



## COVID-19 Literature Digest – 04/12/2020

Dear all,

This week's guest editor is Emma Bennett - Principal Epidemiologist in the Emergency Response Department's Epidemiology and Modelling group. As part of the COVID-19 response, Emma has also been working for the past ten months in the Joint Modelling Cell.

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

*Striking a balance between safeguarding public health and protecting the economy remains to be a complex challenge within the COVID-19 pandemic.*

*The first paper I would like to recommend ([Livestock plants and COVID-19 transmission](#)) considers the relationship between livestock processing plants and COVID-19 transmission in the United States. Understanding the public health risks posed by large industry, particularly food supply industries, is vital for tackling disease spread but also for assessing potential impacts of policy interventions. The study uses a range of analyses (including an event study, instrumental variables (IVs), and matching) to examine the potential relationship between livestock-processing plants (beef, pork and poultry) and local community transmission of the disease. Findings suggest that the public health risk posed by livestock processing extends beyond that of meatpacking companies and their employees and into the local community. Although not able to demonstrate causality, the study suggests that, as of July 21<sup>st</sup> 2020, proximity to livestock plants in the US was associated with 236,000 to 310,000 excess cases (6 to 8% of all US cases) and 4,300 to 5,200 excess deaths (3 to 4% of all US deaths), with the vast majority occurring among people who do not work at livestock plants. Other findings suggest that temporary closure of high-risk plants was followed by lower rates of case growth; smaller, decentralized facilities did not appear to contribute to transmission and plants that had increased their production-line speeds saw more county-wide cases.*

*A Comment in The Lancet Infectious Diseases, my second chosen paper ([SARS-CoV-2 and the human-animal interface: outbreaks on mink farms](#)), addresses another concern around animal-related industries, that of intensive farming of mink for fur. The circulation of SARS-CoV-2 in animals in Denmark and the 'spill back' from mink farms into the community, has generated widespread concern, particularly since accumulated mutations in the spike protein gene might affect the utility of vaccines that are currently in production. First reported in the Netherlands in April, this spillover has also been seen in Spain, Italy, USA, Sweden and Greece. One of the major concerns is the potential formation of a non-human reservoir, from where the virus could be reintroduced once circulation of SARS-CoV-2 is suppressed, or even stopped in humans, thus posing a continual public health threat. The Comment supports the announcement of a new WHO study into the origins of SARS-CoV-2, but stresses that it will also need to consider the role of animals kept for food, fur and other products. The fact that there is no global overview of where mink farms are located (and ECDC estimates that there are around 2750 in Europe alone) and no mandatory surveillance programme, means the scale of these industries, and therefore the threat to our public health, are unknown.*

*Due to the impact of the pandemic, a reduced number of attendees were expected at an annual 10-day Sturgis motorcycle rally in South Dakota's Black Hills (7<sup>th</sup> - 16<sup>th</sup> August 2020). However, as it turned out, over 460 000 people from across the United States turned up. By continuing to hold the rally this year the state's authorities, it has been suggested, put economic interest ahead of public health and the potential for a super-spreading event. Understandably though, with an annual income of around \$800*

million for the state's economy, the balance is a difficult one to strike. My third paper ([COVID-19 Outbreak Associated with a 10-Day Motorcycle Rally in a Neighboring State – Minnesota, August–September 2020](#)) reports that, following the rally, at least 86 Minnesota residents (state bordering South Dakota) developed COVID-19; 51 confirmed primary event-associated cases, 21 secondary cases, and five tertiary cases. An additional nine likely rally-associated secondary or tertiary cases also occurred. Four patients were hospitalized, and one died. To put this in context, approximately one third of counties in Minnesota reported at least one case epidemiologically-linked to this event. The findings suggest that this rally not only had a direct impact on the health of attendees, but also led to subsequent SARS-CoV-2 transmission among household, social, and workplace contacts of rally attendees upon their return to Minnesota. The report also highlights that the motorcycle rally was held in a state that did not have policies regarding event size and mask use (unlike in Minnesota) and demonstrates the need for consistent mitigation measures across states. Furthermore, although the findings did not capture the impact of the motorcycle rally on residents of other states, analyses published in a discussion paper by the IZA Institute of Labor Economics in September (*The Contagion Externality of a Superspreading Event: The Sturgis Motorcycle Rally and COVID-19* (<http://ftp.iza.org/dp13670.pdf>), suggest that the rally was potentially responsible for more than 250 000 cases reported between the 2<sup>nd</sup> of August and the 2<sup>nd</sup> of September, and generated a potential \$12.2 billion in public health costs.

