Institution: Lancaster University		
Unit of Assessment: 3, Allied Health Professions, Dentistry, Nursing and Pharmacy		
Title of case study: Informing national and international government's policy responses to the 2020 SARS-CoV-2 pandemic through epidemiological intelligence		
Period when the underpinning research was undertaken: 2015 – 2020		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	**Role(s) (e.g. job title):**	**Period(s) employed by submitting HEI:**
Jonathan Read Chris Jewell	Senior Lecturer Senior Lecturer	2016 – present 2015 – present
Period when the claimed impact occurred: 01/2020 – 12/2020		
Is this case study continued from a case study submitted in 2014? N		

1. Summary of the impact

Building on their early epidemic modelling work identifying the pandemic potential of the emerging outbreak of SARS-CoV-2 in China in January 2020, Jewell and Read have provided timely research evidence to the Scientific Pandemic Influenza Group on Modelling (SPI-M) of the government's Scientific Advisory Group on Emergencies (SAGE). For example, identifying the scale of within-hospital infections, the impact of school reopening, the efficacy of household isolation measures, and spatial disease risk prediction across the UK. Their research has directly informed the development of national, international and regional disease control policies, such as local lockdown measures, resource planning, and travel restrictions. US government policy and their COVIDTracer planning tool were informed by their research.

2. Underpinning research

The underpinning research by Jewell and Read builds on previous work and expertise. Read previously used airline passenger data to understand epidemic exportation/importation risks for emerging epidemics (2015-2019). Read also made the first large-scale quantification of social contact patterns for viral transmission in China (2014). Since 2018, building on previous work undertaken at Liverpool University, Read has also helped quantify and characterise human interaction patterns in several low and middle-income countries, in many cases providing the first such characterisation (2009-2019).

Jewell's expertise in real-time inference on, and prediction from, epidemic models using Bayesian statistical methods has been critical in informing the underpinning work. Jewell's work on computational Bayesian methods for epidemic models has allowed detailed spatial analysis of outbreaks in a variety of species and demographic settings (2009-2015). More recently these analyses have been applied in the realm of outbreak management applied to diseases, developing computational frameworks to apply these methods to large datasets in both human (e.g., food-borne illness, anti-microbial resistance, and visceral leishmaniasis) and livestock (e.g., foot and mouth disease, avian influenza, and bovine theileriosis) diseases (2015-2019).

The combination of Jewell's expertise in epidemic model fitting and Read's experience in using international flight data enabled them to rapidly develop the first transmission model of the SARS-CoV-2 pandemic fitted to case data, and to publish it online as a preprint on 24 January 2020 [R1]. This unique work, using Markov-chain Monte Carlo (MCMC) to fit a network-based deterministic epidemic model, leveraged temporal-spatial information on cases arising to directly estimate key epidemiological parameters (including R0, infectious period and ascertainment ratio) of the emerging epidemic. This was significantly more informative than other contemporaneous simpler analyses, presenting very early evidence of the pandemic potential of the outbreak in Wuhan and other cities in Hubei province.

Read and Jewell's combined research expertise has enabled them to further engage with the COVID-19 pandemic modelling effort in the following ways:

Modelling of contact tracing and school closure/reopening
Read developed a model of SARS-CoV-2 transmission in the UK that incorporated empirical data on contact patterns in the UK (collected through a national survey by Read) to identify how effective contact tracing would need to be to control the epidemic (Mar-Apr 2020) [R2]. Read also developed a model exploring the impact of school re-openings on epidemic dynamics and the extent to which contact tracing would be required to counteract the negative effects of school reopening on disease dynamics (Apr-May 2020) [R3].

Clinical cohort analysis of COVID-19 mortality risk factors
Read also analysed data collected by the COVID-19 Clinical Information Network (CO-CIN) study [R4], comprising a large cohort of hospitalised COVID-19 patients from across the UK (March 2020 onwards). The current cohort consists of more than 100k enrolled COVID-19 patients. The initial study paper [R4] analysed the first 20,133 patients enrolled before mid-April 2020, and was the first to identify the comorbidities, age groups and sex risk factors associated with mortality for UK patients (March-May 2020). The paper also described the symptoms these early COVID-19 patients presented with, providing relative frequency and symptom groupings, enabling contemporary case definitions to be assessed and refined. Read contributed to the overall analysis plan and the analysis itself, specifically the characterisation of symptoms upon admission, drawing on his experience of quantitative analysis of hospital and infectious disease health data.

