Response to Module 2 of the UK Covid-19 Public Inquiry Reference: M2/SAGE/01/MJK

Prof Matt Keeling OBE

Personal Data

University of Warwick

24th September 2022

1. A brief overview of your qualifications

Question 1. Overview of Qualifications

Full Name and Title: Prof. Matthew James Keeling OBE

Department: Mathematics Institute and School of Life Sciences (joint position)

Current appointment: Professor, Director of Zeeman Institute for Systems Biology and Infectious Disease Epidemiology Research, Deputy Director of MathSys CTD.

I am a Professor at the University of Warwick, and Director of the Zeeman Institute for Systems Biology and Infectious Disease Epidemiology Research. I have worked in the

field of epidemiological modelling since 1997, and have studied a large number of infectious diseases from childhood infections (such as measles) to sexually transmitted infections (such as HPV and Monkeypox) to livestock infections (such as foot-and-mouth disease). I have considerable experience in leading successful research grants, having won in excess of £11M as PI and £33M as Co-I in my career. I have written or co-authored over 200 publications, mostly in infectious disease epidemiology, with a h-index of 73 (meaning that I have 73 publications that have been cited 73 or more times). I have been the director of the Zeeman Institute since its inception in 2016, and I have played a dominant role in two successful EPSRC-funded MathSys CDT programmes. I have been closely involved with the UK response to Foot-and-Mouth (2001 & 2007) and Pandemic Influenza (2009), as well as providing model-based advice to the Dept of Health and Social Care on gender-neutral vaccination again HPV and age-targeting of the seasonal influenza vaccine.

I have been intensely involved with modelling the COVID-19 pandemic since the early stages of the outbreak: producing a string of model projections for policy and co-authoring over 30 papers on COVID-19 dynamics. My long-standing membership of SPI-M and JCVI since 2009, during both the swine-flu and the COVID pandemics is unique and has given me a strong understanding of the use of mathematical models for underpinning key public health decisions. I co-led the JUNIPER consortium (2020-2023) which brought together epidemiological modellers from across the UK to produce rapid policy advice and provide an interface with government and the wider research community.

Education/Qualifications:

Oct 1995. Ph.D. ³The EcRORg\ aQd EYROXWiRQ Rf SSaWiaO HRVW-SaUaViWe V\VWePV´. Mathematics Institute, University of Warwick, with Prof. David Rand.

June 1992. Certificate of Advanced Study in Mathematics (Part III), MMath. Dept of Applied Maths & Theoretical Physics, Cambridge University.

June 1991. First class honours degree in mathematics, BA/MA. Trinity College, Cambridge University.

1. A brief overview of your qualifications

Appointments held:

Jan 02 ± Lecturer (2002-2005), Reader (2005-2007), Professor (2007-), joint between the Mathematics Institute and the School of Life Sciences, University of Warwick

Oct 98 ± Oct 06 Royal Society University Research Fellowship. Initially held at Dept. of Zoology, Cambridge, transferred to University of Warwick

Oct 98 ± Mar 02 King¶s College Fellowship in the Spatial Extended Dynamics Group at the King¶s Research Centre, Cambridge University

Oct 95 ± Oct 98 Wellcome Trust Post-Doctoral Research Training Fellowship in Mathematical Biology. Working with Dr. Bryan Grenfell at the Department of Zoology, Cambridge University.

Peer Reviewed Journals: 205 articles, h-index 73. Selected examples:

1. Keeling, M.J., Dyson, L., Tildesley, M.J., Hill, E.M & Moore, S. (2022) Comparison of the 2021 COVID-19 roadmap projections against public health data in England. *Nature Comms.* **13** 4924.
2. Leng, T., Hill, E.M., Holmes, A., Southall, E., Thompson, R.N., Tildesley, M.J., Keeling, M.J. & Dyson L. (2022) Quantifying pupil-to-pupil SARS-CoV-2 transmission and the impact of lateral flow testing in English secondary schools. *Nature Comms.* **13**, 1106.
3. Brand, S.P.C. et al (2021) COVID-19 transmission dynamics underlying epidemic waves in Kenya. *Science* **374,** 989-994.
4. Dyson, L., Hill, E.M., Moore, S., Curran-Sebastian, J., Tildesley, M.J., Luthgoe, K.A., House, T., Pellis, L, Keeling, M.J. (2021) Possible future waves of SARS-CoV-2 infection generated by variants of concern with a range of characteristics. *Nature Comms*. **12**, 5730.
5. Tennant, W.S.D., Cardinale, E., Cêtre-Sossah, C., Moutrofi, Y., Le Godais, G., Colombi, D., Spencer, S.E.F., Tildesley, M.J., Keeling, M.J., Charafouddine, O., Colizza, V., Edmunds, W.J & Métras, R. (2021) Modelling the persistence and control of Rift Valley fever virus in a spatially heterogeneous landscape. *Nature Comms.* **12**, 5593.
6. Datta, S., Pink, J., Medley, G.F., Petrou, S., Staniszewska, S., Underwood, M., Sonnenberg, P. & Keeling, M.J. (2019) Assessing the cost-effectiveness of HPV vaccination strategies for adolescent girls and boys in the UK. *BMC Infectious Diseases* **19,** 552.
7. Hill, E.M., Petrou, S., de Lusignan, S., Yonova, I, & Keeling M.J. (2019) Seasonal influenza: Modelling approaches to capture immunity propagation. *PLoS Comp Biol.* 1007096.
8. Brooks-Pollock, E., Roberts, G.O. and Keeling, M.J. (2014) A dynamic model of bovine tuberculosis spread and control in Great Britain. *Nature* **511,** 228-231.
9. Keeling, M.J., Danon, L., Vernon, M.C., and House, T.A. (2010) Individual identity and movement networks for disease metapopulations. *Proc Natl Acad Sci USA* **107,** 8866-70.
10. Tildesley, M.J., Savill, N.J., Shaw, D.J., Deardon, R., Brooks, S.P., Woolhouse, M.E.J., Grenfell, B.T. and Keeling, M.J. 2006 Optimal reactive vaccination strategies for a foot-and mouth outbreak in the UK. *Nature* **440,** 83-86.
11. Keeling, M.J. and Rohani, P. 2008 *Modelling Infectious Diseases*, Princeton University Press.

1. A brief overview of your qualifications

Support from Current and Recent Research Grants.

