewed) / Article	<ul style="list-style-type: none"> Using U.S. insurance claims data from 390,517 vaccinated and 1,524,153 matched unvaccinated individuals, vaccination effectiveness (VE) was estimated at 79% for COVID-19 and 81% for COVID-19-related hospitalisations. VE was highest in those <50 years and lower in immunocompromised patients. In areas where the Delta variant was prevalent, effectiveness against infection was 78% and 85% for hospitalisations. Non-randomized data across the U.S. show high and stable vaccine effectiveness of Ad26.COV2.S over time before the Delta variant emerged to when the Delta variant was dominant

13.09.2021	Spread of SARS-CoV-2 Delta variant infections bearing the S:E484Q and S:T95I mutations in July and August 2021 in France	medRxiv (non peer reviewed) / Article	<ul style="list-style-type: none"> • Authors report increase in infections caused by Delta variants bearing E484Q mutation in Paris area. • Most of these sequences belong to a phylogenetic cluster and also bear the S:T95I mutation. • Further monitoring needed to determine if trend driven by undocumented superspreading events or an early signal of future viral evolutionary dynamics
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Diagnostics and genomics

Publication Date	Title/URL	Journal / Article type	Digest
16.09.2021	Characterisation of vaccine breakthrough infections of SARS-CoV-2 Delta and Alpha variants and within-host viral load dynamics in the community, France, June to July 2021	Euro Surveill / Article	<ul style="list-style-type: none"> • Authors compared French community level positive PCR results, 14.06.2021-30.07.2021, as Delta replacing Alpha. • In asymptomatic individuals, quantification cycle (Cq) values (also called cycle threshold (Ct)) significantly higher in fully vaccinated individuals. • In symptomatic individuals and controlling for time since symptoms, the difference vanished ($p = 0.26$). • Infections with Delta had lower Cq values at symptom onset than with Alpha. • Cq values are a proxy, linked to viral load, which is associated with probability of transmission.
15.09.2021	Emergence of SARS-CoV-2 Resistance with Monoclonal Antibody Therapy	medRxiv (non peer reviewed) / Article	<ul style="list-style-type: none"> • In ACTIV-2/A5401, non-hospitalized participants with symptomatic SARS-CoV-2 infection were randomized to 66 bamlanivimab (700mg or 7000mg) or placebo to investigate whether in vivo emergence of SARS-CoV-2 resistance mutations alters either viral replication dynamics or therapeutic efficacy. • Treatment-emergent resistance mutations were significantly more likely detected after bamlanivimab 700mg treatment (7% of 11) than placebo (0% of 112). • There were no treatment-emergent resistance mutations among the 48 participants who received bamlanivimab 7000mg. • Study provides evidence that mAb monotherapy can rapidly select for SARS-CoV-2 resistance, with viral populations able to completely shift from fully sensitive to fully resistant viruses within 24 hours,

leading to dramatic viral rebound and worsened symptom severity. These findings have implications for the design and use of antiviral therapeutics and provide insights into the prevention of SARS-CoV-2 resistance.

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Epidemiology and clinical - long-term complications / sequelae

Publication Date	Title/URL	Journal / Article type	Digest
10.09.2021	Post-COVID syndrome. A case series and comprehensive review	Autoimmunity Reviews	<ul style="list-style-type: none"> • Findings from a series of 100 consecutive patients, (53 women, median age 49) found post-COVID syndrome (PCS) is mainly characterized by musculoskeletal, pulmonary, digestive and neurological involvement including depression. • PCS is independent of severity of acute illness and humoral response. Long-term antibody responses to SARS-CoV-2 infection and a high inter-individual variability were confirmed. Future studies should evaluate the mechanisms by which SARS-CoV-2 may cause PCS and the best therapeutic options
16.09.2021	Technical article: Updated estimates of the prevalence of post-acute symptoms among people with coronavirus (COVID-19) in the UK, 26 April 2020 to 1 August 2021	Gov.uk / Official statistics	<ul style="list-style-type: none"> • Experimental estimates of the prevalence of symptoms that remain 12-weeks post-infection, or "long COVID" range from 3.0% based on tracking specific symptoms, to 11.7% based on self-classification of long COVID, using data to 01.08.2021. • This analysis focusses on the number of Coronavirus Infection Survey (CIS) participants with post-acute symptoms out of those with laboratory-confirmed COVID-19 • Irrespective of the approach to measurement, post-acute symptom prevalence was highest in females, adults aged 50 to 69 years, people with a pre-existing health condition, and those with signs of high viral load at the time of infection.

