



## COVID-19 Literature Digest – 11/12/2020

Dear all,

**This week's guest editor is Dr Sian Evans – Associate Director Local Knowledge and Intelligence Service East of England and Deputy Theme lead, East of England Applied Research Collaboration, Population Evidence and Data Science theme.**

### **If you only read three papers this week...**

The first paper I want to highlight is [an observational study](#) on the use of longitudinal, self-reported data from users of the COVID Symptoms Study app. Varsavsky et al modelled data from over 120 million reports from more than 2.8 million users across England. Data from the app was combined with the results from RT-PCR (swab) tests offered to app users who developed symptoms. On Sept 28, they estimated a national incidence of 15 841 (95% CI 14 023–17 885) daily cases, a prevalence of 0.53% (0.45–0.60), and R(t) of 1.17 (1.15–1.19). They report that their national estimates showed a similar sensitivity to changes to the ONS and REACT-1 studies. At subnational level, the modelling identified a relatively high proportion of areas that had also been highlighted from government testing data. The app data has limitations; app users were not representative of the wider population, it relied on user self-reporting and the likelihood of using the app might be dependent on the likelihood of having COVID-19. The authors conclude that their method could help to detect rapid case increases where testing provision is lower and that mobile technology can be used to provide real-time data on the national and local state of the pandemic, enabling policy makers to make informed decisions in a quickly moving pandemic.

The second paper is a first [systematic review and meta-analysis](#) examining the risk of thromboembolism among people with COVID-19 and the associated mortality risk. Early reports indicated that COVID-19 may be associated with coagulation dysfunction. Malas et al report on a meta-analysis of 42 studies involving 8,271 patients, providing pooled estimates of venous and arterial thromboembolism. They report overall rates of deep vein thrombosis of 20% (95%CI 13-28%) and pulmonary embolism of 13% (95%CI 11-16%) while the arterial thromboembolism rate was 2% (95%CI 1-4%). Rates were higher among patients in ICU compared to those not in ICU. The pooled odds of mortality among patients with thromboembolism was 74% higher compared to patients with no thromboembolism (OR 1.74, 95%CI 1.01-2.98, P=0.04). Malas et al comment that the pooled estimates for venous thromboembolism in their meta-analysis are higher than might be expected for hospitalised patients with acute infection. They conclude that COVID-19 poses a significant risk of thromboembolism and that strategies that succeed in preventing the development of thromboembolism could reduce COVID-19 mortality.

Finally, I wanted to highlight a [letter](#) from Richard Armitage and Laura Nellums who used monthly data from NHS England to report on antibiotic prescribing in general practice. The number of antibiotic prescriptions made in general practice between April 1, and Aug 31, was 15% lower than the corresponding period in 2019. However, due to the decrease in absolute number of appointments over the period, prescriptions were 6.7% higher than expected - a statistically significant increase. They suggest that the data support evidence that antibiotic prescribing rates are higher in remote consultations, possibly due to greater diagnostic uncertainty in a remote setting. While rates of telephone appointments in general practice remain high, they highlight the need for good antimicrobial stewardship to curb the emergence of antimicrobial resistance.

Sian

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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 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.

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Best wishes,

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

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**Report for 11.12.2020** (please note that papers that have **NOT been peer-reviewed** are highlighted in red).

Sections:

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[Guidance and consensus statements \(no digest\)](#)

[Overviews, comments and editorials \(no digest\)](#)

## Serology and immunology

Publication Date	Title / URL	Journal / Article type	Digest
26.11.2020	<a href="#">Low-Avidity CD4(+) T Cell Responses to SARS-CoV-2 in Unexposed Individuals and Humans with Severe COVID-19</a>	Immunity / Article	<ul style="list-style-type: none"> <li>• Authors examine antigen avidity and clonality of SARS-CoV-2-reactive CD4+ T cells ("cells"), as well as the relative contribution of common cold coronavirus (CCCoV) cross-reactivity.</li> <li>• The cells were present in virtually all unexposed individuals examined, displaying low functional avidity and multiple, highly variable cross-reactivities not restricted to CCCoVs.</li> <li>• Cells from COVID-19 patients lacked cross-reactivity to CCCoVs, irrespective of strong memory T cell responses against CCCoV in all donors analysed.</li> <li>• In severe but not mild COVID-19, the cells displayed low functional avidity and clonality, despite increased frequencies.</li> </ul>

