Institution: University of Warwick

Unit of Assessment: B10 – Mathematical Sciences

Title of case study: Mathematical modelling to simulate the spread of foreign animal diseases in the US: informing policy and influencing response planning

Period when the underpinning research was undertaken: 2013-2020

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:**
Michael Tildesley	Associate Professor	2011 – 2013, Apr 2016 – Present
Matt Keeling	Professor	Oct 2009 – Present

Period when the claimed impact occurred: 2014 - December 2020

Is this case study continued from a case study submitted in 2014? N

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

Warwick researchers Dr Mike Tildesley and Professor Matt Keeling have been integral in helping the US, one of the world's largest producers of beef, to develop the first national-scale model to simulate potentially devastating outbreaks of foot-and-mouth disease (FMD) and, later, bovine Tuberculosis (bTB) within the country. In a collaboration with Colorado State University in the US and Linköping University in Sweden, Warwick built upon earlier research into the 2001 outbreak of FMD in the UK to develop two models, the US Disease Outbreak Simulation (USDOS) and the US Animal Movement Model (USAMM), which allows for prediction of animal shipments. The models have enabled the US Department of Agriculture (USDA) since 2014 to develop control policies in the event of outbreaks and to provide operational advice on animal health emergency management before, during and after an incident. These contingency plans, formulated in 2014 and updated in 2020, describe the procedures to be followed in the event of a disease outbreak which could, in a worst-case scenario, cause USD228,000,000,000 of damage.

2. Underpinning research (indicative maximum 500 words)

The US is one of the world's largest producers of beef, with around 93,600,000 cattle across 882,000 farms, and with a market value of USD77,000,000,000 (Census of Agriculture 2017, USDA). Protecting millions of cattle from potential disease outbreaks is thus a crucial part of the nation's economic security, as well as a public health priority. An outbreak of an infectious disease such as foot-and-mouth disease (FMD) could be devastating: FMD is a highly infectious disease which can cause large economic and livestock losses in non-endemic countries. While there has been significant modelling carried out on FMD since the 2001 outbreak in the UK, which cost the country GBP8,000,000,000 (NAO, 2002), this research has typically focused upon transmission dynamics, retrospective analysis of previous epidemics and establishment of optimal control policies that should have been deployed in these outbreaks.

The research of Dr Michael Tildesley and Professor Matt Keeling in Warwick's Mathematics Institute focuses on the development of models of infectious diseases and their utility as predictive tools, particularly in the early stages of a disease outbreak, when there is significant uncertainty regarding its spread (Warwick researchers had previously completed extensive modelling for the UK's 2001 FMD outbreak). However, extending their modelling to the US presented unique challenges: unlike in the UK, individual livestock movements are not tracked, for example. In addition, differences in farm size can be substantial, with the largest cattle ranches in the US being over a hundred times the size of the UK's biggest beef farms. Consequently, a bespoke approach was required.

Between 2013 and 2020, Tildesley and Keeling worked closely with Colorado State University, Linköping University and the US Department of Agriculture (USDA) to develop a novel model framework to simulate the spread of livestock disease at the national scale, for the first time ever, in order to determine intervention policies that could be put in place to minimise the risk of spread should a disease be introduced into the farming industry in the future **[3.1]**.

In 2013 this work produced the first version of the US Disease Outbreak Simulation (USDOS), to enable efficient simulation of outbreaks and evaluation of control strategies in a very large cattle population, without exact locations of premises, and with limited information about shipments. The US Animal Movement Model (USAMM), which accounted for cattle shipments in a statistical sense, was developed to be used in tandem with USDOS. Warwick led on the work for USDOS; Colorado State and Linköping on USAMM.

Further development to overcome the limitations of the early model – it operated only at the county level, dealt just with FMD and did not account for within-farm dynamics – was funded by the US Department of Homeland Security in 2015 **[G1]**, with USDOS-USAMM highlighted as one of their key modelling efforts for disease control in a standard operating procedure (SOP) released in 2014. The model was updated using innovative gridding methodology to optimise the speed of simulations **[3.2]**. The new USDOS model indicated that local infrastructure, cattle density and farm clustering have a significant effect upon the risk of spread of livestock disease, and that bespoke local intervention policies may be necessary to control the spread of that disease **[3.3]**.