Spatial risk and hotspot identification
Jewell and Read conducted the first spatially explicit analysis of COVID-19 incidence within England (May 2020) using spatially-coupled autoregressive time series methods. This represented a rapid response to demonstrating the interdependence of local authority-level case incidence, and wide heterogeneity in case incidence across the country [R5]. Nevertheless, this work revealed a gap in statistical methods for fitting spatial epidemic models at the scale of an entire nation – this was required for measuring spatial reproduction numbers and accurate detection of COVID-19 hotspots in a fast-changing landscape of local “Tier” restrictions.

Jewell addressed this gap, developing a Bayesian spatial stochastic epidemic model based on his previous research in decision support for livestock epidemics. Jewell designed the MCMC-based statistical methodology required to calibrate this mode, and implemented it using cutting-edge GPU computing technology. The results have provided an unprecedented (and to date the only) detailed analysis of COVID-19 spatial dynamics in real-time [R5].

3. References to the research

[R1] **Read, J. M**., Bridgen, J.R., Cummings, D.A., Ho A, & **Jewell, C.P.** (2020). Novel coronavirus 2019-nCoV: early estimation of epidemiological parameters and epidemic predictions. *medRixv,* published online Jan 28 https://doi.org/10.1101/2020.01.23.20018549 In press *Phil Trans Roy Soc B.* (773k reads, 382k downloads, 614 citations in Google scholar).
[R2] Keeling, M.J., Hollingsworth, D., & **Read J.M.** (2020). Efficacy of contact tracing for the containment of the 2019 novel coronavirus (COVID-19). *Journal of Epidemiology & Community Health,* 74(10), 861-8566. https://doi.org/10.1136/jech-2020-214051 (93 citations in Google Scholar).
[R3] Brooks-Pollock, E, **Read J.M.**, Keeling, M.J., & Danon, L. (2020) The impact of reopening schools on COVID-19 transmission in the context of other physical distancing measures. *medRixv* published online Jul 27 https://doi.org/10.1101/2020.06.04.20121434. In press *Phil Trans Roy Soc B.*
[R4] Docherty, A. B., Harrison, E. M., Green, C. A., Hardwick, H. E., Pius, R., Norman, L., Holden, K. A., **Read, J. M.**, et al. (2020). Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: Prospective observational cohort study. *BMJ,* 369, [m1985] https://doi.org/10.1136/bmj.m1985 (963 citations in Google scholar).

[R5] Fronterre, C., **Read, J.M.,** Rowlingson, B., Bridgen, J., Alderton, S., Diggle, P.J**.,** & **Jewell, C.P.** (2020). COVID-19 in England: spatial patterns and regional outbreaks. *MedRxiv,* published online May 20. https://doi.org/10.1101/2020.05.15.20102715

[R6] **Jewell CP** & Brown RG. (2015). Bayesian data assimilation provides rapid decision support for vector-borne diseases. *Journal of the Royal Society Interface,* 12(108), 20150367. https://doi.org/10.1098/rsif.2015.0367 (9 citations in Google Scholar).

4. Details of the impact

Evidence from Read and Jewell's key epidemiological analyses of the SARS-CoV-2/COVID-19 pandemic presented in preprints, peer-reviewed publications and reports and presentations for government advisory groups has influenced the way that governments, both in the UK and US, understand the spread of SARS-CoV-2, and has been instrumental in policy responses to the epidemic.

UK Government Policy

In January 2020, in response to their paper on the China COVID-19 outbreak [R1], Jewell and Read were approached by the Scientific Pandemic Influenza Group on Modelling, Operational sub-group (SPI-M-O, a sub-committee of SAGE). Jewell and Read presented the evidence [R1] to the DHSC/SPI-M-O on 24 January 2020, which informed the situational awareness of the epidemic in early 2020; SPI-M used this evidence to advise SAGE. SAGE subsequently included the evidence from [R1] in their briefings to the UK Government (the DHSC). Since February 2020, Read and Jewell have been members of the SPI-M-O, which continues to report directly to SAGE and Cabinet Office Briefing Rooms (COBR), contributing their research evidence on an ongoing basis to inform policies related to the following topics [S1].