Source of Funds	Title of Project	Duration (Months)	Start date	Role
UKRI	JUNIPER (Joint UNIversity Pandemic and Epidemic Research)	18	Nov-20	Joint PI
NIHR	HPRU in Genomics and Enabling Data	54	Apr-20	Co-I
NIHR	Mathematical & Economic Modelling for Vaccination and Immunisation Evaluation II	36	Oct-19	PI

BBSRC	Investigating the impact of farmer behaviour and farmer-led control of infectious disease outbreaks in livestock	36	Oct-19	Co-I
EPSRC	Mathematics for Real-World Systems II, Centre for Doctoral Training	60	Sep-19	Co-I
NIHR	Global Health Research Group on the Application of Genomics and Modelling to the Control of Virus Pathogens (GeMVi) in East Africa	36	Apr-18	Co-I
NIHR	Vaccine Efficacy Evaluation for Priority Emerging Diseases (VEEPED)	36	Apr-18	Co-I
MRC	Health Data Research UK for the Midlands	36	May-18	Theme lead
Bill & Melinda Gates Foundation	NTD Modelling Consortium: moving towards elimination	36	Apr-18	Co-I
Bill & Melinda Gates Foundation	Human African Trypanosomiasis Modelling and Economic Predictions for Policy	36	Oct-17	Co-I
Bill & Melinda Gates Foundation	Modeling the impact of vaccination strategies on the transmission of schistosomiasis in relation to MDA	12	Jun-17	PI
Bill & Melinda Gates Foundation	Projections on Eliminating Neglected Tropical Diseases (integrating mapping with modeling)	24	Feb-17	Co-I
EPSRC	Cross-scale prediction of Antimicrobial Resistance: from molecules to populations	24	Sep-15	PI
EPSRC / MRC	Mathematics for Real-World Systems Centre for Doctoral Training	60	Sep-14	Co-I
Dept of Health	Infectious Disease Dynamic Modelling in Health Protection	60	Oct-13	PI
EU anihwa ERA-NET	Prediction and Control of Vector- and Movement-Borne Livestock Epidemics	36	Oct-13	PI

PI = principle/lead investigator; Co-I = co-investigator

Questions 2 and 3. Participation in SAGE and sub-groups.

My membership and participation of UK advisory groups between January 2020 and February 2022 included:

SPI-M – I was invited to be a member of SPI-M in early 2009 and am still a member of the reformed group. I was therefore a part of SPI-M-O throughout the entire period of the pandemic and attended over 90 meetings from 27 January 2020 to 23 March 2022. Throughout, I was one of the main epidemiological modellers providing projections and a range of scientific advice and insight. I also liaised closely with the SPI-M-O chairs (Profs Medley & McLean) and the secretariat.

As part of SPI-M-O, I attended and presented findings at the weekly Medium-Term-Projection meeting later organised by UKHSA (from August 2020, although short-term forecast meetings began in April 2020) and at the weekly Spatial Heterogeneities sub-group (February 2021 to March 2022).

SAGE – I was a participant in 14 SAGE meetings (69, 70, 80, 81, 90, 92, 93, 97-103) during the pandemic. In each I was there to answer questions on specific pieces of work submitted through SPI-M-O, including the impact of Tiers and the Roadmap steps to relaxation of controls.

Vaccine Effectiveness Expert Panel – I have been a member of the VEEP panel since its foundation in June 2021; I provided input on vaccine effectiveness from both analysis and literature.

SAGE Task and Finish Groups on Impact of Interventions, Celebrations & Observances and Children – I was a member of these SAGE subgroups during 2020. For each I provided input based on multiple modelled scenarios and analysis of available date. For the Children¶s Task and Finish group I considered the consequences of pupils returning to the classroom and the likely implications for both this age-group and the wider community.

JCVI (included although not a SAGE subgroup) – I was a member of JCVI from 2009 until mid 2022, where I provided model-based advice and assessment of vaccination policy and impact. I attended over 100 meetings of the COVID-19 group, and regularly presented a range of findings and projections.

4. Summary of documents for the purpose of advising SAGE and/or its related subgroups.

Question 4. Summary of Documents.

In total, myself and the Warwick team generated around 200 documents, including presentations, publications and pieces of work for SPI-M-O, SAGE, JCVI or the DHSC. Many of these were with researchers that were part of the JUNIPER consortium. Here I summarise the main results where I was a leading author that were submitted to SPI-M-O or SAGE. These are grouped into 12 sections:

Early Dynamics. Work from February to April 2020 considering the early growth of the outbreak in the UK (often in comparison to the data from China), the role of asymptomatically infected individuals in the epidemic and the longer-term consequences of relaxing controls. **Exiting the first wave**. Documents from May to August 2020, considering how the dynamics were likely to unfold as restrictions were lifted; these included reasonable worse case scenarios and thoughts on reopening large events.

School Closures, Reopening and Dynamics. Modelling estimates and analysis from March 2020 to March 2022 showing that school attendance had only a relatively small impact on the dynamics of the epidemic, the implications of test and isolate for year groups or bubbles, and analysing the dynamics once schools reopened. This also includes work on reopening universities. **Social Bubbles**. From May 2020 this series of three documents set out the implications of social bubbles to lessen the isolation of single or dual occupancy households, or households with small children.

Precautionary Breaks. In September 2020 it was clear that additional control measures would be needed to prevent public health services being overwhelmed. This body of work suggested that a short-ŧeđm plannedŤockdo‖n ‖oẑld ha|e mođe limiŧed Ɛocial and economic conƐeqẑences but would retard the epidemic growth rate. It was followed by a set of projections for the November lockdown, followed by an analysis of the Welsh firebreak.

The Impact of Tiers. Tiers were introduced in October 2020 as a method of regionally differentiated control; this work systematically analysed the impact of Tiers 1-4 on changes to the epidemic growth rate.

Vaccination. A large number of documents that charted the early questions around the optimal deployment of vaccination, the need to slowly relax NPIs until vaccination was complete and the long-term implications of control by vaccination. This is part of a larger body of work that was presented to JCVI.

Roadmaps. Throughout 2021 six major documents were produced to project the expected dynamics as we relaxed legislation on social mixing after the January 2021 lockdown. **Variants (Alpha and Delta)**. Variants have played a major role in sustaining the pandemic, researchers in Warwick and part of the JUNIPER consortium provided key analysis of the early dynamics of Alpha (December 2020) and Delta (June 2021).

Omicron. A series of seven documents were produced during December 2021 and January 2022 developing projections of the plausible epidemic trajectory as more detailed data became available. These projections were compared to the realised data in the March 2022 document.

Other Documents. Nine other documents on a range of subjects including testing and data analysis.

Regular Activities. These documents summarise the three regular (weekly) activities that continued for much of the pandemic: estimating R and generating medium term projections; analysis of spatially resolved data to find hot-spots of infection; and an analysis of testing in school aged children and school absence data.