As the last outbreak of foot-and-mouth disease in the US occurred in 1929, there is uncertainty regarding how disease may spread in the future. In order to investigate this, from early 2016 to late 2017 **[G2]** Tildesley and Keeling developed a novel real-time modelling approach that fitted Warwick's foot-and-mouth model to the most up-to-date data that are accrued during an ongoing outbreak, and explored how model predictions change during an epidemic. A dynamic epidemic model fitted to the data of two contrasting outbreaks of FMD, in the UK in 2001 and in Miyazaki, Japan in 2010, was used to evaluate alternate control strategies, thereby simulating real-time decision making. The results demonstrated that the optimal control policy is selected with available data in the early stage of an outbreak, even with high levels of uncertainty **[3.4]**.

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

All research papers were published in peer-reviewed journals

[3.1] Buhnerkempe, M. G., **Tildesley, M. J.**, Lindström, T., Grear, D. A., Portacci, K., Miller, R. S., Lombard, J. E., **Werkman, M.**, **Keeling, M. J.**, Wennergren, U. and Webb, C. T. (2014) *The Impact of Movements and Animal Density on Continental Scale Cattle Disease Outbreaks in the United States.* PLOS ONE, 9 (3). pp. e91724. doi:10.1371/journal.pone.0091724

[3.2] Sellman, S., Tsao, K., **Tildesley, M. J.**, Brommesson, P., Webb, C. T., Wennergren, U., **Keeling, M. J.** and Lindström, T. (2018) *Need for speed: An optimized gridding approach for spatially explicit disease simulations*. PLOS Computational Biology, 14 (4). pp. e1006086. doi:10.1371/journal.pcbi.1006086

[3.3] Tsao, K., **Sellman, S.**, Beck-Johnson, L. M., Murrieta, D. J., Hallman, C., Lindström, T., Miller, R. S., Portacci, K., **Tildesley, M. J.** and Webb, C. T. (2020) *Effects of regional differences and demography in modelling foot-and-mouth disease in cattle at the national scale*. Interface Focus, 10 (1). pp. 20190054. doi:10.1098/rsfs.2019.0054

[3.4] Probert, W. J. M., Jewell, C. P., Werkman, M., Fonnesbeck, C. J., Goto, Y., Runge, M. C., Sekiguchi, S., Shea, K., **Keeling, M. J.**, Ferrari, M. J. and **Tildesley, M. J.** (2018) *Real-time decision-making during emergency disease outbreaks*. PLoS Computational Biology, 14 (7). pp. e1006202. doi:10.1371/journal.pcbi.1006202

Grants

[G1] Webb, C. T. (PI) and **Tildesley, M. J. (Co-I)**, *U.S. Animal Movement Model (USAMM) and Disease Outbreak Simulation (USDOS): Incorporating within Herd Dynamics and Consequences for Control*. **Sponsor:** US Department of Homeland Security [D15PC00278] **Duration:** Sep 2015 - Sep 2019 **Award:** USD965,456.

[G2] Tildesley, M. J. (PI) and **Keeling, M. J. (Co-I)**, *US-UK Collab Linking models and policy: Using active adaptive management for optimal control of disease outbreaks*. **Sponsor:** BBSRC [BB/K010972/4] **Duration:** Apr 16 - Dec 17 **Award:** GBP193,973.

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

Impact on Government policy: informing USDA's strategic guidelines and operating procedures

In the US, outbreak preparedness and response strategy, including vaccine prioritisation, is the responsibility of USDA's Animal and Plant Health Inspection Service (APHIS). As recognised experts in infectious disease modelling, Tildesley and Keeling have collaborated with the USDA and US Department of Homeland Security for over 10 years to inform US policy in this area **[5.1]**. The [text removed for publication] USDA Centre for Epidemiology and Animal Health, calls this collaboration "*an excellent example of an effective Federal-Academic partnership*." She continues: "*The transfer of knowledge from researchers in the UK such as Dr Tildesley has improved the ability to plan for and respond to agricultural diseases in the United States."* **[5.1]**

