Institution: University of Sussex		
Unit of Assessment: 10 – Mathematical Sciences		
Title of case study: Mathematical modelling of COVID-19 shapes Ukraine's national public health intervention and underpins regional decision-making in the UK		
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:**
Dr Yuliya Kyrychko	Reader in Mathematics	1 Oct 2010 – present
Dr Konstantin Blyuss	Reader in Mathematics	1 Oct 2010 – present
Prof Anotida Madzvamuse	Professor in Applied Mathematics	1 Sep 2006 – present
Dr James Van Yperen	Postdoctoral Research Fellow	1 Aug 2020 – present
Period when the claimed impact occurred: Mar 2020 – Dec 2020		
Is this case study continued from a case study submitted in 2014? N		

1. Summary of the impact

Research by the Mathematics Applied to Biology Group at Sussex has supported COVID-19 control measures at the levels of (1) national policy (in Ukraine) and (2) regional healthcare management in East and West Sussex, and Brighton & Hove (in the UK). Sussex research co-produced by academics and decision makers within the Ukrainian equivalent of the Scientific Advisory Group for Emergencies (SAGE) fed directly into public health policy interventions that have subsequently been implemented by Ukraine's Cabinet and the National Security and Defence Council. As a result, the Ukrainian Government devolved implementation of control measures to regional administrations (June 2020) and moved to a tiered system and adaptive quarantine measures (July 2020). These measures enabled the Ukrainian government to make the best-informed policy decisions they could, which the government confirms were as effective as possible in slowing the spread of the pandemic. In parallel, research at Sussex has (a) underpinned decision making with respect to hospital and mortuary demand in East Sussex, West Sussex, and Brighton & Hove. This research has also helped Public Health Local Authorities to (b) translate UK-SAGE national guidelines to regional level for decision making, (c) prevent or mitigate miscalculations in ward and body storage planning, thereby avoiding monetary and resource mismanagement, and (d) provided key scientific evidence for Urgent Community Response's (UCR) successful business case which secured £1.63 million for care services in West Sussex to deal with the additional burden brought about by COVID-19.

2. Underpinning research

The COVID-19 pandemic, which has already caused over 94 million cases and over 2 million deaths worldwide (at the time of writing), has led to an unprecedented mobilisation of scholarly efforts in order to shed light on the biology of the virus, its means of transmission and to support the development of scientific-evidence-based interventions and policies locally and nationally. The Mathematics Applied to Biology Group has a strong track record in developing and applying epidemiological models to real world problems [R1-3]. The need for designing robust and effective intervention measures has brought into focus the need for mathematical models that could provide important insights into disease dynamics and its subsequent spread, as well as a quantitative comparison of the effects of different intervention scenarios.

Mathematicians at Sussex, in particular Blyuss and Kyrychko, have a track record of developing models with non-Markovian incubation and recovery periods [R1-3] which is a natural feature of the virus' biology. Although this is often overlooked for the sake of model simplicity, this is an essential feature of the disease. Building on this work, they developed a mathematical model for the spread of SARS-Cov-2 which featured the inclusion of realistic distributions of incubation and recovery periods, and population age structure in different regions [R1]. The latter feature accounts for the strong age effect in mortality rates due to COVID-19. This model was first parametrised using UK regional data, and its results demonstrated the major role of the region-specific age distribution of the population on the effectiveness of lockdowns. Whereas many papers analysed the effects of UK lockdown at national level or compared the effects of age distribution on the spread in different countries, as far as Sussex is aware, the work by Blyuss and Kyrychko was the first to demonstrate the significant impact of age distribution on *local epidemic dynamics* and the effectiveness of local lockdown [R1].