4. Summary of documents for the purpose of advising SAGE and/or its related subgroups.

Early Dynamics

28/02/20	Age-Structured Model Results for COVID-19 dynamics (UK-China comparison). Keeling & Hilton	SPI-M
Summary. Models of a single uncontrolled outbreak in an age-structured population. This work shows transmission from asymptomatic individuals was considered in modelling in February 2020: "there will be some transmission from asymptomatic infections (or from individuals with mild symptoms), but we would not expect this to be the equal across all individuals irrespective of symptoms"		

19/03/20	Simple Age-structured Model from Warwick, Exploring uncertainty in the unknown parameters. Keeling & Hilton	SPI-M
Summary. Extends the earlier work on age-structure and asymptomatic transmission to consider the likely dynamics in terms of distributions of infection and disease across age-groups. Sets the fundamental modelling framework used throughout the pandemic. This work was later discussed ;ϬϬϬϮϬϬJ ‖hen ‖e ƐƵbmiŧŧed a moɗe deŧailed deƐcɗipŧion of oƵɗ aƐƐƵmpŧionƐ̀ Symptomatic / Asymptomatic incidence and Assumptions in the Warwick Model This was an early version of work published as: Hilton, J., and Keeling, M. J. (2020). Estimation of country-level basic reproductive ratios for novel Coronavirus (COVID-19) using synthetic contact matrices. *PLoS Comp. Biol.* **16**(7): e1008031. https://doi.org/10.1371/journal.pcbi.1008031		

22/03/20	Short- and Long-Term predictions from the Warwick age-structured model for COVID-19. An assessment of social-distancing on cases, hospitalisations and deaths. Keeling	SPI-M SAGE 19
Summary. First look at long-term dynamics with different levels of control. Work suggests an uncontrolled peak of 20,000 hospitalisation and 4500 deaths per day, if there was no change in behaviour or no measures were introduced. In broad qualitative agreement with Imperial Report 9 from 16/03/2020. Updated on 23/03/2020 to include the impact of short duration (6-week) control measures. This was an early version of work published as: Keeling, M. J., Hill, E., Gorsich, E., Penman, B., Guyver-Fletcher, G., Holmes, A., McKimm, H., Tamborrino, M, Dyson, L., and Tildesley, M. (2020). Predictions of COVID-19 dynamics in the UK: short-term forecasting and analysis of potential exit strategies. *PLoS Comp. Biol.* **17**(1): e1008619. https://doi.org/10.1371/journal.pcbi.1008619		

30/03/20	Warwick predictions considering controls from 13th April. Keeling	SPI-M
Summary. Using the Warwick ODE-based model, partitioned into the 7 English regions. The work looked at possible dynamics due to a relaxation of control policies on 13th April, projecting that a rapid lifting of restrictions could lead to a large rebound in the number of cases, hospital admissions and deaths.		

27/04/20	Assessment of Changes to Lock-Down and Other Controls. Keeling, Tildesley, Dyson, Hill, Gorsich, Penman Tamborrina, Hutton, McKimm, Leng, Guyver-Fletcher, Holmes.	SPI-M SAGE 29
Summary. This work examined (i) targetting lockdown at the elderly, (ii) controls that were responsive to local ICU burden, and (iii) the impact of waning compliance in the population. We state: "Of the strategies investigated here, very few do not lead to a sizeable second or third wave" and "If we knew when a vaccine would be available, this would completely change the perspective on many of these calculations, as one option becomes containing the infection until mass immunisation is possible." **SAGE link**: https://www.gov.uk/government/publications/university-of-warwick-assessment-of changes-to-lockdown-and-other-controls-26-april-2020		

4. Summary of documents for the purpose of advising SAGE and/or its related subgroups.

Exiting the first wave.

04/05/20	Simulations of Potential Exit Strategies. Keeling, Tildesley, Dyson, Hill, Gorsich, Penman Tamborrina, Hutton, McKimm, Leng, Guyver-Fletcher, Holmes	SPI-M SAGE 33
Summary. This work examined the relaxation of the first lockdown over four phases (from 11th May to 15th August). It assumed that some measures would remain in place and that high levels of contact tracing would be in operation. We also considered sensitivity to compliance, looking at compliance declining over time. We stated that In general the proposal of gradually opening schools, workplaces and leisure activities, together with contact tracing limits the chance of a second wave"; however, we caveat this by noting that with poor tracing we projected a notable epidemic peak in Nov/Dec 2020. **SAGE link**: https://www.gov.uk/government/publications/university-of-warwick-simulations-of potential-exit-strategies-3-may-2020		

13/05/20	Reasonable Worse Case Scenarios. Keeling, Dyson, Hill, Tildesley & the Warwick Team.	SPI-M SAGE 38
Summary. Performed a set of scenarios in which (i) *R* increases for a short period before settling to *R*=1 - this generates an increase in cases, which is then maintained until herd immunity is reached; and (ii) *R* is increased for a period, it then is reduced to 0.7 before settling at 1 - this generates a spike in cases before plateauing at a low level. These were used as part of SPI-M-O: COVID-19 short-term forecasts to SAGE 38.		

28/07/20	Warwick Reasonable Worst Case (RWC) Narrative. Keeling, Hill, Tildesley, Dyson & the Warwick Team	SPI-M

Summary. This document discussed five RWC (reasonable worse case) scenarios for the immediate future: importations from tourists returning to UK; increase in *R* in the approach to winter; increased mixing over Christmas & New Year (particularly the movement of students); general apathy towards control measures; lack of protection against infection by the vaccine and reduced efficacy in the elderly.

17/08/20 26/08/20 01/09/20	Intermediate Predictions: Best Guesses at the Dynamics for the Next 2 Months. Keeling	SPI-M SAGE 56
Summary. We conclude that the relaxations that have occurred in recent months (June-August 2020) have eroded any spare capacity required for the opening of schools. In addition, the parameter inference does not explicitly include any impact of the recent relaxation of mass gatherings. Even under our assumptions, where we generally see school pupils playing a relatively minor role, new measures will be necessary to allow schools to reopen without pushing *R* above 1, and therefore we expect a rise in cases. A SPI-M-O summary of this information was presented at SAGE 56.		

4. Summary of documents for the purpose of advising SAGE and/or its related subgroups.

19/08/20	QƵeƐtionƐ onTadgeđ e|enŧƐ and |enƵeƐ. Keeling	SPI-M SAGE 52
Summary. General thoughts on the return of large events. Feeds into the 19/08/2020 SPI-M-O statement on gatherings: https://www.gov.uk/government/publications/spi-m-o-consensus statement-on-events-and-gatherings-19-august-2020/spi-m-o-consensus-statement-on-events and-gatherings-19-august-2020		

School Closures, Reopening and Dynamics

16/03/20	Impact of School Closures. Keeling	SPI-M SAGE 17
Summary. Early work looking at the impact of school closure. We estimate that this could reduce the level of cases from children by ~60%, but would only cause a ~5% drop in ICU admissions across the population. **SAGE link**: https://www.gov.uk/government/publications/impact-of-school-closures-18-march 2020		

29/04/20	Impact of Changes to School Attendance. Keeling	SPI-M SAGE 31

Summary. This paper finds that reopening schools generally leads to a small increase (<10%) in the total number of cases and deaths. In general, we find that the impact of opening schools is a lot less than any changes to the population-wide policy of lockdowns. Keeping class sizes to a minimum (where practical) reduces the impact of re-opening schools still further. We note that reopening secondary schools is likely to have a greater impact than reopening primary schools. We state that models are insufficiently detailed to differentiate between many of the potential options based on the epidemiological, social / educational needs will probably drive the decision. This work was passed to the Children's Task and Finish group.

