Public Health England

COVID-19 Literature Digest – 21/12/2020

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 The reports include both preprints, which should be treated with caution as they are NOT peer-reviewed and may be subject to change, and also research that has been subject to peer review and wider scrutiny.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

Bláthnaid Mahon, James Robinson
On behalf of the PHE COVID-19 Literature Digest Team

Report for 21.12.2020 (please note that papers that have **NOT been peer-reviewed** are highlighted in red).

Sections:

Serology and immunology

Publication Date	Title / URL	Journal / Article type	Digest
17.12.2020	T cell and antibody responses induced by a single dose of ChAdOx1 nCoV-19 (AZD1222) vaccine in a phase 1/2 clinical trial	Nat Med / Article	• Describes exploratory analyses of the immune responses in adults, aged 18–55 years, up to 8 weeks after vaccination with a single dose of ChAdOx1 nCoV-19 in this trial, demonstrating an induction of a Th1-biased response characterized by interferon-γ and tumour necrosis factor-α cytokine secretion by CD4+ T cells and antibody production predominantly of IgG1 and IgG3 subclasses. CD8+ T cells, of monofunctional, polyfunctional and cytotoxic phenotypes, were also induced. • Taken together, these results suggest a favourable immune profile induced by ChAdOx1 nCoV-19 vaccine, supporting the progression of this vaccine candidate to ongoing phase 2/3 trials to assess vaccine efficacy.

Vaccine development

Publication Date	Title / URL	Journal / Article type	Digest
17.12.2020	Phase 1/2 trial of SARS-CoV-2 vaccine ChAdOx1 nCoV-19 with a booster dose induces multifunctional antibody responses	Nat Med / Article	• Previously, the authors reported early immunogenicity and safety outcomes of a viral vector coronavirus vaccine, ChAdOx1 nCoV-19 (AZD1222), in a single-blinded phase 1/2 randomized controlled trial of healthy adults aged 18–55 years. • Now they describe safety and exploratory humoral and cellular immunogenicity of the vaccine, from subgroups of volunteers in the trial, who were subsequently allocated to receive a homologous full-dose (SD/SD D56; n = 20) or half-dose (SD/LD D56; n = 32) ChAdOx1 booster vaccine 56 d following prime vaccination. • A booster dose of vaccine induced stronger antibody responses than a dose-sparing half-dose boost, although the magnitude of T cell responses did not increase with either boost dose. These data support the two-dose vaccine regime that is now being evaluated in phase 3 clinical trials.

Diagnostics and genomics

Publication Date	Title / URL	Journal / Article type	Digest
20.12.2020	Threat Assessment Brief: Rapid increase of a SARS-CoV-2 variant with	European Centre for Disease Prevention and Control / Risk assessment	• The new variant is defined by multiple spike protein mutations (deletion 69-70, deletion 144, N501Y, A570D, D614G, P681H, T716I, S982A, D1118H)

	multiple spike protein mutations observed in the United Kingdom		present as well as mutations in other genomic regions. • Preliminary analysis in the UK suggests that this variant is significantly more transmissible than previously circulating variants, with an estimated potential to increase the reproductive number (R) by 0.4 or greater with an estimated increased transmissibility of up to 70%. • There is no indication at this point of increased infection severity associated with the new variant. • A few cases with the new variant have to date been reported by Denmark and the Netherlands and, according to media reports, in Belgium. • The aim of this Threat Assessment Brief is to summarise the findings, assess potential public health implications of this new variant, provide options for response and point out limitations, unknowns and needs for further studies and investigations.
20.12.2020	COVID-19 (SARS-CoV-2): information about the new virus variant	Gov.uk / News story	• Data from Whole Genome Sequencing, epidemiology and modelling suggest the new variant 'VUI – 202012/01' transmits more easily than other strains. • The way to control this virus is the same, whatever the variant. It will not spread if we avoid close contact with others. Wash your hands, wear a mask, keep your distance from others, and reduce your social contacts. • There is currently no evidence to suggest that the Pfizer vaccine would not protect people against the new strain. Further laboratory work is currently being undertaken as a priority to understand this. • Labs have been issued with guidance to adapt processes to ensure that PCR tests can detect this variant.
18.12.2020	Preliminary genomic characterisation of an emergent SARS-CoV-2 lineage in the UK defined	Virological (non-peer reviewed) / Article	• A distinct phylogenetic cluster (named lineage B.1.1.7) recently detected within the COG-UK surveillance dataset and has been growing rapidly over the past 4 weeks, in both case numbers and

