Institution: University of Warwick		
Unit of Assessment: B10 Mathematical Sciences		
Title of case study: Rapid-response modelling of the COVID-19 pandemic		
Period when the underpinning research was undertaken: 2010-2020		
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:**
Matt Keeling	Professor	Jan 2002 – Present
Louise Dyson	Associate Professor	May 2015 – Present
Michael Tildesley	Associate Professor	2011 – 2013, Apr 2016 – Present
Edward Hill	Research Fellow	June 2017 - Present
Period when the claimed impact occurred: 2020		
Is this case study continued from a case study submitted in 2014? N		

1. Summary of the impact (indicative maximum 100 words)

Mathematical modellers from Warwick's Zeeman Institute for Systems Biology and Infectious Disease Epidemiology Research (SBIDER) have played leading roles in providing the Scientific Advisory Group for Emergencies (SAGE) with quantitative modelling to underpin its advice to the UK Government on policy response to the Covid-19 crisis. The so-called "Warwick model" is an age-structured, regional scale compartmental model that was rapidly developed in response to the emerging crisis. It has been used on an ongoing basis as an input to SAGE's regular published estimates of the R number. In summer 2020, it was used to establish the "Reasonable Worst-Case Scenario" that formed the planning basis for the winter pandemic preparedness plan. It has also been used to formulate advice on specific policies and interventions including school closures, social bubbles, circuit-breakers and vaccine prioritisation.

2. Underpinning research (indicative maximum 500 words)

SBIDER researchers Matt Keeling, Louise Dyson, Ed Hill and Mike Tildesley specialise in understanding and predicting the spread and control of many infectious diseases using statistical and mathematical modelling. Highlights of relevant research done prior to the 2020 SARS-Cov-2 outbreak include modelling of vaccination strategies against pandemic and seasonal influenza **[3.1, 3.2]** and modelling of public health interventions against Ebola **[3.3]**. Since the emergence of the novel SARS-Cov-2 virus, they have provided mathematical modelling for multiple agencies responsible for providing scientific advice to decision makers about the pandemic. These include the Scientific Pandemic Influenza Group on Modelling (SPI-M), the sub-group of SAGE responsible for modelling, the Joint Committee on Vaccination and Immunisation (JCVI), the UK body responsible for vaccination strategy, and the World Health Organisation Strategic Advisory Group of Experts (WHO SAGE). While research has been supported by peer reviewed grants from the MRC **[G1]** and NIHR **[G2]**, most of the relevant new SARS-Cov-2 modelling described below has been published in preprint form but has not yet been peer reviewed. This is to be expected given the emergency nature of the work.

Quantifying the effectiveness of contact tracing: In collaboration with Hollingsworth (Oxford) and Read (Lancaster), Keeling combined social encounters information with predictive models of contact tracing and control **[3.4]**. This allowed evaluation of the efficacy of contact tracing and quantification of the trade-offs between resources deployed and effect of untraced infections.

Development of the Warwick model of Covid-19: The Warwick Covid-19 model, was initially described in **[3.5]** and has continued to evolve. It is a bespoke model, rapidly developed in response to the developing pandemic. It is a deterministic, age-structured, compartmental model in which the UK population is stratified by infection status (susceptible, exposed, infected, recovered) and symptoms (symptomatic/asymptomatic). Importantly, it is regional in resolution to account for regional differences. It is calibrated against real-time data on hospitalisations and deaths, together with Pillar 2 test results and serological surveys. The model predicts epidemic spread and estimates the reproduction number (*R*).

Simulation of lockdown exit strategies: In **[3.6]**, the Warwick model was used to evaluate the relaxation of early lockdown social distancing measures from 7th May 2020. Scenarios modelled included age-based easing of the lockdown and reintroduction of local lockdown measures based on local ICU capacity. The number of patients requiring inpatient and critical care treatment, and deaths, were estimated. It was found that relaxation must be cautious to prevent a second wave.

Estimation of the consequences of re-opening schools: By matching to the early age-distribution of UK cases and observed dynamics, the Warwick model was used in **[3.7]** to evaluate eight strategies for re-opening schools in England. The research modelled the impact of different combinations of years and class sizes on contact patterns, secondary infections, changes in clinical cases and sensitivity to reductions in social distancing compliance. It was found that approaches enabling half-sized classes or focused on younger children were unlikely to push *R* above one.

Vaccine prioritisation strategy: The Warwick model was extended in **[3.8]** to determine optimal UK ordering (by age, comorbidities etc.) of vaccination for different potential vaccine types. For all scenarios considered, targeting older age groups first was found to be optimal. It was also found that a second wave could be avoided if the vaccine prevented transmission as well as disease.