This was an early version of work published as: Keeling, M. J., Tildesley, M. J., Atkins, B. D., Penman, B., Southall, E., Guyver-Fletcher, G., Holmes, A., McKimm, H., Gorsich, E., Hill, E. M., and Dyson, L. (2021). The impact of school reopening on the spread of COVID-19 in England. *Phil. Trans. R. Soc. B*. **376** (1829): 20200261. https://doi.org/10.1098/rstb.2020.0261

SAGE link: https://www.gov.uk/government/publications/university-of-warwick-impact-of changes-to-school-attendance-28-april-2020

17/05/20	Thoughts on School Closures and Workplaces. Keeling	SPI-M
Summary. Following the strict track-and-trace rules, any school class with an identified case needs to close with the children being quarantined. We address two key questions: (i) What are the implications of closing for any suspected case? (ii) What are the implications for closing only for test-positive cases. It is noted that with the first-wave parameters, it is impossible to generate large-scale symptomatic outbreaks in a class-room setting."		

4. Summary of documents for the purpose of advising SAGE and/or its related subgroups.

07/07/20	Thoughts on School Closures Assessing False Positives. Keeling & the Warwick Team	SPI-M
Summary. A major issue with closing for suspected cases is the potential for false positives ' closing classes because of illness that is not COVID-19. Here we examine this problem for schools of different sizes and for mean levels of childhood illness; we conclude that "even if there is no transmission within schools, we expect large schools to commonly reach the threshold of 2 or more cases in 14 days"		

08/08/20	Predicted Primary & Secondary School Absences. Keeling	SPI-M
Summary. Here we use Pillar 2 positives over the last 2 weeks to simulate the expected number of children testing positive in the primary and secondary school age-groups. If we assume that each of these positives generates a 14-daLJ quarantining of their associated school bubble then we can derive primary and secondary absences due to quarantining.		

17/12/20	Report on COVID-19 in schools in England, September - December 2020. Southall, Holmes, Atkins, Dyson, Hill, Keeling & Tildesley	SPI-M SAGE 74

Summary. Paɗt of ŧhe Childɗeɲɛ Taɛk and Finiɛh pɗeɛenŧaŧion ŧo SAGE, analysing school data from September to December 2020. Three main conclusions are drawn: (i) infection is higher in secondary compared to primary schools, although this does not apply to teachers; (ii) community restrictions in the North seem to be suppressing school cases compared to London and East of England; (iii) cases in pupils increased during the first two weeks of the November lockdown although declined in many areas later in the lockdown, in contrast cases in teachers declined in most areas throughout the lockdown. **SAGE link:** https://www.gov.uk/government/publications/tfc-children-and-transmission-update paper-17-december-2020

13/01/21	COVID-19 and Universities: Report from the Higher Education working group at the Isaac Newton Institute. Higher Education working group at the Isaac Newton Institute (including Keeling)	SPI-M SAGE 76
Summary. Work considering the implications of reopening Universities include staggered starts, asymptomatic testing, risk in student halls and transmission to and from the community. Reductions in adherence to NPIs (including case and household isolation) will have more impact than any marginal benefits generated from a staggered return of students to university. The emergence of more transmissible new variants results in impaired effectiveness of mass asymptomatic testing. We observe evidence of spillover transmission between higher education and the wider community in some, but not all, settings. **SAGE link**: https://www.gov.uk/government/publications/isaac-newton-institute-covid-19-and universities-13-january-2021		

4. Summary of documents for the purpose of advising SAGE and/or its related subgroups.

03/03/21	The impact of uptake and adherence on transmission and absences resulting from secondary school reopening strategies involving rapid testing. Leng, Hill, Thompson, Tildesley, Keeling & Dyson	SPI-M SAGE 83
Summary. This document assesses the impact on transmission and absences resulting from school reopening strategies using lateral flow device tests (LFTs), and quantifies the impact of uptake (pupils agreeing to participate in rapid testing), adherence (participating pupils actually taking tests at home), close contact group size, and transmission on within-school test days. We note that mass testing, with isolation or serial contact testing, can result in high levels of absences ' as more infections are detected. There is therefore a trade-off between minimising infection (which required high levels of testing coupled with isolation) and minimising school absence (which occurs when testing is limited and few infections are detected. **SAGE link**: https://www.gov.uk/government/publications/university-of-warwick-impact-of uptake-and-adherence-on-transmission-and-absences-resulting-from-secondary-school reopening-strategies-involving-rapi		

Social Bubbles.

06/05/20	Potential Impact of Bubbles. Keeling & Leng	SPI-M
11/05/20	Short up-date on Modelling Bubbles. Flasche, Leng & Keeling	SPI-M

13/05/20	The effectiveness of extended social bubbles as a soft exit strategy from the COVID-19 lockdown. Leng, Keeling, Flasche	SPI-M SAGE 36

Summary. Thi Ɛ bodLJ of ‖oɗk edžamineƐ allo‖ing additional Ɛocial conɬacɬƐ ɬhɑ̄oƵgh ƀƵbbleƐ̇ We note that clustering of additional contacts within a social bubble is a highly effective means of controlling the increase in *R* while allowing more contacts. Allowing all households to expand their social bubble may increase *R* above 1. However, some targeted approaches only generate a marginally increase in *R*, these include: Paring of single or dual occupancy households; pairing of households with primary school age children. Young children are at least risk and likely to benefit most from allowing close contact with peers because of their ineffective communication digitally or with a 2m distance.