## Vaccine development

Publication Date	Title / URL	Journal / Article type	Digest
10.12.2020	<a href="#">Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine</a>	N Engl J Med / Article	<ul style="list-style-type: none"> <li>• In an ongoing multinational, placebo-controlled, observer-blinded, pivotal efficacy trial, the authors randomly assigned persons 16 years of age or older in a 1:1 ratio to receive two doses, 21 days apart, of either placebo or the BNT162b2 vaccine candidate (30 µg per dose).</li> <li>• 43,448 participants received injections (21,720 with BNT162b2 / 21,728 with placebo). 10 cases of severe Covid-19 with onset after first dose, of which 9 occurred in placebo recipients.</li> <li>• BNT162b2 was 95% effective in preventing Covid-19 (95% credible interval, 90.3 to 97.6). Similar vaccine efficacy (generally 90 to 100%) observed across subgroups defined by age, sex, race, ethnicity, baseline body-mass index, and presence of coexisting conditions.</li> <li>• A two-dose regimen of BNT162b2 conferred 95% protection against Covid-19 in persons 16 years of age or older. Safety over a median of 2 months similar to that of other viral vaccines.</li> </ul>

## Diagnostics and genomics

Publication Date	Title / URL	Journal / Article type	Digest
09.12.2020	<a href="#">Analytical validity of nanopore sequencing for rapid SARS-CoV-2 genome analysis</a>	Nat Commun / Article	<ul style="list-style-type: none"> <li>• Adoption of Oxford Nanopore Technologies (ONT) sequencing for SARS-CoV-2 surveillance has so far been limited due to concerns around sequencing accuracy.</li> <li>• The authors performed viral whole-genome sequencing (WGS) with ONT and Illumina platforms on 157 matched SARS-CoV-2-positive patient specimens and synthetic RNA controls.</li> <li>• Despite elevated error rates observed in ONT sequencing reads, highly accurate consensus-level sequence determination was achieved, with single nucleotide variants detected at &gt;99% sensitivity and &gt;99% precision above a minimum ~60-fold coverage depth.</li> <li>• ONT sequencing also identified a surprising diversity of structural variation within SARS-CoV-2 specimens that were supported by evidence from short-read sequencing on matched samples.</li> <li>• However, ONT sequencing failed to accurately detect short indels and variants at low read-count frequencies.</li> </ul>

## Epidemiology and clinical – children / pregnancy

Publication Date	Title / URL	Journal / Article type	Digest
09.12.2020	<a href="#">Priorities for the child public health response to the COVID-19 pandemic recovery in England</a>	Arch Dis Child / Review	<ul style="list-style-type: none"> <li>• This review highlights a range of risks to child health in England, resulting from the unintended consequences of the COVID-19 response.</li> <li>• Long-term risks may result from diversion of healthcare, interruption of schooling, impact on mental health and increased social inequalities, among other things.</li> <li>• A considered and multidisciplinary policy response that prioritises children's right to health is required in order to mitigate against rising inequalities.</li> </ul>
10.12.2020	<a href="#">Severity of COVID-19 in children with cancer: Report from the United Kingdom Paediatric Coronavirus Cancer Monitoring Project</a>	Br J Cancer / Article	<ul style="list-style-type: none"> <li>• Review incidence and outcomes from SARS-CoV-2 in children with cancer attending UK hospitals for treatment. 54 cases: 15 (28%) asymptomatic, 34 (63%) mild infections, 5 (10%) moderate, severe or critical infections.</li> <li>• No deaths, only 3 patients required intensive care support. Estimated incidence of hospital identified SARS-CoV-2 infection in children with cancer under 16 was 3%.</li> <li>• Children with cancer with SARS-CoV-2 infection do not appear at increased risk of severe infection compared to the general paediatric population.</li> </ul>