Estimation of the consequences of social bubbles: A new individual-based model for a synthetic population of households was developed in **[3.9]** to evaluate different social bubble strategies, where members of one household are permitted to form a social unit with another household to increase social interactions while limiting the risk of infection. The model indicated that social bubbles reduced cases and fatalities by 17% compared to an unclustered increase of contacts. They were particularly effective when directed at small, isolated households with the greatest need for additional social interactions and support such as single occupancy households or those with young children.

Circuit breakers: The effects of short, “circuit breaker” lockdowns were modelled in **[3.10]**. A simplified “ready-reckoner” model was used to demonstrate the effect of a short period of reduced transmission, in which R was pushed below 1, and the results validated using the more realistic Warwick model. The results were expressed as taking the epidemic “back in time” and showed that such a break has the largest effect when growth rates are low but can also provide a break on increasing infections when the growth rate is higher.

3. References to the research (indicative maximum of six references) **Warwick = Bold**

[3.1] Keeling, M. J. and White, P. J. (2011) *Targeting vaccination against novel infections: risk, age and spatial structure for pandemic influenza in Great Britain*. Journal of The Royal Society Interface, 8 (58). pp. 661-670. doi:10.1098/rsif.2010.0474

[3.2] Hill, E. M., Petrou, S., Forster, H., de Lusignan, S., Yonova, I. and **Keeling, M. J.** (2020) *Optimising age coverage of seasonal influenza vaccination in England: A mathematical and health economic evaluation*. PLOS Computational Biology, 16 (10). pp. e1008278. doi:10.1371/journal.pcbi.1008278

[3.3] Li, S.-L., Bjørnstad, O. N., Ferrari, M. J., Mummah, R., Runge, M. C., Fonnesbeck, C. J., **Tildesley, M. J.**, **Probert, W. J. M.** and Shea, K. (2017) *Essential information: Uncertainty and optimal control of Ebola outbreaks*. Proceedings of the National Academy of Sciences of the United States of America, 114 (22). pp. 5659-5664. doi:10.1073/pnas.1617482114

[3.4] Keeling, M. J., Hollingsworth, T. D. and Read, J. M. (2020) *Efficacy of contact tracing for the containment of the 2019 novel coronavirus (COVID-19)*. Journal of Epidemiology and Community Health, 74 (10). pp. 861. doi:10.1136/jech-2020-214051
[3.5] Keeling, M. J., **Dyson, L.**, **Guyver-Fletcher, G.**, **Holmes, A.**, Semple, M. G., ISARIC4C Investigators, **Tildesley, M. J.** and **Hill, E. M.** (2020) *Fitting to the UK COVID-19 outbreak, short-term forecasts and estimating the reproductive number*. medRxiv (preprint). doi:10.1101/2020.08.04.20163782
[3.6] Keeling, M. J., **Hill, E. M.**, **Gorsich, E. E.**, **Penman, B.**, **Guyver-Fletcher, G.**, **Holmes, A.**, Leng, T., McKimm, H., Tamborrino, M., Dyson, L. and Tildesley, M. J. (2021) *Predictions of COVID-19 dynamics in the UK: Short-term forecasting and analysis of potential exit strategies*. PLOS Computational Biology, 17 (1). pp. e1008619. doi:10.1371/journal.pcbi.1008619 (**first made publicly available in 2020** as a medRxiv preprint, doi:10.1101/2020.05.10.20083683)
[3.7] Keeling, M. J., **Tildesley, M. J.**, **Atkins, B. D.**, **Penman, B.**, **Southall, E.**, **Guyver-Fletcher, G.**, **Holmes, A.**, **McKimm, H.**, **Gorsich, E. E.**, **Hill, E. M.** and **Dyson, L.** (2020) *The impact of school reopening on the spread of COVID-19 in England*. medRxiv (preprint, accepted in Philosophical Transactions of the Royal Society B). doi:10.1101/2020.06.04.20121434
[3.8] Moore, S., **Hill, E. M.**, **Dyson, L.**, **Tildesley, M.** and **Keeling, M. J.** (2020) *Modelling optimal vaccination strategy for SARS-CoV-2 in the UK*. medRxiv (preprint, accepted in PLoS Computational Biology). doi:10.1101/2020.09.22.20194183
[3.9] Leng, T., **White, C.**, **Hilton, J.**, Kucharski, A., Pellis, L., Stage, H., Davies, N., CMMID-Covid-19 WG, **Keeling, M. J.** and Flasche, S. (2020) *The effectiveness of social bubbles as part of a Covid-19 lockdown exit strategy, a modelling study*. medRxiv (preprint). doi:10.1101/2020.06.05.20123448
[3.10] Keeling, M. J., **Guyver-Fletcher, G.**, **Holmes, A.**, **Dyson, L.**, **Tildesley, M. J.**, **Hill, E. M.** and Medley, G. F. (2020) *Precautionary breaks: planned, limited duration circuit breaks to control the prevalence of COVID-19*. medRxiv (preprint). doi:10.1101/2020.10.13.20211813