This was an early version of work published as: Leng, T., White, C., Hilton, J., Kucharski, A., Pellis, L., Stage, H., Davies, N., CMMID-Covid-19 WG, Keeling, M.J., Flasche, S. (2021) The effectiveness of social bubbles as part of a Covid-19 lockdown exit strategy, a modelling study. *Wellcome Open Res* **5**:213. https://doi.org/10.1268/wellcomeopenres.16164.2
SAGE link: https://www.gov.uk/government/publications/university-of-warwick-and-lshtm-the effectiveness-of-extended-social-bubbles-as-a-soft-exit-strategy-from-the-covid-19-lockdown-13- may-2020

4. Summary of documents for the purpose of advising SAGE and/or its related subgroups.

Precautionary Breaks

20/09/20	Circuit Breakers Ready Reckoners: Implementing (partial) Lockdown for 2 weeks over Half-Term. Keeling	SPI-M SAGE 57
29/09/20	Circuit Breaker / 2-week intensive control. Keeling	SPI-M SAGE 59
14/10/20	Precautionary Breaks Press Statement. Keeling & Tildesley	SPI-M
31/10/20	Preliminary Look at November Lockdown. Keeling	SPI-M
04/11/20	No Evidence of Decline in Welsh Pillar 2 data	SPI-M
10/11/20	Evidence of Sharp Decline in Welsh Pillar 2 Data	SPI-M

Summary. Circuit breakers or short-term imposition of stronger measures were investigated in a series of documents and a publication. Using simple analysis and full models matched to the pandemic, we show how these breakers lead to a decline in cases and hence a temporary respite from a growing wave of cases. (Figure shows the number of new cases reported in Wales in late 2020, dashed lines show the trend in exponential growth or decay, the impact of the Welsh firebreak, ‖hich occƶđɛ afŧeđ a ‖eeḳɛ đepoɗŧing delaL̨ is clear).

In addition, the pressure on the health-service is due to high peaks in demand, such peaks can be prevented by lockdown-type control measures - although this comes at the cost of spreading the burden over a longer period, but this prevents the health services being overwhelmed. As shown in this work circuit breakers buy time, and in an epidemic time is valuable - it allows the development of novel treatments and vaccines.

Note, we state on 14/10/20 that: "While such precautionary breaks are potentially powerful tools, three important questions remain: (1) Does a pre-planned short duration break have a less harmful impact on the economy and society? (2) Will the general public support, and abide by, another period of tighter controls? (3) What action will be taken after the break to ensure that we do not return to the same situation?"

This work was later published as: Keeling, M.J., Guyver-Fletcher, G, Holmes, A., Dyson, L., Tildesley, M.J., Hill, E.M. and Medley, G.F. (2021) Precautionary breaks: Planned, limited duration circuit breaks to control the prevalence of SARS-CoV-2 and the burden of COVID-19 disease. *Epidemics* https://doi.org/10.1016/j.epidem.2021.100526

SAGE links: https://www.gov.uk/government/publications/university-of-warwick-circuit-breakers implementing-partial-lockdown-for-2-weeks-over-half-term-14-september-2020 and https://www.gov.uk/government/publications/circuit-breakers-implementing-partial-lockdown for-2-weeks-over-half-term-24-september-2020

4. Summary of documents for the purpose of advising SAGE and/or its related subgroups.

The Impact of Tiers

03/11/20	Evidence of the Impact of Tiers on Pillar 2 dynamics. Keeling	SPI-M SAGE 67
18/11/20	Evidence of the Impact of Tiers on Pillar 2 dynamics. Keeling	
19/11/20	Evidence of the Impact of Tiers on Pillar 2 dynamics. Keeling	
19/11/20	Evidence of the Impact of Tiers on Pillar 2 dynamics. Keeling & McLean	SPI-M SAGE 69
24/11/20	Evidence of the Impact of Tiers on Pillar 2 dynamics. Keeling	
26/11/20	Updated evidence of the impact of tiers. Keeling & McLean	SPI-M SAGE 70

Summary. Tiers were introduced on 12th October 2020, and placed different regions of England under different mitigation measures (Tiers 1-4). Using relatively similar statistical analysis, we compared the growth rate in LTLAs (lower tier local authorities) before and after the imposition of different levels of Tiers. This body of work addressed three questions: What interventions were made, where and when? How fast did epidemics shrink or grow before and after those interventions? And what can we learn from ŧhiɛ aƶŧƶmṅɛ effoɖŧɛ ŧo conŧɖol ŧhe ɛpɖead of COVID 19 in the UK?

We show that only the highest levels of Tiers (shown in red in the figure) have a substantial impact on the growth rate in a region. Comparable analysis of controls in the devolved nations is also included.

SAGE links: https://www.gov.uk/government/publications/impact-of-interventions-tfg-the-uks-4- nations-autumn-interventions-19-november-2020 and https://www.gov.uk/government/publications/impact-of-interventions-tfg-the-uks-4-nations autumn-interventions-update-26-november-2020

4. Summary of documents for the purpose of advising SAGE and/or its related subgroups.

Vaccination

07/11/20	Optimisation of Rapidly Delivered Vaccine. Moore & Keeling	SPI-M
03/12/20	COVID vaccine deployment scenarios. Moore, Hill, Tildesley, Dyson, Keeling	SPI-M SAGE 72
17/01/21	COVID vaccine impact forecast	SPI-M
21/01/21	COVID vaccine impact forecast	SPI-M SAGE 76
31/01/21	Relaxation of NPI as vaccination proceeds	SPI-M
03/02/21	Relaxation of NPI as vaccination proceeds	SPI-M SAGE 79
09/03/21	Comparison of realised strategy vs second dose prioritisation	SPI-M
11/10/21	Speculations on the long-term dynamics of COVID-19: 2022 and beyond	SPI-M

Summary. Although much of my work on vaccination went to JCVI, it is impossible to consider projection of the epidemic without taking account of the action of vaccination. The earliest work looked at the potential for vaccination to reduce R, this was performed with very limited data on the behaviour of vaccines and we conclude that the vaccine will have the greatest impact when targeted to the elderly and vulnerable ' it is better to give protection to those most likely to experience severe illness, rather than those most responsible for transmission. This work was later published as: Moore, S., Hill, E.M., Dyson, L., Tildesley, M., Keeling, M.J. (2021) Modelling optimal vaccination strategy for SARS-CoV-2 in the UK. *PLoS Comp. Biol.* **17**(5): e1008849. https://doi.org/10.1371/journal.pcbi.1008849

The next series of papers looked in more detail at the timing of vaccination and whether this allowed the rapid relaxation of non-pharmaceutical interventions. This work was repeated as we needed to account for both the emergence of the Alpha variant and changing data on vaccination efficacLJ We conclƶde ŧhaŦ A high efficacy vaccine that provides a high level of transmission blocking offers a means of eventually relaxing controls without suffering a large subsequent wave of hospitalisations and deaths ho‖e|eđ ‖e noŧe ŧhaŧ đeladžaŧion of conŧđolɛ haɛ ŧo be ɛlo‖ ŧo avoid a rapid spike in cases and severe disease. This work was later published as: Moore, S., Hill, E.M., Tildesley, M., Dyson, L., Keeling, M.J. (2021) Vaccination and non-pharmaceutical interventions for COVID-19: a mathematical modelling study. *Lancet Infectious Diseases.* **21**(6): 793-802. https://doi.org/10.1016/S1473-3099(21)00143-2

More recent work looks at the long-term dynamics under different annual vaccination strategies. We conclƶde Our projections suggest that an effective booster campaign (in the over 50s) could generate manageable waves in 2022 before a long decline. However, weaker boosters that wane
quickly can lead to large outbreaks in 2022. In the long-term, regular (annual) boosting of over 50s appears to be a necessary strategy if hospital admissions and deaths are to remain within manageable limits.