Household isolation

As part of SPI-M-O, Jewell and Read used their previous experience in epidemics research to provide evidence to SPI-M-O from epidemic modelling theory on the likely efficacy of whole-household isolation as a response to the infection of an individual with COVID-19. SPI-M-O used the research, which showed that the policy was robust to non-compliance, as evidence for household isolation as a means of controlling disease spread. Jewell presented the report, 'Effect of compliance with whole household isolation in the COVID-19 outbreak', to SPI-M in March 2020 [S1(b)]. It demonstrated that household isolation for 14 days in response to 1 person being infected was likely to be effective at keeping the basic reproduction number below 1, even with only 40% compliance. Additionally, on 11 March 2020, Read provided results from his new analysis to SPI-M-O of the potential for social contact reduction to control the COVID-19 epidemic in the UK. In reference to this work, the Chief Scientific Advisor to the MoD and Deputy Government Chief Scientist stated, "*These analyses have been important factors in shaping UK Government policy on controlling the pandemic. Isolation of the entire household when one person is infected has been the cornerstone of our efforts to control COVID-19. This work had an immediate impact on policy and an effective and enduring impact on the control of community transmission*" [S2].

Schools

Evidence from a collaboration by Read with Bristol University, Essex University and Warwick University on the likely impact of re-opening schools on the virus's R number in the UK was presented to SPI-M on 27 April 2020 and subsequently on 22 May 2020 to SAGE (see SPI-M-O: Comments on Social Distancing Measures 1 and SPI-M-O: Comments on Social Distancing Measures 2) [R3]. The Chief Scientific Advisor to the UK Government stated that the evidence was critical in forming advice to the government on the reopening of schools and on the need for an effective testing and contact tracing system to absorb the additional transmission and cases that reopening might generate [S3]. Schools were reopened in August/September across all nations of the UK, with profound impacts on the economy (enabling parents to return to work), children's welfare, education and future life prospects. The Chief Scientific Advisor to the MoD and Deputy Government Chief Scientist stated, "*Understanding the role of children and schools in the spread of COVID-19 has been one of the most difficult tasks for SAGE...Having the thoughtful,* *careful, brilliant analyses provided by Dr Jewell and Dr Read has been essential for SAGE to be able to offer clear advice to HMG. As everyone knows the strong policy decision has been taken to keep schools open – second only in importance to our strategic direction that the NHS should keep functioning. HMG relies on SAGE for the science advice that underpins that decision and Dr Jewell and Dr Read played an essential role in generating that advice"* [S2].

Hospital transmission

In April 2020, Read was specifically tasked by SPI-M-O to analyse the CO-CIN study data from UK hospitals to identify the scale of nosocomial (within-hospital) transmission of SARS-CoV-2. Building on the analysis conducted in [R4], Read conducted additional real-time statistical analysis, identifying the scale and heterogeneity of within-hospital transmission in the UK during the first wave of the pandemic, and the results were presented to SAGE on 30/04/2020. This was the first dedicated analysis of SARS-CoV-2 transmission in UK hospitals and identified the scale of the problem and heterogeneities by NHS trust. The results were reported to SAGE and NHS leadership. From 12 April 2020, Read presented weekly analyses of the CO-CIN UK COVID-19 patient study data to SPI-M-O, indicating a continuing significant level of nosocomial transmission in UK hospitals during the first wave of the pandemic, with regional variation. SAGE used the analysis provided by Read to advise the government and the NHS about the risk of the spread of SARS-CoV-2 in hospitals, which was key to policy responses, as evidenced by the following statement from the Chief Scientific Advisor to the MOD and Deputy Government Chief Scientist, "[SAGE] *advice to the government and to the NHS on hospital transmission at this stage of the epidemic was reliant on the analysis conducted by Lancaster on the CO-CIN data*. (…) *When people ask me "what do you wish you had known in February that you now know", I say, "I wish we'd known COVID spreads so well in hospitals". It was thanks to this expert and timely analysis of the CO-CIN data that we knew as fast as we did how much nosocomial infection there was. The policy response has been to introduce frequent testing of all staff and, where possible, to keep COVID-19 patients separated from others"* [S2].

Spatial analysis and "hotspot" detection

Jewell and Read's work with SAGE, the Joint Biosecurity Centre (JBC), and Public Health England (PHE) to identify local 'hotspots' of cases [R5] supported PHE's recommendations for the application of local restrictions applied to regions with high numbers of cases. Extending this work and previous work developing adaptive management tools for livestock epidemics [R6], in collaboration with researchers at Warwick University and Google Research, Jewell led the development of a fully Bayesian spatial stochastic model of COVID-19 transmission in England. Early work demonstrating the high level of spatial heterogeneity in case incidence across England [R5] was presented to the Minister of Defence (Con Wyre & Preston North, 30th May 2020), kick-starting the interest in spatial trends in viral transmission and leading to the provision of publicly available COVID-19 case data at Local Authority-level for local planning and research purposes.