In collaboration with Dr Igor Brovchenko, chair of the Special Committee of the National Academy of Sciences of Ukraine on Mathematical modelling of dynamics and containment of COVID-19, and building on the research in [R3], Blyuss and Kyrychko developed a model for the spread of COVID-19 in Ukraine [R4]. This model was based on extensive clinical and epidemiological data collected by Ukraine's Ministry of Health in April-May 2020, which provided accurate parameterisation of incubation, hospitalisation, recovery and death, as well as age-dependent characteristics of the disease. In [R4], they reproduced observed time course of disease, developed short-term forecasts of epidemic dynamics, and also considered the effects of different intervention scenarios on mitigating the effects of the disease. They found that on a longer timescale, a 30% reduction in contacts within the working population resulted in a more substantial reduction in total cases and deaths than a similar reduction in school contacts, or a 50% shielding of people over 60 years of age.

An important component of epidemic models is their integration of real-world data for the purpose of parameter estimation and forecasting. Madzvamuse has a wealth of expertise in Bayesian and other inference methods for more complex systems such as partial differential equations [R4]. Building on his links with experimental biologists, Madzvamuse and his team, including Van Yperen, were tasked with developing a model for forecasting hospital and mortuary demand in East Sussex, West Sussex, and Brighton & Hove. The team used local NHS datasets from the NHS Situational Reports and Office of National Statistics to generate a data-driven ordinary differential equation model with the necessary parameter inference component, which relied on previous approaches developed by Madzvamuse and colleagues [R5]. In particular, the research showed that one can recover estimates of parameters which reflect the impact of the epidemic locally and that, whilst some of these estimates are in line with nationally derived parameters, others are different [R5]. This in part confirmed the views of local authorities across Sussex that the burden on Sussex was significantly less compared to other regions, like Kent or Manchester. Madzvamuse and his team built an online prototype translational toolkit (https://alpha.halogen-health.org) which provides a description of the model derived in [R5], its assumptions, its methodology, and its outputs, in a user-friendly format and language accessible to non-academics. This tool allows users to carry out scenario-based forecasting driven by the rigorous research in [R5], and provides an educational environment that gives users a hands-on experience of mathematical modelling.

3. References to the research

[R1] K.B. Blyuss, Y.N. Kyrychko. Effects of latency and age structure on the dynamics and containment of COVID-19, Published online April 2020, medRxiv. doi: 10.1101/2020.04.25.20079848. Subsequently in J. Theor. Biol., 2021; 513, 110587: DOI: 10.1016/j.jtbi.2021.110587.

[R2] N. Sherborne, K.B. Blyuss, I.Z. Kiss. Dynamics of multi-stage infections on networks. Bull. Math. Biol., 2015; 77: 1909-33. DOI: 10.1007/s11538-015-0109-1.

[R3] Y.N. Kyrychko, K.B. Blyuss, I. Brovchenko. Mathematical modelling of the dynamics and containment of COVID-19 in Ukraine. Sci. Rep., 2020; 10:1-11. DOI: 10.1038/s41598-020-76710-1.

[R4] E. Campillo-Funollet, C. Venkataraman, A. Madzvamuse. Bayesian Parameter Identification for Turing Systems on Stationary and Evolving Domains. Bull. Math. Biol., 2019; 81: 81–104. DOI: 10.1007/s11538-018-0518-z. *Research supported by Leverhulme Trust Research Project Grant* [G1]

[R5] E. Campillo-Funollet, J. Van Yperen, P. Allman, M. Bell, W. Beresford, J. Clay, G. Evans, M. Dorey, K. Gilchrist, A. Memon, G. Pannu, R. Walkley, M. Watson, A. Madzvamuse. Predicting and forecasting the impact of local outbreaks of COVID-19: Use of SEIR-D quantitative epidemiological modelling for healthcare demand and capacity. Published online August 2020, DOI: 10.1101/2020.07.29.20164566. Subsequently under review in Int. J. Epidemiol. *Research supported by Research England/HEIF Grant* [G1]

[G1] Leverhulme Trust (Unravelling new mathematics for 3D cell migration, Madzvamuse, A. (PI), Styles, V. (Co-I), Venkataraman, C. (Co-I); University of Sussex, 09/2014-12/2017; RPG-2014-149, £258,593).