SAGE Links: https://www.gov.uk/government/publications/spi-m-o-insights-from-early vaccination-modelling-9-december-2020
https://www.gov.uk/government/publications/university-of-warwick-covid-19-vaccine-impact forecast-13-january-2021
https://www.gov.uk/government/publications/university-of-warwick-relaxation-of-npis-as vaccination-proceeds-4-february-2021

4. Summary of documents for the purpose of advising SAGE and/or its related subgroups.

RoadMaps

06/02/21	Roadmaps for Relaxation of NPIs. Moore & Keeling	SPI-M SAGE 80/81
29/03/21	Road Map Scenarios & Sensitivity. Keeling, Moore, Dyson, Tildesley & Hill	SPI-M SAGE 85
04/05/21	Road Map Scenarios and Sensitivity: Steps 3 and 4. Keeling, Dyson, Hill, Moore & Tildesley.	SPI-M SAGE 88

08/06/21	Road Map Scenarios and Sensitivity: Step 4. Keeling, Dyson, Hill, Moore & Tildesley.	SPI-M SAGE 92/93
06/07/21	Road Map Scenarios and Sensitivity: Step 4. Keeling, Dyson, Hill, Moore & Tildesley.	SPI-M SAGE
12/10/21	Projections of SARS-CoV-2 transmission and COVID-19 disease until June 2022. Keeling, Dyson, Hill, Moore & Tildesley.	SPI-M SAGE 96

Summary. Throughout 2021, there were a series of Roadmap documents that looked at the potential for relaxation of controls from the January lockdown to an absence of restrictions. Each of the above documents only refers to the final version of each of the six Roadmaps, whereas each document was the result of an iterated process, sharing preliminary results with the SPI-M-O group and SAGE before producing the final set of results.
The initial document helped provide the forward projections enabling the selection of the time frame over which relaxation would occur. The next four documents were produced before each Step in the relaxation process and generally provided confidence to the government that none of the step-changes would overwhelm health-care resources. The initial Step 4 document on 08/06/21 demonstrated the uncertainty in Step 4, due to the recent invasion of the Delta variant into the UK, and concerns that there may have been limited vaccine protection. The final document on 12/10/21, considered the longer-term dynamics. Each of the documents shows increasing complexity and a deeper understanding of the roles of vaccination and human behaviour.
A scientific summary document and retrospective examination of the Roadmap projections (including a comparison to subsequent data) is now published: Keeling, M.J., Dyson, L., Tildesley, M.J. Hill, E.M. & Moore, S. (2022) Comparison of the 2021 COVID-19 roadmap projections against public health data in England. *Nature Communications* **13**: 4924. https://doi.org/10.1038/s41467- 022-31991-0

SAGE links: https://www.gov.uk/government/publications/university-of-warwick-relaxation-of npis-as-vaccination-proceeds-4-february-2021
https://www.gov.uk/government/publications/university-of-warwick-roadmaps-for-relaxation-of npis-6-february-2021
https://www.gov.uk/government/publications/university-of-warwick-roadmaps-for-relaxation-of npis-18-february-2021
https://www.gov.uk/government/publications/university-of-warwick-road-map-scenarios-and sensitivity-29-march-2021
https://www.gov.uk/government/publications/university-of-warwick-roadmap-scenarios-and sensitivity-steps-3-and-4-5-may-2021
https://www.gov.uk/government/publications/university-of-warwick-road-map-scenarios-and sensitivity-step-4-9-june-2021
https://www.gov.uk/government/publications/university-of-warwick-roadmap-scenarios-and sensitivity-step-4-6-july-2021
https://www.gov.uk/government/publications/university-of-warwick-projections-of-sars-cov-2- transmission-and-covid-19-disease-until-june-2022-the-action-of-waning-efficacy-and-boosters 12-oc

4. Summary of documents for the purpose of advising SAGE and/or its related subgroups.

Variants

22/12/20	Juniper on new variant to SPI-M 22nd Dec 2020. JUNIPER consortium (including Keeling)	SPI-M SAGE 74
Summary. Statistical investigation of the Alpha variant (B.1.1.7), as identified by S-gene target failure. This work showed substantial growth advantage of the new variant and the clear spread from the South East. It also considered the distribution within age-groups and the dynamics without households and hospitals. Consideration was given to a different generation time for Alpha compared to Wildtype, which although not relevant here improved our understanding of the Omicron wave. **SAGE link**: https://www.gov.uk/government/publications/juniper-consortium-notes-on-the-new sars-cov-2-variant-22-december-2020		

02/06/21	Estimating the Transmission Advantage for B.1.617.2. Keeling	SPI-M SAGE 91
02/06/21	Comparing temporal trends in the demographics of S+ and S- COVID cases. Overton, Gog, Keeling, Brooks-Pollock, Pellis, Danon & the JUNIPER consortium	SPI-M SAGE 91
Summary. These two papers consider the rise of B.1.617.2 (Delta) variant from the early data on S-gene detection (using the TaqPath system Alpha is S-gene negative, while Delta is S-gene po£i†i|eJ The fi∂£† pape∂ conclƶde£ †ha† We estimate that the B.1.617.2 variant has a 42% (CI 13-57%) transmission advantage over the B.1.1.7 variant, although ignoring the anomalous results for the North East and Yorkshire our estimate rises to 45% (CI 33-57%). The £econd docƵmen† dig£ deepe∂ in†o †he di£†∂ibƵ†ion of Del†a ca£e£ no†ing †ha† some regions (Bolton, Leicester, Birmingham, Blackburn, and Manchester), S+ [Delta] cases have disproportionately affected individuals with an Asian ethnicity since early April. **SAGE links**: https://www.gov.uk/government/publications/university-of-warwick-estimating-the transmission-advantage-for-delta-variant-b16172-3-june-2021 https://www.gov.uk/government/publications/juniper-comparing-temporal-trends-in-the demographics-of-s-and-s-covid-cases-3-june-2021		

Omicron

06/12/21	Early Omicron Results	SPI-M
08/12/21	Early Omicron Results	SPI-M SAGE 99
Summary. The first in a series of documents that provided early model-based projections of the Omicron wave. Here we examined the impact of differential transmission (80-150% of Delta), vaccine efficacy (50%-100% compared to Delta), and different protection from prior infection. We assumed that some control would be achieved through a booster vaccination programme to over 18s or over 40s, but concluded "There is definitely the clear potential for overwhelming public health problems". The second document highlighted scenarios that most closely match the extremely high early growth in the UK. **SAGE link**: https://www.gov.uk/government/publications/university-of-warwick-early-omicron results-13-december-2021		

4. Summary of documents for the purpose of advising SAGE and/or its related subgroups.

14/12/21	Early Omicron Results. Keeling, Guzman-Rincon, Tildesley & Dyson	SPI-M
Summary. This document attempted to match the relative growth rate of Omicron compared to Delta of 0.3-0.4 per day. It included early data on vaccine efficacy (lower than against Delta and rapidly waning) and considered the lower Omicron severity and the impact of 'NPIs' (or behaviour change). We stated that "Estimation of both hospital admissions and deaths are confounded by unknown severity of Omicron and unknown VE (second-dose and boosters) against severe disease. We have explored a range of Severities, from as severe as Delta to just 10%."		