Both USDOS and USAMM early model versions were first featured as part of the USDA's Foreign Animal Disease Preparedness and Response Plan (FAD PReP) in 2014, following the development of USDOS at Warwick in 2013 **[3.1]**. For the plan, both models were incorporated in the *Overview of Modeling and Assessment Tools* standard operating procedure (SOP), with SOPs constituting formalised step-by-step guidance to be followed under specific circumstances **[5.2a]**. In this context, this overall series of SOPs provides the USDA – one of the USA's federal executive departments – with operational details *'for conducting critical activities, such as communication and biosecurity, that are essential to effective preparedness and response to an FAD outbreak*' **[5.2b]**.

Series of SOPs are often incorporated into larger strategic documents, and this is no different for the USDA. First published in 2014 and reissued in 2020, the *FAD PReP Foot-and-Mouth Disease (FMD) Response Plan: The Red Book* provides the holistic approach taken by US government officials in response to an FMD or other foreign animal disease outbreak. The Red Book acknowledges the importance of mathematical models as part of this approach, mandating that the USDA should bring together "*epidemiologists, disease agent experts, economists, and affected commodity experts to undertake risk assessments to inform policy makers as required*" **[5.3]**. Further, the FAD PReP series of SOPs are featured throughout the 2020 Red Book, with the 2014-published *Overview of Modeling and Assessment Tools* SOP spotlighted as outlining appropriate modelling contingencies, including its provision of "*current models and assessment tools*" which encompasses USDOS and USAMM **[5.3]**.

Overall, the USDOS and USAMM models have remained relevant and useful to US agricultural policy from their initial integration into the still active 2014 SOP **[5.2a]**, through further refinement in 2016/2017, and finally with the models being officially transferred to the USDA **[5.1]** in 2019 for use in the prediction of future disease risk through livestock movements. The [text removed for publication] USDA Centre for Epidemiology and Animal Health says: "*Use of [the USAMM and USDOS] models provide information for various analyses important to mitigating the risk of disease spread within the US livestock industry and have been applied to support the Federal Emergency Management Agency Food, Agriculture, and Veterinary response exercise in collaboration with USDA.*" **[5.1]**. The models were extended in 2018 to simulate bovine tuberculosis outbreaks.

The 2020 version of the Red Book reflects knowledge gained and lessons learned during APHIS's testing of its response capabilities with FAD outbreaks in 2016, 2017, 2018 and 2019, as well as the planning and execution of the 2018 ARMAR (Agriculture Response Management and Resources) foot-and-mouth disease (FMD) functional exercise (see Impact on response planning, below). Among other things, compared to prior versions: it includes policy that explicitly recognises vaccination as a likely response tool in an FMD outbreak, as well as new surveillance sections revised by the Center for Epidemiology and Animal Health; it highlights available training resources and often overlooked planning considerations; and it incorporates policy guidance prepared for ARMAR on managing a national movement standstill **[5.3]**.

Impact on response planning: highlighting the importance of a national-scale analysis

USDOS gives the USDA the capacity to determine the optimal control policy that should be introduced dependent upon where the disease might start and how it might spread in the early stages of an outbreak. Run on a laptop or supercomputer, USDOS efficiently simulates outbreaks by local (aerosol) and long-range transmission (animal movement) **[5.4]**. USDOS can investigate the impact of a suite of movement restrictions, ring culling, vaccination and diagnostic testing strategies. Warwick's novel real-time modelling approach for FMD is able to use the most up-to-date data during an ongoing outbreak to advise policy makers on the most effective intervention strategies when there is significant uncertainty during the early stages of an outbreak, and adapt policies as more is learned about epidemic behaviour. Shortening the duration of an epidemic could mean significantly lower economic losses.