**Epidemiology and clinical – risk factors**

Publication Date	Title / URL	Journal / Article type	Digest
09.12.2020	<a href="#">Occupation and risk of severe COVID-19: prospective cohort study of 120 075 UK Biobank participants</a>	Occup Environ Med / Article	<ul style="list-style-type: none"> <li>• UK Biobank data (2006–10) for England were linked to SARS-CoV-2 test results from Public Health England (16 March to 26 July 2020). Of 120 075 participants, 271 had severe COVID-19.</li> <li>• Higher risk of severe COVID-19: healthcare workers (RR 7.43, 95% CI 5.52 to 10.00), social &amp; education workers (RR 1.84, 95% CI 1.21 to 2.82), other essential workers (RR 1.60, 95% CI 1.05 to 2.45).</li> <li>• Medical support staff (RR 8.70, 95% CI 4.87 to 15.55), social care (RR 2.46, 95% CI 1.47 to 4.14) and transport workers (RR 2.20, 95% CI 1.21 to 4.00) had highest risk within broader groups.</li> <li>• Non-white non-essential workers had a higher risk (RR 3.27, 95% CI 1.90 to 5.62) and non-white essential workers had the highest risk (RR 8.34, 95% CI 5.17 to 13.47).</li> </ul>
09.12.2020	<a href="#">Male sex identified by global COVID-19 meta-analysis as a risk factor for death and ITU admission</a>	Nat Commun / Article	<ul style="list-style-type: none"> <li>• Authors present a meta-analysis of 3,111,714 reported global cases: whilst no difference in proportion of males and females with confirmed COVID-19, male patients have almost three times the odds of requiring intensive treatment unit (ITU) admission (OR = 2.84; 95% CI = 2.06, 3.92) and higher odds of death (OR = 1.39; 95% CI = 1.31, 1.47) compared to females.</li> <li>• With few exceptions, the sex bias observed in COVID-19 is a worldwide phenomenon.</li> <li>• An appreciation of how sex is influencing COVID-19 outcomes will have important implications for clinical management and mitigation strategies for this disease.</li> </ul>
10.12.2020	<a href="#">Analyses of Risk, Racial Disparity, and Outcomes Among US Patients With Cancer and COVID-19 Infection</a>	JAMA Oncol / Original investigation	<ul style="list-style-type: none"> <li>• US patients with cancer were at significantly increased risk for COVID-19 infection and worse outcomes, which was further exacerbated among African Americans.</li> <li>• Recent cancer diagnosis significantly increased COVID-19 risk (aOR, 7.14 [95% CI, 6.91-7.39]; P &lt; .001), especially leukemia (aOR, 12.16 [95% CI, 11.03-13.40]; P &lt; .001), non-Hodgkin lymphoma (aOR, 8.54 [95% CI, 7.80-9.36]; P &lt; .001), and lung cancer (aOR, 7.66 [95% CI, 7.07-8.29]; P &lt; .001).</li> <li>• African Americans had significantly higher risk than White patients; especially breast cancer (aOR, 5.44 [95% CI, 4.69-6.31]; P &lt; .001), prostate cancer (aOR, 5.10 [95% CI, 4.34-5.98]; P &lt; .001), colorectal cancer (aOR, 3.30 [95% CI, 2.55-4.26]; P &lt; .001), and lung cancer (aOR, 2.53 [95% CI, 2.10-3.06]; P &lt; .001).</li> <li>• Patients with cancer and COVID-19 had significantly worse outcomes</li> </ul>

(hospitalization, 47.46%; death, 14.93%) than patients with COVID-19 without cancer or with cancer without COVID-19 .

#### Epidemiology and clinical – long-term complications / sequelae

Publication Date	Title / URL	Journal / Article type	Digest
08.12.2020	<a href="#">Characterising long-term covid-19: a rapid living systematic review</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• A living systematic review in response to the rapidly evolving evidence base for long covid included 28 studies (16 cohort studies, 10 cross-sectional, and 2 large case series) comprising 9,442 adults with Covid-19 from 13 countries.</li> <li>• A wide range of systemic, cardiopulmonary, gastrointestinal, neurological, and psychosocial symptoms was reported, of which the most common were breathlessness, fatigue, smell and taste disturbance, and anxiety.</li> <li>• Persistent symptoms were described across both previously hospitalised and non-hospitalised populations.</li> <li>• Findings are subject to limitations including: high risk of bias and heterogeneity; limited external validity; lack of control subjects; inconsistent data collection methods; and few studies conducted in primary care or low- and middle-income countries.</li> </ul>

