Institution: The University of Manchester		
Unit of Assessment: 10 (Mathematics)		
Title of case study: Modelling in a pandemic: advising the UK response to COVID-19, and protecting enclosed communities.		
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:**
Lorenzo Pellis	Senior Research Fellow (Sir Henry Dale Fellow)	2017 – present
Ian Hall	Reader	2018 – present
Thomas House	Senior Lecturer (2015 – 2017), Reader (2017 – present)	2015 – present
Christopher Overton	Postdoctoral Research Associate	2020 – present
Helena Stage	Postdoctoral Research Associate	2018 – present
Stefan Güttel	Reader	2012 – present
Period when the claimed impact occurred: January 2020 – December 2020		
Is this case study continued from a case study submitted in 2014? N		

1. Summary of the impact

The Unit's expertise in modelling/analysis of epidemics, and particularly transmission in enclosed communities, has enabled impact on both regional and national scales throughout the COVID-19 pandemic. Their work was delivered through direct collaboration with both national and regional bodies, and to Government *via* the Scientific Advisory Group for Emergencies (SAGE) and Public Health England (PHE). The dominant impacts are

i. In March 2020, the timing of the first national lockdown was driven by the Unit's modelling that identified a three-day infection doubling time, displacing the previous five-to-six day figure;
ii. In collaboration with the Office for National Statistics (ONS) the COVID-19 infection survey was developed and used to inform restriction tiering and national intervention decisions;
iii. Modelling results shaped infection control procedures for enclosed communities (notably in prisons and hospitals, but also care homes and schools), and is credited with minimising outbreak risk and saving lives;
iv. Modelling also underpinned hospital resource planning in the North West, which permitted elective non-COVID life-threatening work to continue, and is also credited with having saved lives.

2. Underpinning research

From 2015, strategic appointments to the Unit's Statistics research theme, at the interface with the Life Sciences theme, led to the establishment of an epidemiology and public health group. Researchers from this group have been conducting epidemiological modelling research, which encompasses statistical and mathematical modelling of infectious disease dynamics, branching into public health, non-infectious disease epidemiology, ecology, evolution and data science.

Notable underpinning work prior to the COVID-19 pandemic includes **[1]**, in which the researchers developed a household-based model framework and applied it to care homes, thus providing the mathematical underpinning for understanding the infection process in those enclosed communities. The careful numerical benchmarking experiments were key for guiding the trade-off between model complexity/accuracy in the face of restricted time and computational resources (relevant to emergency response). This was followed by **[2]**, in which the researchers developed insight and a model framework for dealing with age structure in households, the prime example of epidemiologically relevant enclosed communities.

The combined expertise of the above-named researchers provided a basis for the Unit's COVID-19 modelling group. Prior to the UK's first national lockdown, the researchers developed an initial set of tools described in **[3]**, which formed the primary set of methods used by the modelling group. They include a range of statistical and mathematical models, beyond simple 'SIR'-type differential equation models, for analysing the early stages of an outbreak and assessing interventions. Particularly, the researchers used parameter estimation in the presence of known biases in data, and the effect of non-pharmaceutical interventions in enclosed communities, such as households and care homes.

Publication **[4]** analysed confirmed COVID-19 cases, deaths and hospital data to quantify epidemic growth rates from various European nations. This work describes the estimated three-day infection doubling time at the beginning of the pandemic. Additionally, using methods developed in **[3]** to estimate time intervals between events from right-censored data, the researchers identified a nine-day delay between implementation of an intervention and its measurable effect in the hospitalisation data, which was (at that time) the only reliable data available *in lieu* of testing. The researchers then developed more refined time-between-events methods in **[5]**. These were used to estimate hospital length of stay, comparing results using an Accelerated Failure Time (AFT) survival model, a truncation corrected method (TC), and a multi-state (MS) survival model. The latter was also implemented directly by the Manchester University NHS Foundation Trust (MFT) and all NHS Trusts in the North West, to provide Trust-specific length of stay and severity estimates and as a planning tool to predict bed occupancy.