Warwick and colleagues' real-time modelling of disease outbreaks contributed to the development of an app, USAMM-Shiny App, to make it easier for public officials and livestock farmers to predict cattle shipments and prepare for disease outbreaks **[5.5a]**. The interactive app allows users to create heat maps to visualise the movement of cattle across the US: the visualisation of movement data can help to inform risk assessments, develop scenarios and trace back efforts to predict where cattle shipments may occur in the United States using the USAMM model **[5.5b]**. This information allows the USDA to determine high-risk counties for disease introduction; it also underpins the outbreak simulation capability provided by USDOS, as shipment-based disease spread is a required input into the model and there are no complete records of animal shipments in the US to otherwise rely on.

Disease preparation exercises remain a core activity of APHIS, which sponsors or participates in an average of 3 or 4 such exercises annually (41 exercises over 11 years) for FMD **[5.6]**. Prior to the transition of the models into the USDA, governmental uptake of the USAMM model was demonstrated by APHIS and other collaborators in a 2017 assessment exercise **[5.7]**. This marks an important use-case for USAMM which the USDA actively participated in, highlighting the integration of real-world data on cattle imports with the model priorities for surveillance of specific state counties.

In 2019, the US Government Accountability Office (GAO) was asked by Congress to review USDA's efforts to prepare for an FMD outbreak. The resulting report **[5.6]** recommends that USDA follow its procedures to prioritise and monitor the completion of corrective actions that the agency had previously identified for FMD preparedness. Efficient allocation of limited vaccine resources in the event of an outbreak was identified as an area of concern. The GAO notes that APHIS has "*used predictive models to evaluate different vaccination strategies*" at the state level **[5.6]** and recommends that "*a similar analysis at the national level … could help inform USDA's vaccine prioritization decisions in advance of an outbreak*". Such national-scale analyses are only now possible due to the novel capabilities provided by the USDOS/USAMM models.

Although there has not been an outbreak of FMD in the US for almost 100 years, a constant risk of reintroduction remains. The importance of the capability provided by the USAMM/USDOS model is reflected by the fact that the country has over 882,000 cattle farms, with over 93,600,000 beef and dairy animals. According to the GAO, "*an FMD outbreak would have serious economic impacts, in part because trade partners would likely halt all imports of U.S. livestock and livestock*

products until the disease was eradicated. These imports were valued at more than $19 billion [USD19,000,000,000] *in 2017*" **[5.6]**. This is expanded on further in the 2020 Red Book: "*A U.S. outbreak contained to California could cost $6–14 billion; a nation-wide agroterrorism attack could reach $228 billion* [USD228,000,000,000]" **[5.3]**. These stark figures reflect the importance of effective contingency planning for US agriculture in the face of an outbreak: the need to reduce the risk of large-scale transmission through national-scale modelling cannot be overstated.

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

[5.1] Statement (March 2020) from [text removed for publication] the USDA Centre for Epidemiology and Animal Health

[5.2a] Foreign Animal Disease Preparedness and Response Plan (FAD PReP) standard operating procedure (SOP) for the Overview of Modeling and Assessment Tools (2014) https://tinyurl.com/463q9jhf; **[b]** FAD PReP SOP webpage description (expanding the Standard Operating Procedures tab) https://tinyurl.com/nfc4v36o

[5.3] The USDA Foot and Mouth Disease Response Plan (The "Red Book", 2020): https://tinyurl.com/nivv6rc0

[5.4] Source code and documentation for the USDOS model along with a full set of references to the underpinning research: https://webblabb.github.io/usammusdos/usdos.html

[5.5a] Newswise article (Aug 2017) on development of the USAMM model in collaboration with Warwick: https://tinyurl.com/18g5n4rj **[5.5b]** Source code and documentation for the USAMM model and implementation as a runnable Shiny app: https://usamm-gen-net.shinyapps.io/usamm-gen-net

[5.6] GAO-19-103 (March 2019) US Government Accountability Office report, USDA's Preparedness for Foot-and-Mouth Disease: https://www.gao.gov/assets/700/697467.pdf

[5.7] Gorsich, E. E., McKee, C. D., Grear, D. A., Miller, R. S., Portacci, K., Lindström, T. and Webb, C. T. (2018) *Model-guided suggestions for targeted surveillance based on cattle shipments in the U.S*. Preventive Veterinary Medicine, 150. pp. 52-59. doi:10.1016/j.prevetmed.2017.12.004