	by a novel set of spike mutations		regions affected. • B.1.1.7 has an unusually large number of genetic changes, particularly in the spike protein. • Mutation N501Y is one of six key contact residues within the RBD and has been identified as increasing binding affinity to human and murine ACE2. • The spike deletion 69-70del has been described in the context of evasion to the human immune response but has also occurred in association with other RBD changes. • Mutation P681H is immediately adjacent to the furin cleavage site, a known location of biological significance.
15.12.2020	SIREN protocol: Impact of detectable anti-SARS-CoV-2 on the subsequent incidence of COVID-19 in 100,000 healthcare workers: do antibody positive healthcare workers have less reinfection than antibody negative healthcare workers?	medRxiv (non-peer reviewed) / Article	• Describes a proposed large-scale prospective longitudinal cohort study of healthcare staff across the UK to examine whether prior SARS-CoV-2 infection in healthcare workers confers future immunity to reinfection. • Participants will undergo antibody and viral RNA testing at 1-4 weekly intervals throughout the study period and will complete enrolment and fortnightly questionnaires on exposures and symptoms. • Follow-up will be for at least 12 months from study entry. • Primary outcome will be reinfection with SARS -CoV-2 during the study period. Secondary outcomes will include incidence and prevalence (both RNA and antibody) of SARS-CoV-2, viral genomics, viral culture, symptom history and antibody/neutralising antibody titres.

Epidemiology and clinical – risk factors

Publication Date	Title / URL	Journal / Article type	Digest
18.12.2020	COVID-19: pre-existing health conditions and ethnicity	Gov.uk / Research and analysis	• Report assessing whether the inequalities in diagnosis and death from COVID-19 between ethnic groups can be explained by pre-existing health conditions.

			• This report shows that, in the first wave of the COVID-19 pandemic in England, among people with a similar history of previous hospital admission mentioning pre-existing health conditions, there were ethnic differences in the numbers of cases and deaths involving COVID-19. • In addition, ethnic inequalities in survival following diagnosis of COVID-19 were not explained by differences in such patterns of admission with pre-existing health conditions between ethnic groups. • This conclusion is consistent with other studies reviewed in this document.
18.12.2020	Impact of Sex and Metabolic Comorbidities on COVID-19 Mortality Risk Across Age Groups: 66,646 Inpatients Across 613 U.S. Hospitals	Clin Infect Dis / Accepted manuscript	• This study aimed to determine the association between common patient characteristics and mortality across age-groups among COVID-19 inpatients. • Among 66,646 (6.5%) admissions with a COVID-19 diagnosis, across 613 U.S. hospitals, 12,388 (18.6%) died in-hospital. • In multivariable analysis, male sex was independently associated with 30% higher mortality risk (aRR, 1.30, 95% CI: 1.26 – 1.34). • Diabetes without chronic complications was not a risk factor at any age (aRR 1.01, 95% CI: 0.96 – 1.06), and hypertension without chronic complications was only a risk factor in 20-39 year-olds (aRR, 1.68, 95% CI: 1.17 – 2.40). • Diabetes with chronic complications, hypertension with chronic complications, and obesity were risk factors in most age-groups, with highest relative risks among 20-39 year-olds (respective aRRs 1.79, 2.33, 1.92; p-values ≤ 0.002).
18.12.2020	Does the prolonged use of face-masks by HCWs interfere with the respiratory system by inducing oxidative stress and blood oxygen/carbon dioxide imbalance?	HSE / Evidence summary	• The average face mask does not limit the flow of oxygen to the lungs, even in people with severe lung diseases. • Effects of prolonged mask and respirator use in healthcare settings include headaches, skin sensitivity, acne, itchy nose, and excessive sweating around the mouth. • Frequent breaks, improved hydration and rest, skin care, and newly designed, more comfortable masks are recommendations for future management of adverse effects related to prolonged mask use.