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Epidemiology and clinical – risk factors

Publication Date	Title/URL	Journal / Article type	Digest
05.09.2021	COVID-19 in Liver Transplant Recipients: A Systematic Review	J Clin Med / Review	<ul style="list-style-type: none"> • Systematic review of Liver transplant (LT) recipients. PubMed search , Nov 2019 - 30 May 2021, to explore (i) outcome and clinical course; (ii) immunological response after COVID-19; (iii) vaccination response. Considered 35, 4, and 5 articles, respectively, • Despite heterogeneity of reports, gastrointestinal symptoms were common. Outcomes not per se worse compared to general population. • Conflicted data about acquired immunity after SARS-CoV-2 infection. Vaccine immunogenicity appeared to be low.
10.09.2021	Estrogen and COVID-19 symptoms: Associations in women from the COVID Symptom Study	PLoS One / Article	<ul style="list-style-type: none"> • COVID Symptom Study app data May - June 2020 analysed for links between COVID-19 rates and: 1) menopausal status; 2) combined oral contraceptive pill (COCP) use; 3) HRT use. • Post-menopausal women aged 40-60 years (n=44,268): higher rates of predicted COVID-19 (P=0.003) and a corresponding range of symptoms, with consistent, but not significant trends observed for tested COVID-19 and disease severity. • Women aged 18-45 years taking COCP (n =295,689): significantly lower predicted COVID-19 (P=8.03E-05) / reduction in hospital attendance (P=0.023). • Post-menopausal women using HRT or hormonal therapies (n=151,193) didn't exhibit consistent associations, including increased rates of predicted COVID-19 (P=2.22E-05) for HRT users alone. • Being pre-menopausal appears to have a protective effect against COVID-19 in a large community survey. • HRT findings should be treated with caution due to lack of data on HRT type, route of administration, duration of treatment, and potential comorbidities. • Preprint previously included.
10.09.2021	Evaluation of antithrombotic use and COVID-19 outcomes in a nationwide atrial fibrillation cohort	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • From 972,971 individuals with atrial fibrillation (AF) and a CHA2DS2-VASc score\geq2, 88.0% (n=856,336) had pre-existing antithrombotic (AT) use, 3.8% (n=37,418) had a COVID-19 related hospitalisation and 2.2% (n=21,116) died.

			<ul style="list-style-type: none"> • Factors associated with no AT use included comorbidities that may contraindicate AT use (liver disease and history of falls) and demographics (socioeconomic status and ethnicity). • Pre-existing AT use was associated with lower odds of death but higher odds of hospitalisation. The same pattern was observed for anticoagulants (AC) vs antiplatelets (AP) but not for direct oral anticoagulants (DOACs) vs warfarin. • Pre-existing AT use may offer marginal protection against COVID-19 death, with AC offering more protection than AP. Although this association may not be causal, it provides further incentive to improve AT coverage for eligible individuals with AF.
13.09.2021	Association between COVID-19 vaccination, infection, and risk of Guillain-Barre syndrome, Bell's palsy, encephalomyelitis and transverse myelitis: a population-based cohort and self-controlled case series analysis	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • UK study included 1,868,767 ChAdOx1 and 1,661,139 BNT162b2 vaccinees; 299,311 people infected with COVID-19; and 2,290,537 from the general population. • No consistent association was found between either vaccine and any of the studied neuro-immune adverse events. • A 5-fold increase was observed in the risk of Guillain-Barre syndrome and an 11-fold of encephalomyelitis following COVID-19 infection
10.09.2021	Risk of severe COVID-19 outcomes associated with immune-mediated inflammatory diseases and immune modifying therapies: a nationwide cohort study in the OpenSAFELY platform	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • In a cohort of 17,672,065 adults 1,163,438 (7%) had immune-mediated inflammatory diseases (IMIDs). 19,119 people received targeted immune modifying drugs, and 200,813 received standard systemics. • Analysis provides evidence of increased COVID-19-death and hospitalisation in individuals with IMIDs overall compared to individuals without IMIDs of the same age, sex, deprivation and smoking status. • No evidence was found of increased COVID-19 deaths with targeted compared to standard systemic treatments, or in those prescribed TNF inhibitors, IL-12/23, IL7, IL-6 or JAK inhibitors compared to standard systemics.