Publication **[6]** highlights the challenges in interpreting established models within enclosed communities without better data (including identifiable sub-groups such as residents and staff) and the larger scale interaction routes to the outside population. This approach was a key driver in the push for better quality fine-grained data gathering, particularly in vulnerable care home communities.

3. References to the research

The bulk of underpinning research arose during the COVID-19 pandemic in 2020. Consequently, **[4, 5, 6]** are available as pre-prints. Work exemplifying expertise, techniques and insights as applied to epidemics and enclosed community transmission **[1, 2, 3]** is published in peer-reviewed journals. Authors from UoM are highlighted in bold text.

[1] **Kinyanjui, T.**; Middleton, J.; **Güttel, S.**; Cassell, J.; Ross, J.; & **House, T.**, "Scabies in residential care homes: Modelling, inference and interventions for well-connected population sub-units", **2018**, *PLoS Comput. Biol.*, *14*, e1006046. DOI: 10.1371/journal.pcbi.1006046
[2] **Pellis, L.**; Cauchemez, S.; Ferguson, N. M.; Fraser, C., "Systematic selection between age and household structure for models aimed at emerging epidemic predictions", **2020**, *Nat. Commun.*, *11***,** 906. DOI: 10.1038/s41467-019-14229-4
[3] **Overton, C.**; **Stage, H. B.**; Ahmad, S.; **Curran-Sebastian, J.** *et al.* "Using statistics and mathematical modelling to understand infectious disease outbreaks: COVID-19 as an example", **2020**, *Infect. Dis. Mod.*, *5*, 409-441 (14/19 authors from UoM). DOI: 10.1016/j.idm.2020.06.008
[4] **Pellis, L.**; Scarabel, F.; **Stage, H. B.**; **Overton, C. E.** *et al.* "Challenges in control of COVID-19: short doubling time and long delay to effect of interventions", **2020**, *arXiv* (preprint, submitted 31 March 2020. 12/17 authors from UoM). DOI: arxiv.org/abs/2004.00117
[5] **Vekaria, B.**; **Overton, C. E.**; **Wisniowski, A.**; Ahmad, S. *et al.* "Hospital length of stay for COVID-19 patients: Data-driven methods for forward planning", **2020**, *BMC Infect. Dis.* (preprint, submitted 25 August 2020. 13/16 authors from UoM). DOI: 10.21203/rs.3.rs-56855/v1
[6] **Hall, I.**; **Pellis, L.**; **House, T.**; **Lewkowicz, H.**; Sedgwick, J.; Gent, N., "Rapid increase of Care Homes reporting outbreaks a sign of eventual substantial disease burden", **2020**, *medRxiv* (preprint, submitted 11 May 2020, to appear in *Phil. Trans. Roy. Soc. A*), DOI: 10.1101/2020.05.07.20089243
The research was supported by competitive grant funding from the EPSRC, MRC, Wellcome Trust, and Royal Society, with total funding in excess of GBP1,700,000.

4. Details of the impact

Pathways to impact

Pellis and Hall are contributing members to PHE's Joint Modelling Cell, comprising PHE employees, academics, NHS representatives and others **[A]**. This group is part of PHE's Incident Response structure, and provides analyses and information to the Incident Director, as well as PHE's Silver Command (Chief Executive Officer) and Gold Command (the UK Chief Medical Officer and relevant officials from the Department of Health and Social Care, DHSC) **[A]**. PHE's Senior Medical Advisor characterises the Unit's contribution to pandemic response, saying, "*I* *cannot commend too highly the **excellent, substantial, and authoritative role of the Department of Mathematics, whose advice is highly trusted and valued both by ourselves in PHE and across Government***" **[A]**.