Emma

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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 04.12.2020** (please note that papers that have **NOT been peer-reviewed** are highlighted in red).

Sections:

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

### Serology and immunology

Publication Date	Title / URL	Journal / Article type	Digest
03.12.2020	<a href="#">Durability of Responses after SARS-CoV-2 mRNA-1273 Vaccination</a>	N Engl J Med / Correspondence	<ul style="list-style-type: none"><li>• Authors describe immunogenicity data 119 days after first vaccination (90 days after second vaccination) in 34 healthy adult participants who received two injections of vaccine at a dose of 100 µg.</li><li>• Results show that despite a slight expected decline in titres of binding and neutralizing antibodies, mRNA-1273 has the potential to provide durable humoral immunity.</li><li>• Findings provide support for the use of a 100-µg dose of mRNA-1273 in an ongoing phase 3 trial, which has recently shown a 94.5% efficacy rate in an interim analysis.</li></ul>

### Diagnostics and genomics

Publication Date	Title / URL	Journal / Article type	Digest
24.11.2020	<a href="#">Clinical, laboratory, and radiologic characteristics of patients with initial false-negative SARS-CoV-2 nucleic acid amplification test results</a>	Open Forum Infectious Diseases / Article	<ul style="list-style-type: none"><li>• Authors retrospectively reviewed test results from 15,011 U.S adults who underwent ≥1 SARS-CoV-2 nucleic acid amplification tests (NAATs); 2,699 had an initial negative NAAT and repeat testing.</li><li>• Sixty of 2,699 (2.2%) had a false-negative (FN) result. Weekly frequency of FNs among subjects with repeat testing peaked at 4.4%, coinciding with peak NAAT positivity (38%).</li><li>• 18/60 FN NAATs (30%) were performed early (i.e., ≤1 day of symptom onset), and 18/60 (30%) were performed late (i.e., &gt;7 days after symptom onset) in disease.</li><li>• 17 subjects with two consecutive FNs on NP NAATs, 9 (53%) provided lower respiratory tract (LRT) specimens for testing, all of which were positive.</li></ul>

			<ul style="list-style-type: none"> <li>• Findings support repeated NAATs among symptomatic patients, particularly during periods of higher COVID-19 incidence. Prioritise LRT testing to increase yield among patients with high clinical suspicion for COVID-19.</li> </ul>
01.12.2020	<a href="#">Extrapolation of United Kingdom Pillar 2 Care home Covid-19 test data to ascertain effectiveness of lateral flow testing in low prevalence settings</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• The authors utilise Pillar 2 test data from the University of Birmingham test laboratory, and by extrapolation against the validate limit-of-detection of the UK lateral flow assay, provide a potential sensitivity for the test in a comparable low prevalence population captured in the Pillar 2 program.</li> <li>• Data suggests the lateral flow assay should successfully capture around 85% of all PCR positive tests performed in the Pillar 2 laboratory, and that a fully designed comparative study of lateral flow versus PCR testing is merited in a real life environment.</li> </ul>
30.11.2020	<a href="#">Is Point-of-Care testing feasible and safe in care homes in England? An exploratory usability and accuracy evaluation of Point-of-Care Polymerase Chain Reaction test for SARS-COV-2</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• Point-of-care PCR for SARS-COV2 (POC) was evaluated in four UK care homes (278 participants), and test agreement with laboratory real-time PCR and usability and use errors were assessed.</li> <li>• POC and laboratory tests returned uncertain results or errors for 17 and 5 specimens respectively.</li> <li>• In agreement analysis of 256 specimens, asymptomatic specimens showed 83.3% positive agreement and 98.7% negative agreement, with overall prevalence and bias-adjusted kappa (PABAK) of 0.965.</li> <li>• Symptomatic specimens showed 100% positive agreement and 100% negative agreement, with overall PABAK of 1.</li> <li>• No usability-related hazards emerged from this exploratory study.</li> <li>• Agreement between POCT and laboratory PCR was good. Further diagnostic accuracy evaluations and in-service evaluation studies should be conducted, if the test is to be implemented more widely, to build greater certainty on this initial exploratory analysis.</li> </ul>
30.11.2020	<a href="#">Prospective mapping of viral mutations that escape antibodies used to treat COVID-19</a>	bioRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• The authors map how all mutations to SARS-CoV-2's receptor-binding domain (RBD) affect binding by the antibodies in Regeneron's REGN-COV2 cocktail and Eli Lilly's LY-CoV016.</li> <li>• Uncovers a single amino-acid mutation that fully escapes the REGN-COV2 cocktail, which consists of two antibodies targeting distinct structural epitopes.</li> <li>• Identifies viral mutations that are selected in a persistently infected patient treated with REGN-COV2, as well as in lab viral escape selections.</li> <li>• Reveals that mutations escaping each individual antibody are already present in circulating SARS-CoV-2 strains.</li> <li>• Overall, these complete escape maps enable immediate interpretation of the consequences of mutations observed during viral surveillance.</li> </ul>