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Epidemiology and clinical – other

Publication Date	Title/URL	Journal / Article type	Digest
14.09.2021	Oral Manifestations of COVID-19: Updated Systematic Review With Meta-Analysis	Front Med (Lausanne) / Systematic Review	<ul style="list-style-type: none"> • Systematic review including 74 studies on oral manifestations in patients with COVID-19. Of these 74 records, 10 were prevalence studies and the remaining 64 were case reports and case series on oral manifestations • The literature describes a relatively high frequency of xerostomia and aphthous lesions in patients with COVID-19 but the authors highlight the paucity of available evidence
13.09.2021	Trends in Covid-19 hospital mortality in women and men	medRxiv (non peer reviewed) / Article	<ul style="list-style-type: none"> • Multicentre study across 17 Spanish hospitals used sociodemographic, clinical, and mortality data from all patients with Covid-19 (n=3390, of which 1330 women), who had been discharged alive, or had died after being admitted, between March 2020 and February 2021 • Death was reported for 451 patients. There was a significant decreasing trend in mortality by time of admission for the whole year. This trend was significant for men but not women. • Treatments that mainly address the immune response to the infection, which is implicated in the higher mortality for men, may explain why the death rate in women does not improve. Behavioural changes among women, around the prevention of Covid-19, care for relatives, or seeking medical help, during the pandemic, may have increased their risk.
13.09.2021	Deaths involving COVID-19 by vaccination status, England: deaths occurring between 2 January and 2 July 2021	Office for National Statistics / Analysis	<ul style="list-style-type: none"> • Between 02.01.2021 – 02.07.2021, there were 51,281 deaths involving COVID-19 in England; 640 occurred in people who were fully vaccinated, including some who had been infected before they were vaccinated. • The risk of death involving COVID-19 was consistently lower for people who had received two vaccinations compared to one or no vaccination, as shown by the weekly age-standardised mortality rates (ASMRs) for deaths involving COVID-19. • There were 256 breakthrough deaths in this period, 61.1% of which occurred in males. • The median age of breakthrough deaths was 84, compared to 82 for other COVID-19 deaths and for non-COVID-19 deaths.

			<ul style="list-style-type: none"> • 13.1% of breakthrough deaths occurred in people who were identified as likely to be immunocompromised from hospital episodes or causes of death, compared to 5.4% for other COVID-19 deaths.
14.09.2021	Asymptomatic SARS-CoV-2 infection and the demography of COVID-19	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Detailed surveillance data gathered during COVID-19 resurgences in six cities of China at the beginning of 2021 to investigate trends in asymptomatic infection by age and location and their contribution to the pandemic • The proportion of asymptomatic infection declines with age, and using an age-stratified compartment model, and overall distribution of cases by the authors explain the geographic differences in the reported numbers of asymptomatic cases • Study estimates that 22-55% of cases would come from asymptomatic cases in an uncontrolled epidemic. Authors conclude that outbreaks will continue to occur if only adults are vaccinated, and surveillance and control measures may still be needed to contain epidemic resurgence.

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Infection control / non-pharmaceutical interventions

Publication Date	Title/URL	Journal / Article type	Digest
13.09.2021	Contact tracing is an imperfect tool for controlling COVID-19 transmission and relies on population adherence	Nat Commun / Article	<ul style="list-style-type: none"> • UK modelling shows well-implemented contact tracing could bring benefit controlling and preventing outbreaks, providing up to a 15% reduction in R. • Reporting and adherence most important predictors of impact; tracing coverage, speed and diagnostic sensitivity also important. • Contact tracing is not currently appropriate as the sole control measure.
09.09.2021	The potential impact of vaccine passports on inclination to accept COVID-19 vaccinations in the United Kingdom: Evidence from a large cross-sectional survey and modelling study	EClinicalMedicine / Research Paper	<ul style="list-style-type: none"> • National survey of 17,611 UK adults (9-27.04.2021) re. introduction of vaccine passports. • Responses stratify along socio-demographic lines: younger age groups, Black / Black British ethnicities (compared to whites), non-English speakers more likely express lower inclination to vaccinate if introduced.