Pellis, Hall and House are members of the UK Government's Scientific Pandemic Influenza Group on Modelling (SPI-M), a sub-group that provides modelling consensus to SAGE. SAGE assesses evidence alongside other scientific expertise to provide advice and recommendations directly to the UK Government. Hall is co-chair of the SAGE Social Care Working Group (SCWG), has participated in SAGE itself, and is a member of the Environmental Modelling Group. House has participated in the Children's Task and Finish Group.

In addition to the above pathways to national decision-making, the Unit's researchers worked directly with organisations such as the ONS, MFT (an NHS Foundation Trust, which operates independently of UoM), and Her Majesty's Prison and Probation Service (HMPPS).

National response

Modelling from the Unit's researchers influenced the timing of the UK Government policy of a national 'lockdown' from 23 March 2020. On 20 March 2020, an analysis (conducted by the Unit's Pellis) of confirmed cases and deaths from other EU nations, together with data on hospital/ICU COVID-occupied beds from Italy, was presented to SPI-M **[B, C, 4]**. This modelling work demonstrated that the time required for the number of infections to double was three days, challenging SAGE's consensus estimates of a five-to-six-day doubling time based on other groups' analysis of data from China **[C]**. This analysis indicated that the UK pandemic trajectory was approximately two weeks behind Italy, at the lowest end of SAGE's two-to-four-week consensus **[A, B, C, 4]**, and recommended swift and aggressive interventions. The Government's Chief Scientific Advisor (GCSA) says that this was "***key evidence in the decision-making process that led to the Government to close pubs and restaurants that same day***" **[B]**.

Further analysis by Pellis was presented to SPI-M on 23 March 2020, which demonstrated that any effects associated with current mitigation measures would not be apparent in data until nine-to-ten days after their instigation **[A, B, C, 4]**. The GCSA clarifies the significance of this, saying, "*With the established 3-day doubling time, infections would have grown 8-fold placing hospital and ICU bed projections higher than the target limits suggested by the NHS at the time. This **made it clear that decisions had to be taken immediately*** […] *It is hard to quantify the impact in terms of lives saved, but at the speed of growth estimated at the time, even doubling the bed availability would only have bought 3 days of reprieve. Therefore, **just a few days' delay could have led to significantly more infections and associated deaths**, and likely added significant additional strain on the healthcare system.*" **[B]**. For context, there were 237 COVID-19-related daily deaths recorded at the point of lockdown on 24 March 2020.

Part of the UK Government's strategy for monitoring the pandemic was to establish a nationwide survey of community-based infection and behaviour – called the COVID-19 Infection Survey – run by the ONS as part of the UK Statistics Authority. By October 2020, the survey's scale had grown to sampling 150,000 participants per fortnight **[D]**. The survey's protocol and ethical approval, as well as the content of the questionnaire and its operation was "*set up at pace …. in collaboration with* [the Unit's] *Thomas House"* **[D]**. The UK Statistics Authority's National Statistician describes the Unit's researchers' contributions to the survey, saying they "…*played a big part in key analysis we have undertaken, bringing scientific and complex mathematical modelling knowledge to the wider work of the survey. This includes **being pivotal in the understanding of transmission within the household** and producing modelling around a secondary attack rate **which have fed into SAGE discussions around schools and occupations**. This also includes the use of machine learning techniques in order to develop analysis on symptoms of those testing positive to feed into wider discussions around how to identify COVID-19*" **[D]**.

The analyses produced by the COVID-19 Infection Survey have been used in many ways. These include providing up-to-date data on the state of the pandemic for Number 10 briefings; informing restriction tiers and national intervention decisions; assessing the effectiveness of non-pharmaceutical interventions such as face coverings and social distancing; and advising key scientific groups such as SAGE on subjects including new COVID-19 variants **[D]**.