23/12/21	Warwick Omicron Modelling. Dyson and Keeling	SPI-M SAGE 101
Summary. This work looked at the differential impact of continuing with Plan-B or different levels of imposed NPI. It is noted that: "It remains beyond the scope of current models to predict behaviour change in response to the unfolding situation. It is highly likely that there has already been a degree of behaviour change due to concerns about Omicron that are not yet reflected in the epidemiological data; as infection levels continue to build the amount of precautionary behaviour change is likely to increase irrespective of any imposed controls. From this perspective, the Plan B only scenario is likely to be an overestimate of the epidemiological consequences due to self-limiting behaviour." **SAGE link**: https://www.gov.uk/government/publications/university-of-warwick-omicron modelling-22-december-2021		

30/12/21	Short-term Projections based on Early Omicron Variant Dynamics in England. Keeling, Brooks-Pollock, Challen, Danon, Dyson, Gog, Guzman Rincon, Hill, Pellis, Read, Tildesley	SPI-M SAGE 101
Summary. A comprehensive look at the UK Omicron data to that point and projections of likely scenarios (Plan B and shorter tighter NPI controls). The work was available online as: Keeling, Brooks-Pollock, Challen, Danon, Dyson, Gog, Guzman Rincon, Hill, Pellis, Read, Tildesley (2021) Short-term Projections based on Early Omicron Variant Dynamics in England *medRxiv* https://www.medrxiv.org/content/10.1101/2021.12.30.21268307v1 **SAGE link**: https://www.gov.uk/government/publications/university-of-warwick-short-term projections-based-on-early-omicron-variant-dynamics-in-england-23-december-2021		

06/01/22	Warwick Omicron Modelling. Keeling & Dyson	SPI-M SAGE 102

Summary. A comparison of Omicorn projections to early data from the wave. This document considered a shorter generation time as well as lower severity of Omicron compared to Delta. Here we comment that: "We have assumed that there will only be a small change in the behaviour of older adults from the current estimated value to Step2-like behaviour ' given concerns in this age-group the change could potentially be larger." **SAGE link**: https://www.gov.uk/government/publications/university-of-warwick-omicron modelling-6-january-2022

4. Summary of documents for the purpose of advising SAGE and/or its related subgroups.

13/01/22	Long Term Dynamics of COVID-19: Infection and Hospital Admissions. Keeling, Hill, Tildesley & Dyson	SPI-M
Summary. There remains considerable uncertainty over the likely dynamics for the next 6-12 months even without the invasion of any novel variants. Here we have highlighted three sources of uncertainty: the degree to which depletion of susceptibles or behaviour change lead to the reduction in Omicron cases; the time-scale over which behaviour returns to pre-COVID normality; the level of vaccine protection and the time over which this eventually wanes.		

14/03/22	Comparison of Omicron Parameters. Keeling & Dyson	SPI-M
Summary. In a retrospective analysis on the Omicron modelling (see figure from 13th December, with the more recent data over-laid). We conclude: "One surprising aspect of the Omicron wave, which substantially limited the scale and severity of the wave, was the public reaction during December and early January ' with far more testing and far less mixing than had occurred in November. As such early models (from 13th December) that assumed a high level of NPIs are in the closest agreement with the observed number of hospital admissions ' although we had assumed that behaviour change would come from imposed restrictions rather than voluntary action."		

Regular Now-Casting, Medium Term Projections and Spatial Analysis

24/04/20	Preliminary Exceedance Methods. Keeling	SPI-M
11/09/20	Local-scale COVID-19 dynamics in the UK. Keeling	SPI-M
15/09/20	Statistical Estimation of Growth Rate from Pillar 1 and Pillar 2 Data. Keeling	SPI-M
05/03/21	Spatial Variation from Warwick. Guzmán-Rincón & Keeling	SPI-M

Summary. The 24/04/20 document was the first in a long series of spatial exceedance models. Our novel method allowed identification of LTLAs (Lower Tier Local Authorities) that did not conform to the national pattern. In this earliest version of the work "we identify the following high-risk regions: Leicester, Bradford, Kirklees, Barnsley, Rochdale, Oldham, Sheffield, Bolton, Pendle, Rotherham", which were later recognised hot-spots of infection.
This work was updated on a weekly basis and was a part of the long-running SPI-M spatial heterogeneity subgroup. It was adopted by Public Health Scotland, and formed a regular part of their assessment of the epidemic in Scotland from mid-2020.
Later work from 05/03/21 used more robust Gaussian Process methods for the estimation of local growth rates and detection of anomalous behaviour.

This later work is available as a pre-print: Guzmán-Rincón, Hill, Dyson, Tildesley & Keeling (2022) Bayesian Estimation of real-time Epidemic GrowthRates using Gaussian Processes: local dynamics of SARS-CoV-2 in England. *medRxiv*
https://www.medrxiv.org/content/10.1101/2022.01.01.21268131v2

4. Summary of documents for the purpose of advising SAGE and/or its related subgroups.

24/04/20	Now-casting documents. Keeling	SPI-M
02/09/20	Medium term predictions. Dyson & Keeling	SPI-M SAGE
Summary. First in a long series of now-casting and medium term (6-week) projections. Taking the epidemiological observations, re-estimating model parameters and then projecting the dynamics forward over relatively short time scales (assuming no further changes in behaviour or policy). Other estimates were continually produced during 2020, 2021 and early 2022.		

23/09/21	Maps of Pillar 2 cases in school age-groups. Keeling & Tildesley	SPI-M
Summary. This document examined the rapid rise in school cases from September 2021. This work was extended to examine the different age-structured signals that came from LFT and PCR testing, and later included a deep analysis of school absence data. The analysis continued weekly and was presented regularly to SPI-M-O into early 2022.		