			<ul style="list-style-type: none"> • Introducing vaccine passports will likely lower inclination to accept a COVID-19 vaccine once baseline vaccination intent has been adjusted for. • Larger decrease if required for domestic use, not facilitating international travel. • Passports may be viewed less positively among socio-demographic groups that cluster in large urban areas.
15.09.2021	Non-pharmacological measures implemented in the setting of long-term care facilities to prevent SARS-CoV-2 infections and their consequences: a rapid review	Cochrane Database Syst Rev / Review	<ul style="list-style-type: none"> • Search conducted 22 January 2021; 11 observational studies and 11 modelling studies included. • Intervention domains identified: (i) Entry regulation measures; (ii) Contact-regulating and transmission-reducing measures; (iii) Surveillance measures; (iv) Outbreak control measures; (v) Multicomponent measures • Comprehensive framework of non-pharmacological measures implemented in long-term care facilities, but certainty of evidence predominantly low to very low.

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Transmission

Publication Date	Title/URL	Journal / Article type	Digest
14.09.2021	Daily testing for contacts of individuals with SARS-CoV-2 infection and attendance and SARS-CoV-2 transmission in English secondary schools and colleges: an open-label, cluster-randomised trial	Lancet / Article	<ul style="list-style-type: none"> • Cluster-randomised controlled trial of 201 secondary schools/FE colleges in England; 10-week study (19.04.2021-10.05.2021) with Delta predominant. • Close contacts of a proven case: standard 10-day home isolation (control) vs. daily antigen lateral flow testing for 7 days, remaining at school (intervention). • Similar rates of symptomatic infections among students and staff with both approaches. • Daily contact testing of school-based contacts was non-inferior to self-isolation for transmission control. • Associated comment: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)02092-4/fulltext
24.07.2021	Surface contamination with SARS-CoV-2: A systematic review	Sci Total Environ / Systematic Review	<ul style="list-style-type: none"> • Systematic review of 37 provides evidence that SARS-CoV-2 RNA has been detected in a wide range of facilities and surfaces;

			<ul style="list-style-type: none"> • 6 studies have evaluated the viability/infectivity of SARS-CoV-2 from 242 positive surface samples; no viable virus could be isolated from the 242 samples with SARS-CoV-2 RNA detected by RT-qPCR • 17.7% of samples in hospital settings and 10.1% in non-hospital settings were positive for SARS-CoV-2 RNA, using various molecular methods. • As there is no evidence of viable and infectious SARS-CoV-2 on surfaces, authors warn against extrapolating SARS-CoV-2 RNA detection data into decision-making, as this may exaggerate the risk of fomite transmission.
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Treatment

Publication Date	Title/URL	Journal / Article type	Digest
14.09.2021	Remdesivir plus standard of care versus standard of care alone for the treatment of patients admitted to hospital with COVID-19 (DisCoVeRy): a phase 3, randomised, controlled, open-label trial	Lancet Infect Dis / Article	<ul style="list-style-type: none"> • Results from DisCoVeRy phase 3, randomised, controlled trial conducted in 48 sites in Europe. • Patients randomly assigned to standard of care alone (n=428) / in combination with remdesivir (n=429). • No clinical benefit observed from use of remdesivir in adult patients who were admitted to hospital for COVID-19, were symptomatic for more than 7 days, and required oxygen support.

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Modelling

Publication Date	Title/URL	Journal / Article type	Digest
13.09.2021	The Canna model: Assessing the impact of NHS Test and Trace on COVID-19 transmission: June 2020 to April 2021.	Gov.uk (non peer reviewed) / Research and analysis	<ul style="list-style-type: none"> • Modelling framework to evaluate the reduction in transmission from test, trace and self-isolation (TTI), providing a very high-level view of the impact of the whole system. • To determine the marginal impact attributable to NHS Test and Trace (NHSTT) the authors compare full impact of TTI to a hypothetical counterfactual scenario, in which all individuals who tested with