Enclosed communities

(a) Prisons in England and Wales: HMPPS is the Government agency responsible for overseeing the approximately 120 prisons in England and Wales, constituting around 80,000 prisoners and 50,000 staff **[E]**. The Unit's researchers proactively engaged with the PHE Health and Justice team and partners in Ministry of Justice in February 2020, and were further approached by HMPPS in March and April, based on their established expertise in modelling virus incursion and transmission in enclosed groups.

The Unit's researchers produced a Risk of Incursion analysis in May 2020 **[C]**, which provided HMPPS an improved understanding of the high degree of heterogeneity in risk across prisons (based on their size, type, and staffing) **[E]**. As HMPPS' Public Health Advisor notes, this led to "*our introduction of a national four-level classification* system […] *in addition to informing the development of a national framework to determine prison regimes and COVID-secure operational delivery throughout the pandemic*", based on population-level epidemic scenarios performed by the Unit **[E]**. This work "*has helped us make informed decisions concerning when, where and how to intervene in monitoring and controlling COVID-19 transmission in prisons, thus making our efforts more targeted and cost-effective, and equally* ***minimising the risk of outbreaks, ultimately saving lives***" **[E]**.

Further modelling from the Unit's researchers, delivered in June 2020 **[C]**, on routes of incursion into prisons, used estimates in **[4]** (based on methods in **[3]**) to quantify how much risk can be mitigated by using 'reverse cohorting units' (RCUs) for incoming prisoners, isolating them in distinct environments before their introduction to the broader prison population **[E]**. This improved understanding "*has influenced our working practices with respect to RCUs, quantifying the increased risk associated with shorter times spent in the RCU and the mitigation of risk via exit testing on leaving the RCU*". Combined with additional PHE work, the Unit's researchers' work was "***essential*** *in enabling HMPPS and PHE to formulate an effective testing algorithm for release of prisoners from RCU whilst balancing minimal isolation timescales and acceptable levels of risk*" **[E]**.

(b) Manchester University NHS Foundation Trust: The COVID-19 pandemic placed a significant burden on UK hospitals. In March 2020, the UK Government chose to suspend all 'non-essential' clinical services nationally to focus hospital resources on COVID-19 care. Through their direct collaboration with MFT, the Unit's researchers developed and fitted multiple stochastic models to help understand how COVID-19-infected patients progress through hospital care, the resources required for their treatment, and how in-hospital infections spread through the enclosed community **[F, 5]**.

The Unit's work on predicting resource requirements **[5]** enabled MFT's nine hospitals and out-of-hospital services to plan confidently to a very precise operating model, resulting in the "*minimum suspension of clinical services*" during the pandemic **[F]**. As the Joint Group Medical Director also states, "*Your modelling has permitted Greater Manchester and other localities to manage their resources effectively by being able to plan, predict and deliver a system wide response to COVID over the past 11 months* [March 2020 – February 2021]" **[F]**. This model **[5]** has been used across the North West of England, and subsequently adopted "*across other parts of the NHS*", and its value "*has been recognised nationally*" **[F]**.

The risk of in-hospital cross-infection between wards, known as nosocomial infection, has been "*a very difficult problem to address*" for hospitals **[F]**. The network-based models provided by the Unit's researchers have helped MFT to understand how nosocomial infection occurs, and the risk factors associated with it. This has been of great value to MFT, who state, "…*through the work of your team not only have we been able to understand how to minimise cross infection* [and] *the implications of this for our patients… [but also to] …identify which sub populations are more vulnerable to cross infection*" **[F]**. This work allowed MFT to "…*for the first time quantify the risks associated with sharing staff between COVID and non-COVID wards*", providing "…*robust justification for the policy*" of compartmentalisation, which the Trust had previously adopted based on intuitive arguments **[F]**. The Unit's scientific justification, "*when presented to clinicians and nursing staff increased awareness and compliance*" **[F]**.