## Epidemiology and clinical – risk factors

Publication Date	Title / URL	Journal / Article type	Digest
04.12.2020	<a href="#">Rapid Risk Assessment: Risk of COVID-19 transmission related to the end-of-year festive season</a>	European Centre for Disease Prevention and Control / Risk assessment	<ul style="list-style-type: none"> <li>• This document assesses the risk of SARS-CoV-2 transmission to the general population and medically vulnerable individuals in the EU/EEA and the UK, from the perspective of the upcoming end-of-year festive season.</li> </ul>
04.12.2020	<a href="#">Multidisciplinary Community-Based Investigation of a COVID-19 Outbreak Among Marshallese and Hispanic/Latino Communities - Benton and Washington Counties, Arkansas, March-June 2020</a>	MMWR Morb Mortal Wkly Rep / Report	<ul style="list-style-type: none"> <li>• Marshallese and Hispanic persons represented approximately 19% of the population but accounted for 64% of COVID-19 cases and 57% of associated deaths in two Arkansas counties.</li> <li>• Contributing factors include lack of relevant health communications, limited coordination between stakeholders, mistrust of the medical system, financial need to work, and household density.</li> <li>• Reducing COVID-19 disparities requires strengthening coordination of public health, health care, and community stakeholders to provide tailored health education, community-based prevention activities, case management, care navigation, and service linkage.</li> </ul>
04.12.2020	<a href="#">Disproportionate Incidence of COVID-19 Infection, Hospitalizations, and Deaths Among Persons Identifying as Hispanic or Latino — Denver, Colorado March–October 2020</a>	MMWR Morb Mortal Wkly Rep / Report	<ul style="list-style-type: none"> <li>• In Denver, Colorado, the majority of adult COVID-19 cases (55%), hospitalizations (62%), and deaths (51%) were among Hispanic adults, double the proportion of Hispanic adults in Denver (24.9%).</li> <li>• Among adults with COVID-19, Hispanic persons reported larger household sizes and more known COVID-19 household exposure, working in essential industries, working while ill, and delays in testing after symptom onset.</li> </ul>
27.11.2020	<a href="#">Ethnicity, Household Composition and COVID-19 Mortality: A National Linked Data Study</a>	medRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• Authors estimate associations between household composition and COVID-19 mortality in older adults (<math>\geq 65</math> years) using a census-based dataset (<math>n=10,078,568</math>), and investigated whether living in a multi-generational household (MGH) explained some of the elevated COVID-19 mortality amongst ethnic minority groups.</li> <li>• Results suggest living in a MGH was associated with increased risk of COVID-19 mortality.</li> <li>• After adjusting for confounding factors, the hazard ratios (HRs) for living in a MGH with dependent children were 1.13 and 1.17 for older males and females.</li> <li>• The HRs for living in a MGH without dependent children were 1.03 for older males and 1.22 for older females.</li> <li>• Living in a MGH explained between 10% and 15% of the elevated risk of COVID-</li> </ul>