Epidemiology and clinical – other

Publication Date	Title / URL	Journal / Article type	Digest
16.12.2020	All-Cause Excess Mortality and COVID-19-Related Mortality Among US Adults Aged 25-44 Years, March-July 2020	Jama / Research letter	• Examined all-cause excess mortality and COVID-19–related mortality in the early pandemic period among adults aged 25 to 44 years and compared this with data on unintentional opioid deaths, the leading cause of death in this demographic. • Findings indicate the COVID-19 pandemic was associated with increases in all-cause mortality. • In 3 of 10 US Department of Health and Human Services regions, COVID-19 deaths were similar to or exceeded unintentional opioid overdoses occurring during corresponding months of 2018. • In total, 38% of all-cause excess deaths were attributed directly to COVID-19; remaining excess deaths are unexplained, possibly due to inadequate testing. • Study limitations include lower-bound estimates due to reporting lags, and the possibility of simultaneous increases in opioid deaths during the study period.
16.12.2020	Postmortem Stability of SARS-CoV-2 in Nasopharyngeal Mucosa	Emerg Infect Dis / Research letter	• Analyses of infection chains have demonstrated that SARS CoV-2 is highly transmissive. However, data on post-mortem stability and infectivity are lacking. • Authors finding of nasopharyngeal viral RNA stability in 79 corpses showed no time-dependent decrease. Maintained infectivity is supported by virus isolation up to 35 hours post-mortem.
10.12.2020	What is the evidence for waste water surveillance to enhance other forms of surveillance for COVID-19?	HSE / Evidence summary	• Summarises evidence for waste water surveillance to enhance other forms of surveillance for COVID-19. • The WHO say that surveillance of COVID-19 in wastewater and sludge may compliment public health data and provide, for example, information on when cases may spike 5-7 days in advance of such spikes being detected by health facilities and health authorities. The WHO also point out that environmental surveillance should not be used as a substitute for robust surveillance of COVID-19 cases. • The COVID-19 WBE Collaborative was launched in partnership with the Sewage analysis CORe group Europe (SCORE)network and the Global Water Pathogen Project as a hub to coordinate and promote the efforts of research groups undertaking WBE for COVID-19. • From Sept, the Netherlands adopted a national wastewater

			surveillance strategy, and samples from over 300 water treatment plants will be tested daily. • The UK have commenced testing wastewater samples from 44 treatment sites and researchers are pioneering waste water analysis as part of a nationwide programme.

Treatment

Publication Date	Title / URL	Journal / Article type	Digest
17.12.2020	Update to living systematic review on drug treatments for covid-19	BMJ / Research	• This living systematic review by Siemieniuk and colleagues has been updated. • The latest version includes results for new interventions azithromycin, colchicine, interferon beta, interferon gamma, interferon kappa plus trefoil factor 2, rhG-CSF, tocilizumab (but certainty is low or very low); evidence that remdesivir may not reduce mortality (low certainty) or time to symptom resolution (moderate certainty); evidence that glucocorticoids probably reduce length of ICU stay (low certainty) and increase ventilator-free days (moderate certainty).

Guidance and consensus statements

Publication Date	Title / URL	Journal / Article type
17.12.2020	COVID-19 rapid guideline: vitamin D	NICE / Guideline
18.12.2020	National protocol for COVID-19 mRNA vaccine BNT162b2 (Pfizer/BioNTech)	Gov.uk / Guidance

Overviews, comments and editorials

Publication Date	Title / URL	Journal / Article type
18.12.2020	Calling for pan-European commitment for rapid and sustained reduction in SARS-CoV-2 infections	Lancet / Correspondence
18.12.2020	Infectivity of asymptomatic versus symptomatic COVID-19	Lancet / Correspondence
17.12.2020	COVID-19 as the Leading Cause of Death in the United States	JAMA / Viewpoint

Produced by the PHE COVID-19 Literature Digest Team

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