[G2] Research England/HEIF (COVID Rapid Response – HEIF Programme, Madzvamuse, A. University of Sussex, 04/2020 – 12/2020, £75,280).

4. Details of the impact

The mathematical modelling outlined above has supported COVID-19 control measures at the levels of (1) national policy (in Ukraine) and (2) regional healthcare management in East and West Sussex, and Brighton & Hove (in the UK).

4.1 Impact on the design and implementation of COVID-19 control measures in Ukraine

In Ukraine, the majority of scientific research is done in research institutes of the state-funded National Academy of Sciences of Ukraine (NASU). Prior to emergence of COVID-19, there was no dedicated scientific committee in Ukraine that specialised in modelling epidemics and advising government on strategy. To address the growing problem of COVID-19 and to develop strategies for its containment and mitigation, in early April 2020, the National Security and Defence Council of Ukraine (NSDCU) approached the NASU, which then created the Working Group on "Mathematical modelling of problems related to the coronavirus SARS-CoV-2 epidemic in Ukraine" (equivalent of UK's SAGE group), chaired by Dr Igor Brovchenko. Since April 2020, this Working Group provides weekly or bi-weekly forecasts of cases, deaths and recoveries for each of Ukraine's regions to the National Security and Defence Council of Ukraine and the Cabinet of Ministers, who then use those forecasts for policy decisions. It is the only scientific committee in Ukraine that directly communicates with the government with regards to monitoring the dynamics of COVID-19, provides forecasts, and models the effects of different types of interventions.

Building on their previous work on COVID-19 dynamics in the UK [R1], Blyuss and Kyrychko worked closely with Dr Brovchenko to develop a mathematical model of COVID-19 dynamics [R3] that was based on detailed clinical and epidemiological data collected by the Ukraine's Ministry of Health. Some of the early results of this work featured in a national press conference given to Ukrainian journalists by the Working Group of the National Academy of Sciences of Ukraine on 28 May 2020, where the Chair of the Working Group explicitly stated that the model developed jointly with researchers at Sussex is far superior and more accurate [S1] compared to the basic model used at that point. *This new model allowed its users to (i) account for regional differences in population age structure and mixing, and (ii) identify which control measures – such as lockdowns or targeted actions to reduce mixing among the working-age population – lead to the most significant reduction in disease burden.* The President and the Head of the Working Group of NASU confirm in their gratitude letter [S5] that the set of "Specific measures that were subsequently introduced on the basis of these results" included:

a. On 13 June 2020, Ministry of Health introduced a requirement for local authorities to modify working hours at local companies to reduce mixing between working-age people during rush hour [S2].
b. On 20 June 2020, the Cabinet modified its guidance and allowed regional administrations to make local decisions on anti-epidemic measures and local lockdowns for different regions depending on their current levels of infection, starting from 22 June 2020 [S3, S5].
c. On 22 July 2020, the Cabinet introduced the tiered system ("green", "yellow", "orange", "red") for characterisation of severity of epidemiological situation in each of Ukraine's 25 major administrative regions, starting from 1 August 2020. This tiered system was designed based on the following quantitative measures: the percentage of hospital bed occupancy, the rolling average of the percentage of positive PCR tests per capita, the local growth rate of cases, and the per capita weekly number of administered PCR tests. On the basis of these quantitative measures, restrictions and/or closure of shops, hospitality, sports venues, schools, universities, colleges, public transport were instigated [S4-5].

These measures meant that the Ukrainian Government could:

1. *implement epidemic control measures without a nationwide lockdown; and*
2. *make the best-informed policy decisions they could, and that, in the government's opinion, their interventions were as effective as possible in slowing the spread of the pandemic.*

The President and the Head of the Working Group of NASU confirms these impacts and the work's continuing legacy: "The results of this research and the associated recommendations have been and are being used by the Government of Ukraine and the National Security and Defence Council of Ukraine when making decisions on the strategy of containment of [the] COVID-19 epidemic in Ukraine" [S5].