Jewell now provides SPI-M, the JBC, Scottish Government and the Cabinet Office with weekly reports of the estimated time-evolving reproduction numbers, hotspot detection, and short-term predictions of case incidence and prevalence at the Local Authority District level. They are the only group capable of providing such estimates and predictions on a daily basis from principled statistical analysis using a spatially explicit model. The reports are used to identify future hotspots and provide an evidence base for the development of local tier restriction categories and subsequent evaluation of tier efficacy [S2, S4, S5]. The reports have been used by JBC/Cabinet Office in selecting which data to provide for the Prime Minister's briefing 'dashboard', and for identifying local authorities with especially outlying behaviour compared to the national average. The reports have been, therefore, central to informing the decisions on tier allocations [S5]. The UK government's Chief Scientific Advisor stated that the Lancaster outputs on spatial modelling outputs have led to improved efforts by the national health agencies to provide COVID-19 case data publicly, which are now routinely used by SPI-M to generate ongoing COVID-19 reports [S3]. The

Co-Chair of SPI-M-O said, "*At this level, the Lancaster framework is the best available in the UK…I would be surprised if there were better globally…these interventions have been instrumental in the formation of our advice to Government*" [S4]. Referring to the spatial stochastic model [R6], the Chief Scientific Advisor to the MoD and Deputy Government Chief Scientist stated, "*There is no question that this is the best spatial model that we have*" [S2].

Local Governments in the UK

Jewell and Read have contributed short-term prediction results from the spatial stochastic model [R6] to the local authorities in Lancashire and to the Lancashire Resilience Forum. The North West region, including Lancashire, has experienced the highest infection intensity in England, and Read and Jewell's predictions have provided a key evidence base for public health officials to perform agile planning and allocation of healthcare resources within the county [S6, S7]. This evidence, in particular the weekly regional reproduction number estimates and spatial reports on Pillar 1 and 2 positive testing projections, was critical to the advice provided by the Blackburn authority to schools, local communities and organisations. In addition, Blackburn with Darwen Council and the Lancashire Local Resilience Forum used the evidence to plan a wide range of responses to the pandemic, including resourcing of local contact tracing, understanding demands for council services, and determining potential future impacts on primary and secondary care. Read also provided hospital demand forecasts for the Merseyside Resilience Forum [S8]. The policy decisions by these local government bodies have directly affected communities, impacting a combined total of approximately 2,500,000 residents.

US State Department

Lancaster research [R1] provided some of the first publicly available evidence of the extent and likely magnitude of the COVID-19 outbreak in Wuhan and the threat of a pandemic. The study was exceptionally timely and contributed to full situational awareness of the emerging situation in China and the risks to the United States. In the words of the Director of the US Department of State Office of the Geographer and Global Issues (Bureau of Intelligence and Research), "*Dr Read's work filled critical information gaps as our agency grappled with consequential policy decisions following the emergence of the novel disease, which was not well understood at the time. We incorporated Dr Read's research into our updates for senior US government policy makers, including the US Secretary of State*" [S9]. Additionally, the analysis in R2 was used in a planning tool for contact tracing (COVIDTracer) in response to COVID-19 that was made available online by the US Department of Health and Human services [S10].

5. Sources to corroborate the impact

[S1] Evidence presented to the Scientific Advisory Group for Emergencies (SAGE):
a) Scientific evidence supporting the government response to coronavirus (COVID-19), Modelling inputs (outputs [R1, R2] cited). Last updated November 2020
b) Jewell CP, Neal P. Effect of compliance with Whole Household Isolation in the Covid-19 outbreak, Paper presented by Lancaster University, considered at SAGE 16 on 16 March 2020.
[S2] Testimonial from the Chief Scientific Advisor to the MOD, Deputy Government Chief Scientist, 2020.
[S3] Testimonial from the Government's Chief Scientific Adviser, 2020.
[S4] Co-chair of the Scientific Pandemic Influenza Group on Modelling (SPI-M), 2020.
[S5] a)Testimonial from a health analyst in the Analysis and Data Directorate, C-19 Taskforce, Cabinet Office, 2020, b) feedback from SPI-M secretariat, 2021.
[S6] Testimonial from Director of Public Health, Lancashire County Council, 2020.
[S7] Testimonial from Consultant in Public Health, Blackburn with Darwen Council, 2020.
[S8] Evidence of contribution to MRF: Data and modelling of COVID, 2020.
[S9] Testimonial from the Director of the US Department of State Office of the Geographer and Global Issues, Bureau of Intelligence and Research, 2020.
[S10] Planning Tool, US Department of Health and Human Services, 2020.