			19 death among older females from South Asian background, but very little for South Asian males or people in other ethnic minority groups.
03.12.2020	<a href="#">Clinical characteristics and risk factors associated with severe COVID-19: prospective analysis of 1,045 hospitalised cases in North-Eastern France, March 2020</a>	Eurosurveillance / Research	<ul style="list-style-type: none"> <li>• Objective was to identify risk factors predictive of severe disease and death in France.</li> <li>• Among 1,045 patients, 424 (41%) had severe disease, including 335 (32%) who were admitted to ICU, and 115 (11%) who died.</li> <li>• Mean age was 66 years (range: 20–100), and 612 (59%) were men.</li> <li>• Concluded that overweightedness, obesity, advanced age, male sex, comorbidities, dyspnoea and inflammation are risk factors for severe COVID-19 or death in hospitalised patients.</li> </ul>
02.12.2020	<a href="#">Association between biomarkers and COVID-19 severity and mortality: a nationwide Danish cohort study</a>	BMJ Open / Original research	<ul style="list-style-type: none"> <li>• Nationwide study of 1,310 patients, aged ≥18 years, admitted to Danish hospitals with COVID-19. 352 (26.9%) experienced the composite endpoint and 263 (20.1%) died.</li> <li>• Elevated levels of CRP, leucocytes, procalcitonin, urea, troponins and D-dimer, and low levels of eGFR were associated with higher standardised absolute risk of death/ICU admission within 30 days.</li> </ul>

#### Epidemiology and clinical – other

Publication Date	Title / URL	Journal / Article type	Digest
03.12.2020	<a href="#">Metformin and risk of mortality in patients hospitalised with COVID-19: a retrospective cohort analysis</a>	Lancet Healthy Longevity / Article	<ul style="list-style-type: none"> <li>• Aim was to identify whether metformin reduced COVID-19-related mortality and whether sex-specific interactions exist.</li> <li>• 6256 of the 15 380 individuals with pharmacy claims data from Jan 1 to June 7, 2020 were eligible for inclusion. 3302 (52.8%) of 6256 were women.</li> <li>• Concluded that metformin was significantly associated with reduced mortality in women with obesity or type 2 diabetes who were admitted to hospital for COVID-19. Prospective studies are needed to understand mechanism and causality. If findings are reproducible, metformin could be widely distributed for prevention of COVID-19 mortality, because it is safe and inexpensive.</li> </ul>
03.12.2020	<a href="#">Characteristics of Adults aged 18-49 Years without Underlying Conditions Hospitalized with Laboratory-Confirmed COVID-19 in the United States, COVID-NET - March-August 2020</a>	Clin Infect Dis / Article	<ul style="list-style-type: none"> <li>• Mar 1st –Aug 1st, 44,865 U.S patients hospitalized with COVID-19 identified through COVID-NET. Adults aged 18–49 years old represented 31.8% (n=13,167) of all hospitalized patients.</li> <li>• Among 513 hospitalized adults aged 18–49 years without underlying medical conditions, 22% were admitted to ICU; 10% required mechanical ventilation; and three patients died (0.6%).</li> <li>• These data demonstrate that healthy younger adults can develop severe COVID-19.</li> </ul>

## Infection control / non-pharmaceutical interventions

Publication Date	Title / URL	Journal / Article type	Digest
02.12.2020	<a href="#">Effective in-vitro inactivation of SARS-CoV-2 by commercially available mouthwashes</a>	bioRxiv (non-peer reviewed) / Article	<ul style="list-style-type: none"> <li>• The authors evaluate the efficacy of SARS-CoV-2 inactivation by seven commercially available mouthwashes with a range of active ingredients in vitro.</li> <li>• Results showed <math>\geq 4.1</math> to <math>\geq 5.5</math> log<sub>10</sub> reduction in SARS-CoV-2 titre following a one minute treatment with commercially available mouthwashes containing 0.01-0.02% stabilised hypochlorous acid or 0.58% povidone iodine, and non-specialist mouthwashes with both alcohol-based and alcohol-free formulations designed for home use.</li> <li>• In contrast, products containing 1.5% hydrogen peroxide or 0.2% chlorhexidine gluconate were ineffective.</li> <li>• Findings contribute to evidence surrounding virucidal efficacy of mouthwashes/oral rinses against SARS-CoV-2, and have important applications in settings such as dentistry.</li> </ul>