4.2 Impact on decision making and care provision in the Sussex region

In response to the COVID-19 pandemic in the Sussex region, the Sussex Health and Care Partnership developed a Gold Command structure which posed modelling questions of strategic operational significance to the Local Health Resilience Partnership (LHRP) covering East Sussex, West Sussex, and Brighton & Hove (with a combined population of 1.7 million).

While national-scale planning for COVID-19 is underpinned by the modelling conducted by SAGE-NHSE, local decision making and planning requires finer resolution approaches. As a result, leaders from Public Health Intelligence approached Madzvamuse and his team to create a consortium, known as the "Sussex Modelling Cell (SMC)", to undertake COVID-19 epidemiological modelling that is specific to the region [R5]. The work addressed questions of strategic and operational significance for local decision making throughout the pandemic.

a. Forecasting the impact of COVID-19 secondary waves within Sussex [S6-7, S10]. By manipulating the reproduction rate (R number), the model results [R5] showed that if a second wave was to happen *it could cause up to ten times the strain on hospital demand* compared to the experience that incited the first national intervention. On 20 July 2020, this was the basis of LHRP's decision to not reduce the available wards for COVID-19 patients, and for funding to be provided for a one-year postdoctoral research assistant to focus on the future of COVID-19 within Sussex [S6]. Kate Gilchrist, Head of Public Health Intelligence at Brighton & Hove City Council, said "[national modelling] was not an accurate representation of what was happening at the time, as we found out when we started using the modelling outputs the university team [R5] derived, and so without the Sussex Modelling Team we could have easily mis-calculated the necessity for wards and body storage inducing monetary and resource mismanagement" [S10].

b. Translating the reasonable worst-case scenario (RWCS) SAGE national forecast [S8, S10]. With the success of the second wave modelling, on 11 September 2020, Madzvamuse's team undertook research to aid the translation of the SAGE national RWCS document to reflect the impact in Sussex. By working with the official sensitive SAGE documents and through modelling, they *demonstrated that not only should Sussex expect the peak of hospital demand later than nationally modelled, but in fact Sussex was already experiencing less hospital demand than what was expected from the RWCS document.* On 6 October 2020, this underpinned LHRP's decision that healthcare capacity was accounted for until at least the end of January 2021 and no changes were required [S8]. Graham Evans, Head of Public Health Intelligence at East Sussex County Council, referred to the RWCS modelling and said "After reviewing the information and the presentation, Mark Angus (Director of Urgent Care System Improvement, Sussex Clinical Commissioning Group (CCG)) said 'this work has been fundamental to how we have developed our plans for our system and how we monitor our systems as part of our incident management and resilience management.'." [S10].

c. Forecasting demand and capacity for the death management cell (DMC) [S10]. Following the RWCS modelling, on 4 November 2020 the DMC, a subgroup of the Sussex Resilience Forum dealing with excessive deaths, approached the SMC to understand the demand for the potential body storage requirements over the winter period. Madzvamuse's team provided this information and on 7 December 2020 the DMC decided to renew their body storage contracts for the winter period. The forecasting for the DMC is particularly important as *they need at least a month's notice of any large changes in deaths, which would mean the ability to forecast reliably at least two months in advance*, something which is not attainable using the national modelling. Regarding the modelling of death management, Jacqueline Clay, Principal Manager, Public Health and Social Research Unit at West Sussex County Council, said "Without the University of Sussex Mathematics Team, we would have used short term monitoring of deaths by underestimating the lag between infection, illness and death; this would not have provided a sufficient time period to adjust plans. However, the [DMC] knows, ... that the research and forecasting done here was reliable, easily understandable and accessible", and "Halogen [the online tool developed by Sussex based on [R5]] gave me the ability to understand how the mathematical modelling works, something that is crucial for having the confidence that the modelling techniques work…" [S10].