			<p>COVID-like-symptoms are assumed to have self-isolated, without ever taking a test, together with their household contacts</p> <ul style="list-style-type: none"> • During phases of exponential growth, and high incidence, even very small reductions in R_t will prevent many cases. Our study has indicated several periods when TTI brought R_t below 1. This would have prevented exponential growth, bringing incidence rates down, and will have helped to reduce the duration and economic impact of lock down and other social restrictions.
13.09.2021	Vaccinations or Non-Pharmaceutical Interventions: Safe Reopening of Schools in England	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • Authors present results of simulation using individual-based model, JUNE, for school opening after a prior vaccination campaign using an optimistic set of assumptions about vaccine efficacy and the likelihood of prior-reinfection • A scenario-based approach is used to assess the effects of vaccinating those aged 16-17, those aged 12-17, and not vaccinating children at all relative to only vaccinating the adult population. • According to these simulations vaccinating children in the 12-15 age group would have had a significant impact on the course of the epidemic, saving thousands of lives overall, whilst vaccinating only those children aged 16-17 would have a relatively small effect • Simulations indicate that there could still be a significant positive impact on the epidemic (fewer cases, fewer deaths) by continuing NPI strategies in schools; however analysis suggests that the best results are likely derived from a combination of vaccinations and NPIs.
14.09.2021	Common, low-frequency, rare, and ultra-rare coding variants contribute to COVID-19 severity	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • The authors report on the development of an Integrated Polygenic Score (IPGS) model which may provide useful information for developing diagnostics and therapeutics, while also being able to guide bedside disease management. • Common and rare variants from whole exome sequencing data of about 4,000 SARS-CoV-2-positive individuals were used to define an interpretable machine learning model for predicting COVID-19 severity. • Around one quarter of the selected genes are sex-specific, offering insight into the contrasting susceptibility to severe disease. • Pathway analysis of the selected genes associated with COVID-19 severity reflected the multi-organ nature of the disease.
13.09.2021	Analysis of 2.1 million SARS-CoV-2 genomes identifies mutations associated with transmissibility	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> • PyR0, a hierarchical Bayesian multinomial logistic regression model is used to identify numerous substitutions that increase transmissibility,

		<p>including previously identified spike mutations and many non-spike mutations within the nucleocapsid and nonstructural proteins</p> <ul style="list-style-type: none"> • PyRO forecasts growth of new lineages from their mutational profile, identifies viral lineages of concern as they emerge, and prioritises mutations of biological and public health concern for functional characterization • Applied to the full set of publicly available SARS-CoV-2 genomes, it provides a principled, unbiased analysis of the mutations driving increased transmissibility of the virus; the highlighted genetic diversity offers promising targets for follow-up investigation and may open new avenues for therapeutic or public health intervention.
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Guidance and consensus statements

Publication Date	Title/URL	Journal / Article type
13.09.2021	Universal vaccination of children and young people aged 12 to 15 years against COVID-19: Letter from the UK Chief Medical Officers to the UK Health Ministers on COVID-19 vaccination of 12 to 15 year olds.	Gov.uk / Correspondence
10.09.2021	Expert Opinion on COVID-19 Vaccination and the Use of Cladribine Tablets in Clinical Practice	medRxiv (non-peer reviewed) / Consensus statement
14.09.2021	SPI-M-O: Consensus statement on COVID-19, 8 September 2021	Gov.uk (non peer reviewed) / Consensus Statement

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Overviews, comments and editorials

Publication Date	Title/URL	Journal / Article type
10.09.2021	Covid-19: Vaccine passports approved in Scotland despite criticism	BMJ / News
16.09.2021	Covid-19: Unvaccinated face 11 times risk of death from delta variant, CDC data show	BMJ / News
10.09.2021	Covid-19: "Health in all policies" will help protect world from future pandemics, says commission	BMJ / News

04.09.2021	Drug repurposing against coronavirus disease 2019 (COVID-19): A review	J Pharm Anal / Review
14.09.2021	Prevention of host-to-host transmission by SARS-CoV-2 vaccines	Lancet Infect Dis / Personal view
14.09.2021	Covid-19: Boys are more at risk of myocarditis after vaccination than of hospital admission for covid	BMJ / News
09.09.2021	The next phase of SARS-CoV-2 surveillance: real-time molecular epidemiology	Nat Med / Review article
14.09.2021	Covid-19: Booster doses to be offered to 30 million people in UK	BMJ / News
09.09.2021	Long COVID and kidney disease	Nat Rev Nephrol / Comment
08.09.2021	Mass Spectrometry-based Proteomics and Glycoproteomics in COVID-19 Biomarkers Identification: A Mini-review	J Anal Test / Review

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