## Transmission

Publication Date	Title / URL	Journal / Article type	Digest
02.12.2020	<a href="#">Does respiratory co-infection facilitate dispersal of SARS-CoV-2? investigation of a super-spreading event in an open-space office</a>	Antimicrob Resist Infect Control / Research	<ul style="list-style-type: none"> <li>• Authors describe a super-spreading event within a team working in an open-space office and investigate factors potentially having facilitated SARS-CoV-2 transmission.</li> <li>• Of 13 team members, 11 fell ill with COVID-19. Sequence of events and full genome sequence data suggest one person as index case, directly infecting 67 to 83% of the teammates.</li> <li>• The index case and a further individual were diagnosed with an adenovirus serotype 4 co-infection.</li> <li>• Several environmental and behavioural factors identified that probably facilitated the transmission. Relevance of the adenovirus co-infection remains unclear and merits further investigation.</li> </ul>
02.12.2020	<a href="#">Severe Acute Respiratory Syndrome Coronavirus 2 Outbreak Related to a Nightclub, Germany, 2020</a>	Emerg Infect Dis / Article	<ul style="list-style-type: none"> <li>• Authors report COVID-19 outbreak with 74 cases related to a nightclub in Germany in March 2020. Large number of cases from event 1, relatively low median incubation period (4 days) for first-generation cases, close genetic relatedness of sequenced viruses all corroborate transmission from a single person and potential superspreading in a nightclub with no social distancing.</li> <li>• Staff members were particularly affected (attack rate 56%) and likely caused sustained viral transmission after an event at the club.</li> </ul>

- This outbreak illustrates the potential for superspreader events and corroborates current club closures.

### Treatment

Publication Date	Title / URL	Journal / Article type	Digest
02.12.2020	<a href="#">Repurposed Antiviral Drugs for Covid-19 — Interim WHO Solidarity Trial Results</a>	N Engl J Med / Article	<ul style="list-style-type: none"> <li>• At 405 hospitals in 30 countries, 11,330 adults underwent randomization; 2750 were assigned to receive remdesivir, 954 to hydroxychloroquine, 1411 to lopinavir (without interferon), 2063 to interferon (including 651 to interferon plus lopinavir), and 4088 to no trial drug.</li> <li>• These remdesivir, hydroxychloroquine, lopinavir, and interferon regimens had little or no effect on hospitalized patients with Covid-19, as indicated by overall mortality, initiation of ventilation, and duration of hospital stay.</li> </ul>

### Modelling

Publication Date	Title / URL	Journal / Article type	Digest
03.12.2020	<a href="#">Detecting COVID-19 infection hotspots in England using large-scale self-reported data from a mobile application: a prospective, observational study</a>	Lancet Public Health / Article	<ul style="list-style-type: none"> <li>• In this prospective, observational study, the authors did modelling using longitudinal, self-reported data from users of the COVID Symptom Study app in England between Mar 24, and Sept 29, 2020, to track the disease at a local level to identify areas in need of targeted intervention.</li> <li>• Conclude that their method could help to detect rapid case increases in regions where government testing provision is lower. Self-reported data from mobile applications can provide an agile resource to inform policy makers during a quickly moving pandemic, serving as a complementary resource to more traditional instruments for disease surveillance.</li> </ul>

### Guidance and consensus statements (no digest)

Publication Date	Title / URL	Journal / Article type
02.12.2020	<a href="#">Overview of COVID-19 vaccination strategies and vaccine deployment plans in the EU/EEA and the UK</a>	European Centre for Disease Prevention and Control / Technical report
02.12.2020	<a href="#">Guidelines for COVID-19 testing and quarantine of air travellers - Addendum to the Aviation Health Safety Protocol</a>	European Centre for Disease Prevention and Control / Technical report
02.12.2020	<a href="#">Regulatory approval of Pfizer / BioNTech vaccine for COVID-19</a>	Gov.uk / Decision

02.12.2020	<a href="#">Priority groups for coronavirus (COVID-19) vaccination: advice from the JCVI, 2 December 2020</a>	Gov.uk / Independent report
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### Overviews, comments and editorials

Publication Date	Title / URL	Journal / Article type
03.12.2020	<a href="#">Metformin: an inexpensive and effective treatment in people with diabetes and COVID-19?</a>	Lancet Healthy Longevity / Comment
02.12.2020	<a href="#">A Large, Simple Trial Leading to Complex Questions</a>	N Engl J Med / Editorial
02.12.2020	<a href="#">Placebo-Controlled Trials of Covid-19 Vaccines — Why We Still Need Them</a>	N Engl J Med / Perspective
02.12.2020	<a href="#">FDA Approval of Remdesivir — A Step in the Right Direction</a>	N Engl J Med / Perspective

### Produced by the PHE COVID-19 Literature Digest Team

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