Key Grants:

[G1] Tildesley, M. J. (PI), **Keeling, M. J.**, **Dyson, L.** and **Hill, E. M.**, *Mathematical modeling and adaptive control to inform real time decision making for the COVID-19 pandemic at the local, regional and national scale*. **Sponsor:** MRC [MR/V009761/1] **Duration:** May 2020 - Jul 2021 **Award:** GBP243,131
[G2] Keeling, M. J. (PI), **Staniszewska, S.** and Petrou, S., *Mathematical & Economic Modelling for Vaccination and Immunisation Evaluation, and Emergency Response*. **Sponsor:** NIHR [NIHR200411] **Duration:** Oct 2019 – Oct 2022 **Award:** GBP720,706

4. Details of the impact (indicative maximum 750 words)

The main pathway to impact for this research is through membership of the advisory bodies directly responsible for providing scientific input into government policy. Keeling, Dyson, Hill and Tildesley are active members of the SPI-M modelling group which provides scientific advice to SAGE and directly to the Department of Health. Keeling and Tildesley also sit on the Interdisciplinary Task and Finish Group on the Role of Children in Transmission (TFC), an interdisciplinary body of SPI-M, and the Scientific Pandemic Influenza Group on Behaviours (SPI-B). Keeling also sits on the JCVI.

In the year 2020, the Warwick group have authored or co-authored 57 modelling reports to SPI-M, with 19 being sent onto SAGE as a result. The majority of these reports are publicly available alongside the published minutes of SAGE meetings. However, in keeping with civil service norms, the authorship of the papers is not stated. The contributions of the Warwick group to the relevant reports are confirmed in a statement from the UK Government Chief Scientific Adviser **[5.1]**.

Estimation of the R number: The R number is the crude yardstick against which the effectiveness of the public health response to the epidemic is measured. The Warwick model is one of 6 models from 7 UK institutions that have been used throughout the pandemic to form SPI-M's weekly combined estimate of the *R* number for 10 UK regions, together with short and medium term forecasts of the progress of the epidemic **[5.1, 5.2]**. Credible estimates of the R number were critical in the timing and sequencing of the relaxation of social distancing measures after the first lockdown. The need demonstrated in **[3.6]** for a cautious exit from lockdown to avoid a second wave, including the potential for reintroduction of local lockdown measures where ICU occupancy exceeded a given threshold, was largely included in the recommendations **[5.3]** of the 33rd SAGE meeting on 5 May and subsequently adopted by the Government when exiting the first lockdown. Local lockdowns were later introduced in Leicester on 17 July and in the North of England on 31 July on the basis of these recommendations.

Specification of Reasonable Worst-Case Scenario: On 10 March, the 14th SAGE meeting recommended that, for planning purposes, it is not useful to produce a "most likely" scenario given the lack of available data. The Reasonable Worst-Case Scenario (RCWS) was recommended as being the most useful scenario for government planning. Warwick and three other modelling groups subsequently developed several RWCS, which provided similar results once normalised. When the RWCS was reviewed in May at the request of the government, the Warwick model was selected by SPI-M at the 38th SAGE meeting on May 21 as the single model to provide the consensus **[5.4]**. Keeling was subsequently asked to explain the rationale for the RWCS in oral evidence to the House of Lords Select Committee on Science and Technology on 2 June **[5.5]**.

Protocols for reopening of schools in England after the first lockdown: The findings of **[3.7]** were incorporated, along with findings from 3 other models, into a paper **[5.6]** presented at the April 30th SAGE meeting by the TFC. This paper covered 9 separate scenarios from minimal attendance of schools by the children of key workers to full attendance. The main point of consideration was the finding from the Warwick model, supported by other modelling groups, that “the impact of opening schools is a lot less than any changes to the population-wide policy of lockdowns”. A follow-up SAGE meeting was arranged the next day to fully evaluate the detailed findings. At this meeting, the consensus ranking on the 9 different scenarios was supported by SAGE – with precautionary measures advised ahead of re-opening schools **[5.7]**. In June 2020, a phased reopening of schools was announced, focusing initially on early years and primary school settings and smaller class sizes in line with modelling recommendations.