#### Epidemiology and clinical – other

Publication Date	Title / URL	Journal / Article type	Digest
10.12.2020	<a href="#">Community prevalence of SARS-CoV-2 in England from April to November, 2020: results from the ONS Coronavirus Infection Survey</a>	Lancet Public Health / Article	<ul style="list-style-type: none"> <li>• <i>This paper was previously included in the Digest as a preprint.</i></li> <li>• Samples were collected from individuals aged 2 years and older living in private households in England that were randomly selected from address lists and previous ONS surveys in repeated cross-sectional household surveys with additional serial sampling and longitudinal follow-up.</li> <li>• Between Apr 26 and Nov 1, 2020, results were available from 1 191 170 samples from 280 327 individuals; 5231 samples were positive overall, from 3923 individuals.</li> <li>• Important risk factors for testing positive for SARS-CoV-2 varied substantially between the part of the first wave that was captured by the study (Apr to June, 2020) and the first part of the second wave of increased positivity rates (end of Aug to Nov 1, 2020), and a substantial proportion of infections were in individuals not reporting symptoms, indicating that continued monitoring for</li> </ul>

			SARS-CoV-2 in the community will be important for managing the COVID-19 pandemic moving forwards.
10.12.2020	<a href="#">Epidemiological characteristics of COVID-19 cases and estimates of the reproductive numbers 1 month into the epidemic, Italy, 28 January to 31 March 2020</a>	Eurosurveillance / Research	<ul style="list-style-type: none"> <li>• Describes the epidemiology and transmission dynamics of the first COVID-19 cases in Italy amid ongoing control measures.</li> <li>• Of the 98,716 cases of COVID-19 analysed, 9,512 were healthcare workers.</li> <li>• Of the 10,943 reported COVID-19-associated deaths (crude case fatality ratio: 11.1%) 49.5% occurred in cases older than 80 years.</li> <li>• Male sex and age were independent risk factors for COVID-19 death. Estimates of R0 varied between 2.50 (95% confidence interval (CI): 2.18–2.83) in Tuscany and 3.00 (95% CI: 2.68–3.33) in Lazio.</li> <li>• The COVID-19 outbreak in Italy showed a clustering onset similar to the one in Wuhan, China. R0 at 2.96 in Lombardy combined with delayed detection explains the high case load and rapid geographical spread. Overall, Rt in Italian regions showed early signs of decrease, with large diversity in incidence, supporting the importance of combined non-pharmacological control measures.</li> </ul>
08.12.2020	<a href="#">Evidence of SARS-CoV-2 RNA in an Oropharyngeal Swab Specimen, Milan, Italy, Early December 2019</a>	Emerg Infect Dis / Research letter	<ul style="list-style-type: none"> <li>• Authors retrospectively explored a possible etiologic involvement of SARS-CoV-2 in non-measles-linked rash cases.</li> <li>• They identified SARS-CoV-2 RNA in an oropharyngeal swab specimen collected from a child with suspected measles in early December 2019, ≈3 months before first identified coronavirus disease case in Italy.</li> <li>• This finding is of epidemiologic importance because it expands our knowledge on timing and mapping of the SARS-CoV-2 transmission pathways.</li> </ul>

### Infection control / non-pharmaceutical interventions

Publication Date	Title / URL	Journal / Article type	Digest
10.12.2020	<a href="#">Community use of face masks and similar barriers to prevent respiratory illness such as COVID-19: a rapid scoping review</a>	Eurosurveillance / Review	<ul style="list-style-type: none"> <li>• Review to assess effectiveness of wearing face masks in the community to prevent respiratory disease, and recommend improvements to this evidence base.</li> <li>• 33 studies (12 randomised control trials (RCTs)) were included. Mask wearing reduced primary infection by 6% (odds ratio (OR): 0.94; 95% CI: 0.75–1.19 for RCTs) to 61% (OR: 0.85; 95% CI: 0.32–2.27; OR: 0.39; 95% CI: 0.18–0.84 and OR: 0.61; 95% CI: 0.45–0.85 for cohort, case-control and cross-sectional studies respectively).</li> <li>• RCTs suggested lowest secondary attack rates when both well and ill household members wore masks (OR: 0.81; 95% CI: 0.48–1.37). While RCTs might underestimate effects due to poor compliance and controls wearing</li> </ul>