The Unit's statistical model for integrating patient movements and COVID-19 test results was of particular value to MFT, who say it "*…not only allowed **in-hospital outbreaks to be detected faster** but wards where the risk of an outbreak was greater could be flagged up to the Senior Surveillance Officer ahead of time*" **[F]**. This model provided information on which patients had potentially been exposed to COVID-19 and should therefore be monitored **[F]**. MFT's Joint Group Medical Director summarised the impact of the Unit's work by stating, "*I can with some certainty confirm that the work undertaken by* [the Unit's researchers] *has **both saved lives and permitted the elective non-COVID life-threatening work*** […] ***to continue for as long as possible*"** **[F]**. It has also meant that *"…when necessary, any reduction has been the minimum required to permit effective escalation of our response to COVID*" **[F]**.

(c) Care Homes: The COVID-19 pandemic also placed significant pressure on the resources and capacity of the UK's non-hospital healthcare system. This pressure was particularly acute in social care settings, with residential care homes initially experiencing significant outbreaks of COVID-19 and high mortality rates. In England, there are approximately 15,000 care homes with ~450,000 beds **[G]**.

From the first days of the pandemic, it was widely recognized in Government that the severe health consequences of COVID-19 infection in older populations meant care homes were at particularly high risk **[B, G]**. In response to this, Hall formed a multi-disciplinary analytics group in April 2020, which then became the SCWG sub-group of SAGE, with Hall as co-chair. On 9 March 2020, the Unit's researchers submitted a paper to SPI-M **[C]** that quantified the likely impact of unconstrained COVID-19 spread in care homes, in terms of hospitalisations and deaths in hospital **[B, G]**. This paper pre-empted the rapid rise in care home outbreaks and, as data from care homes began to emerge, the Unit's researchers fit them to a bespoke model which projected the severe consequences of these outbreaks **[G, 6]**. As the Government's Chief Scientific Advisor attests, "*This work contributed to a series of policies targeted at care homes, including: interruption of visits, introduction of infection control procedures and other measures to reduce the risk of importation from staff.*" **[G]**.

The Unit's analyses identified the increased risk associated with insufficient data from care homes. Lack of data hinders effective monitoring of the impacts of interventions in care homes, which is crucial for controlling virus spread in these high-risk enclosed communities **[G, 6]**. As the Chief Scientific Advisor notes, "*Good monitoring indicators thus can save lives and drive hypotheses about the way outbreaks occur*" **[G]**. Hall presented a consensus paper to SAGE on 12 May 2020 **[C]** on behalf of SCWG's 30 members, containing multiple analyses and evidence from both his own **[6]** and other members' work. This paper made the case for collecting better-quality data and testing of both residents and staff within care homes **[G, 6]**. This resulted in several impacts associated with data curation, linkage and collection. For example, the Care Quality Commission began to provide information on deaths at individual care-home level, and PHE to provide testing data based on postcode rather than by coarser geographical aggregation, which has been "*…essential to monitor how hard each care home had been hit by COVID-19 and assess transmission within care homes…*" **[G]**. This "*…allowed faster identification of care home outbreaks*" **[G]**. Likewise, Hall and SCWG's recommendation was that "*…if there was insufficient capacity to test all staff* and *residents weekly to focus on weekly staff testing. The policy team was therefore able to directly use this advice by assessing their realistic constraints, and rolled out a policy of weekly staff testing and monthly testing of residents*" **[G]**.

5. Sources to corroborate the impact

[A] Letter from Public Health England's Senior Medical Advisor, 21 January 2021
[B] Letter from the UK GCSA regarding the work of Pellis, 11 February 2021
[C] List of relevant papers submitted to SPI-M, SAGE, SCWG, MFT, PHE, HMPPS
[D] Letter from the Chief Statistician, UK Statistics Authority, 27 January 2021
[E] Letter from the Health Policy Advisor, HMPPS, 21 December 2020
[F] Letter from MFT's Joint Group Medical Director, 1 February 2021
[G] Letter from the UK GCSA regarding the work of Hall, 4 March 2021