JCVI vaccine prioritisation list: The Chief Scientific Advisor confirmed the Warwick researchers’ contribution to scientific prediction of the impact of vaccination presented to JCVI (Joint Committee on Vaccines and Immunisation), SPI-M and SAGE, stating: “The early elements of this research considered the benefits of targeted vaccination and helped inform the JCVI priority list, while later models have focused on how non-pharmaceutical interventions can be relaxed as the vaccine is rolled out across the population.’’ The mathematical modelling in **[3.8]** indicated that the optimal strategy for minimising future deaths or quality adjusted life year (QALY) losses is to offer vaccination to older age groups first. These findings were subsequently cited by the JCVI on 30 December as providing the scientific rationale for the committee’s recommendation that vaccine priority groups should be ranked primarily by age **[5.8]**. This is reflected in the implementation of the Covid-19 vaccination programme.

Introduction of social bubbles as a soft exit from lockdown: The findings of Warwick’s modelling demonstrating the relative safety of social bubbles **[3.9]** were included in a report presented to the 36th SAGE meeting on 13 May **[5.9]**. All models indicated low risks of increase in R from bubbles involving single-occupancy households and single parents with primary school age children. Although SAGE advised against the introduction of bubbles in the short term when other measures have just been lifted, on June 10th the Prime Minister announced that single adult households who live alone or with dependent children would be permitted to form a ‘support bubble’ with one other household **[5.10]**, a policy that remains in place today.

Circuit breakers in Wales and Northern Ireland: The results of **[3.10]** on circuit breakers were included in a paper presented to the 59th SAGE meeting on 24 September **[5.11]**. SAGE noted the estimate of R of 1.2 to 1.5. would result over time in hospitalisations exceeding scenario planning levels unless interventions brought R back below 1. SAGE also advised that a two-week circuit breaker could achieve this. Although the government decided against a proposed circuit breaker in England over half-term, the policy was adopted by the Welsh and Northern Ireland governments who entered circuit breaker lockdowns on 23 October and 27 November respectively.

5. Sources to corroborate the impact (indicative maximum of 10 references)

[5.1] Statement from the Government Chief Scientific Adviser
[5.2] SPI-M-O: Consensus Statement on COVID-19: [20 May 2020, https://tinyurl.com/akdfacyb, plus many of others]
[5.3] SAGE 33 minutes: Coronavirus (COVID-19) response, 5 May 2020 [https://tinyurl.com/5hwcrkht]; SPI-M-O: Consensus view on the potential relaxing of social distancing measures, 4 May 2020 [https://tinyurl.com/4xrjsrs9]
[5.4] SAGE 38 minutes: Coronavirus (COVID-19) response, 21 May 2020 [https://tinyurl.com/3rn769en]; SPI-M-O: COVID-19 planning and reasonable worst-case scenarios, 20 May 2020 [https://tinyurl.com/fzdrmurv]
[5.5] Select Committee on Science and Technology Oral evidence: The science of Covid-19 Tuesday 2 June 2020 [https://committees.parliament.uk/oralevidence/444/pdf/]
[5.6] SAGE 30 minutes: Coronavirus (COVID-19) response, 30 April 2020 [https://tinyurl.com/yfbs7uwx]; TFC: Modelling and behavioural science responses to scenarios for relaxing school closures, 30 April 2020 [https://tinyurl.com/yypevcrk]
[5.7] SAGE 31 minutes: Coronavirus (COVID-19) response, 1 May 2020 [https://tinyurl.com/3r975kye]; TFC: Modelling and behavioural science responses to scenarios for relaxing school closures, 1 May 2020 [https://tinyurl.com/2a9kx4tn]
[5.8] Joint Committee on Vaccination and Immunisation: advice on priority groups for COVID-19 vaccination, 30 December 2020 [https://tinyurl.com/5xpx2cje]
[5.9] SAGE 36 minutes: Coronavirus (COVID-19) response, 14 May 2020 [https://tinyurl.com/77d9nxwa]; SPI-M-O Statement on bubbles, 13 May 2020 [https://tinyurl.com/yc2xhevw]
[5.10] Prime Minister's statement on coronavirus (COVID-19): 10 June 2020 [https://tinyurl.com/jatanzf]
[5.11] SAGE 59 minutes: Coronavirus (COVID-19) response, 24 September 2020 [https://tinyurl.com/ujtpz6cr], Circuit breakers: implementing (partial) lockdown for 2 weeks over half-term, 24 September 2020 [https://tinyurl.com/3uec9rzh]