			<p>masks, observational studies likely overestimate effects, as mask wearing might be associated with other risk-averse behaviours. GRADE was low or very low quality.</p> <ul style="list-style-type: none"> <li>Wearing face masks may reduce primary respiratory infection risk, probably by 6–15%. It is important to balance evidence from RCTs and observational studies when their conclusions widely differ and both are at risk of significant bias. COVID-19-specific studies are required.</li> </ul>
10.12.2020	<a href="#">Evaluation of Cloth Masks and Modified Procedure Masks as Personal Protective Equipment for the Public During the COVID-19 Pandemic</a>	JAMA Intern Med / Original investigation	<ul style="list-style-type: none"> <li>Comparative study of fitted filtration efficiencies (FfEs) of face coverings; mean (SD) FfE of consumer grade masks tested on adult male with no beard ranged from 79.0% (4.3%) to 26.5% (10.5%), with the 2-layer woven nylon mask having the highest FfE.</li> <li>Modifications intended to enhance the fit of medical procedure masks improved FfE measurements from 38.5% (unmodified mask) to as much as 80.2%.</li> </ul>
18.11.2020	<a href="#">Nosocomial Coronavirus Disease Outbreak Containment, Hanoi, Vietnam, March-April 2020</a>	Emerg Infect Dis / Article	<ul style="list-style-type: none"> <li>Report on COVID-19 outbreak during March 2020 at Bach Mai Hospital (BMH) in Hanoi, northern Vietnam's largest hospital complex. After 3 weeks, outbreak contained.</li> <li>Rapid screening of cases, extensive testing, prompt quarantine, contact tracing, and social distancing contributed to prevent community transmission in Hanoi and northern Vietnam.</li> </ul>

### Transmission

Publication Date	Title / URL	Journal / Article type	Digest
10.12.2020	<a href="#">Secondary transmission of COVID-19 in preschool and school settings in northern Italy after their reopening in September 2020: a population-based study</a>	Eurosurveillance / Rapid communication	<ul style="list-style-type: none"> <li>Report epidemiological investigations of transmission of SARS-CoV-2 in 41 classes of 36 schools in Reggio Emilia province, northern Italy, from their reopening on 1 Sept to 15 Oct 2020.</li> <li>The overall secondary case attack rate was 3.2%, reaching 6.6% in middle and high schools. More timely isolation and testing of classmates could be effective in reducing virus transmission in this setting.</li> </ul>

## Modelling

Publication Date	Title / URL	Journal / Article type	Digest
10.12.2020	<a href="#">Report 40 - Optimal scheduling rules for elective care to minimize years of life lost during the SARS-CoV-2 pandemic: an application to England</a>	Imperial College / Report	<ul style="list-style-type: none"><li>• Developed a model to optimally schedule elective hospitalizations and allocate hospital general and critical care beds to planned and emergency patients in England during the pandemic.</li><li>• Applied the model to NHS England data and show that optimized scheduling leads to lower years of life lost and costs than policies that reflect those implemented in England during the pandemic.</li><li>• Overall across all disease areas the model enables an extra 50,750-5,891,608 years of life gained when compared to standard policies, depending on the scenarios. Especially large gains in years of life are seen for neoplasms, diseases of the digestive system, and injuries &amp; poisoning.</li></ul>

## Guidance and consensus statements

Publication Date	Title / URL	Journal / Article type
10.12.2020	<a href="#">Coronavirus disease 2019 (COVID-19) and supply of substances of human origin in the EU/EEA - Second update</a>	European Centre for Disease Prevention and Control / Technical report
09.12.2020	<a href="#">Confirmation of guidance to vaccination centres on managing allergic reactions following COVID-19 vaccination with the Pfizer/BioNTech vaccine</a>	Gov.uk / Press release

## Overviews, comments and editorials

Publication Date	Title / URL	Journal / Article type
10.12.2020	<a href="#">Filtration Efficiency of Face Masks Used by the Public During the COVID-19 Pandemic</a>	JAMA Intern Med / Editor's note
10.12.2020	<a href="#">Face masks and COVID-19: don't let perfect be the enemy of good</a>	Eurosurveillance / Editorial
12.12.2020	<a href="#">Facing up to long COVID</a>	The Lancet / Editorial
10.12.2020	<a href="#">The COVID-19 vaccines rush: participatory community engagement matters more than ever</a>	Lancet / Comment

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