d. Urgent Community Response (UCR) service within West Sussex [S9-10]. With the growing hospital demand throughout the pandemic, there was a need to understand the added burden COVID-19 was having on acute hospital care and post discharge services. The UCR service tries to minimise the burden in acute care by (i) providing potential patients with care at home or in other care establishments (like care homes) and (ii) providing extra support to discharged patients who may need it. The research provided by Madzvamuse's team projected the number of patients discharged throughout the winter period, which – in combination with the discharge pathway analysis by Phil Allman, Head of Performance, Planning and Intelligence for West Sussex at the Sussex CCG – *provided the Sussex CCG with the information to appropriately allocate resources and successfully secure an additional £1.63 million to deal with the burden of COVID-19 within West Sussex* [S9]. *In addition to the typical winter services needed, this extra grant almost doubled the amount requested last year.* Phil Allman said "Without the Sussex Mathematics Team [R5], I would have simply used the national model outputs and scaled them to fit the Sussex regional numbers. This would have been highly ineffective due to the different impact COVID-19 has had nationally in comparison to Sussex, as well as the crude approximation from the reduction in magnitude of numbers. This will not only have either majorly under- or overly-estimated the funding needed, but would have caused the wrong allocation of resources, potentially causing major issues later in the winter period" [S10].

5. Sources to corroborate the impact

[S1] National press conference for Ukrainian journalists by the Special Committee of the National Academy of Sciences of Ukraine (28 May 2020) https://www.youtube.com/watch?v=VWSRpI1-lAI (research mentioned 20m35s – 21m30s). [in Ukrainian, translated transcript of segment supplied].

[S2] Ministry of Health of Ukraine introduced a requirement for local authorities to reduce mixing of working age people by means of modifying working hours and shifting rush hours https://covid19.gov.ua/karantynni-zakhody [in Ukrainian]

[S3] Ukraine's Cabinet of Ministers' directive on delegating decisions on local lockdown measures to individual regions (22 Jun 2020): https://www.kmu.gov.ua/npas/pro-vstanovlennya-karantinu-z-metoyu-zapobigannya-poshirennyu-na-teritoriyi-ukrayini-gostroyi-respiratornoyi-hvorobi-covid-19-sprichinenoyi-koronavirusom-sars-cov-i200520-392 [in Ukrainian]

[S4] Ukraine's Cabinet of Ministers' Directive (22 July 2020) on the introduction of tiered system of epidemic monitoring from 1 Aug 2020: https://www.kmu.gov.ua/npas/pro-vstanovlennya-karantinu-ta-zapr-641 [in Ukrainian, summary from the Ministry of Health together with its English translation is supplied].

[S5] Letter of gratitude from the Special Committee of the National Academy of Sciences of Ukraine detailing the contribution of the work of Kyrychko and Blyuss to mathematical modelling of COVID-19 in Ukraine, including the specific list of anti-epidemic measures that were subsequently implemented by Ukraine's Cabinet and the National and Security Defence Council of Ukraine (26 Oct 2020) [scanned copy supplied].

[S6] Letter documenting supply of Madzvamuse and Van Yperen support to SMC (28 Jul 2020).

[S7] Halogen: Forecast the local impact of COVID-19. Toolkit developed by Madzvamuse, Van Yperen and others to forecast the impact of COVID-19 using their research in an interactive manner: https://alpha.halogen-health.org.

[S8] Action log after the RWCS presentation at the LHRP (9 Oct 2020). Action number 022 (p5) shows the decision to show the official sensitive to Madzvamuse and Van Yperen. Action number 032 (p1) shows that the decision to keep the same number of hospital wards open had been made.

[S9] UCR proposal (5 Oct 2020). Madzvamuse's and Van Yperen's modelling contribution is referenced as "the winter demand capacity modelling" in *The Requirement* section on p4.

[S10] Collection of testimonial letters from Brighton & Hove City Council, East Sussex County Council, West Sussex County Council, Sussex Clinical Commissioning Group (Jan/Feb 2021).