Other Documents

20/08/20	Some Preliminary Thoughts on Pillar 2 swabbing. Keeling	SPI-M
Summary. There is likely a complex feedback between true levels of infection, perceived risk and amount of testing, which obscures the true patterns ' better data on the reason for testing would resolve this. Testing is predominantly focused in the 20-34 age group, which is ideal for detecting cases but is unlikely to be directly correlated with more severe outcomes. Using percentage positive (rather numbers per 100,000 of population) may help to highlight new problem areas where relatively high levels of cases are found with little testing effort.		

13/10/20	Thoughts on Test-and-Trace Targeting. Keeling	SPI-M
Summary. Despite the fact that Test-and-Trace is a control method, if it is to be locally targeted the first priority has to be obtaining a reliable assessment of the state of infection across the UK. Without this targeting is impossible. Potentially the best that can be achieved is a moderate testing capacity in all regions of the country, with additional capacity at regions identified by high growth rates and high proportions of positive tests.		

04/11/20	Christmas Forecasts. Keeling	SPI-M
Summary. This document looked at the potential impact of additional mixing over Christmas 2020; considering that there could have been greater mixing between generations while at the same time less mixing within work-places. This has the potential to shift the age-distribution of infection.		

28/08/21	Multiple Ways of Looking at Pillar 2 Data. Keeling	SPI-M
Summary. We Ɛƚill doṅƚ ƶndeƌƐƚand ǁhLJ people geƚ Pillaƌ Ϯ ƚeƐƚeḋ Whaƚ dƌi|eƐ ƚhe negaƚi|e Pillaƌ 2 tests? Looking at proportions helps to remove biased due to testing behaviour, but may introduce other biases if the relationship between symptoms and testing changes. Since mid-July we have seen a decrease in testing, but an increase in proportions testing positive in the younger (<20s) age groups.		

07/09/21	Examination of the increase in reported positive cases during the EUROS. Keeling	SPI-M
Summary. A spatial and temporal examination of the increase in Pillar 2 (community) cases that occurred during the EUROs football tournament (cases being reported either 1-28 July 2021 or 10- 20 July 2021). Some Lower Tier Local Authorities experienced up to 100% increase in cases during this period, although the average was closer to 40-50% increase.		

13/10/21	Control Options for Mitigating a Rapid Rise in Infections. Keeling, Read, Hill, House, Dyson, Tildesley, Challen	SPI-M SAGE 96
Summary. Here we consider three potential causes of a steep rise in infections, hospital admissions and deaths, and the merits of seven control options that could be enacted to control the rise (improved ventilation, improved public awareness, booster and greater vaccine uptake, test-trace-and-isolate, legal changes to restrictions, antivirals / pharmaceuticals, and travel restrictions). We conclude that a doubling of cases every week (or two weeks) would demand a dramatic change in precautionary behaviour, either voluntarily or enforced, to bring infection under control. **SAGE link**: https://www.gov.uk/government/publications/juniper-control-options-for-mitigating a-rapid-rise-in-infection-12-october-2021		

13/01/22	Toy model of Precautionary Behaviour. Keeling	SPI-M
Summary. One curiosity of the Delta wave has been the long period with near-constant infection levels. A possible explanation for this is the interaction between precautionary behaviour (risk avoidance, mask-wearing, testing) and infection levels. Here we explore this interaction and show that it can generate a relatively high plateau of infection.		

15/02/22	Long Term Dynamics of COVID-19: Infection and Hospital Admissions. Keeling, Hill, Tildesley & Dyson	SPI-M
Summary. This document considered the long-term dynamics out to 100 years looking at the impact of waning immunity and repeat infections on the pattern of infection and hospital admissions. A key outcome of this analysis is that it may take several years before COVID-19 attains a regular cycle.		

16/02/22	Cost Effectiveness of Testing. Keeling	SPI-M
Summary. In this brief note we consider the economic impact of an imminent change of control policy - assumed to be the suspension of LFD testing - through very simple analysis. It illustrates the key point that a change in policy that precipitates a slowing of the epidemic decline may be a false economy.		

5. A summary of any articles you have written, interviews and/or evidence you have given.

Question 5. Articles, Interviews and Evidence

Here I outline 28 major publications on COVID-19 that I have led (or played a main role in formulating), providing a link to each, the date it was first published online and the date it was published by the journal; a list of other publications is also provided. I also provide information on interviews with the media ' primarily the Millennium Maths Plus magazine (which ran explanatory pieces on our work) and through the Science Media Centre ' and evidence given to multiple national and international organisations.

Publications

First online: 17/02/2020	Keeling, M.J., Hollingsworth, T.D. & Read, J.M. (2020) "The Efficacy of Contact Tracing for the Containment of the 2019 Novel Coronavirus (COVID-19)" *J. Epidemiology & Community Health* **74** (10). http://dx.doi.org/10.1136/jech-2020-214051
Published: 23/06/2020	

Summary: Contact tracing together with testing is viewed as a necessary tool in the relaxation of lockdown methods. Work by SBIDER, in collaboration with Oxford and Lancaster Universities, considered the use of contact tracing in the early stages of the outbreak as a means of controlling or containing the pandemic in the UK. Before lockdown, each person had many contacts that were made over a 7-day period (mean contacts 216, mean contacts to trace 36), so contact tracing logistics could soon be overwhelmed with just a few infectious cases. If we are able to trace all the contacts meeting the close contact definition, then our results show that an outbreak could be contained, although the "untraceable" contacts could still give rise to a low number of secondary cases.

First online: 17/02/2020 Published: 02/06/2020	Hilton, J., and Keeling, M. J. (2020). " Estimation of country-level basic reproductive ratios for novel Coronavirus (COVID-19) using synthetic contact matrices" *PLoS Comp. Biol.* **16**(7): e1008031. https://doi.org/10.1371/journal.pcbi.1008031
Summary: The value of the basic reproductive ratio, R_0, changes both according to the epidemiological characteristics of the virus, but also the context in which it spreads. Since susceptibility and transmission of COVID-19 changes with the age of the individual, the age-structure of the population can have a big effect on the value of R_0. This work examines the risk posed by COVID-19 in different areas of the world. For some parameter choices, the large proportion of children in Africa effectively buffer transmission leading to a much lower R_0; notably under these parameters Italy is an obvious hot-spot while Germany has the lowest transmission in Europe.	

5. A summary of any articles you have written, interviews and/or evidence you have given.

First online: 11/05/2020 Published: 22/01/2021	Keeling, M. J., Hill, E., Gorsich, E., Penman, B., Guyver-Fletcher, G., Holmes, A., McKimm, H., Tamborrino, M, Dyson, L., and Tildesley, M. (2020). "Predictions of COVID-19 dynamics in the UK: short-term forecasting and analysis of potential exit strategies" *PLoS Comp. Biol.* **17**(1): e1008619. https://doi.org/10.1371/journal.pcbi.1008619
Summary: In this very early paper we develop the "Warwick model" for COVID-19, and consider how elements of quarantine and isolation can be included into the fundamental SIR-framework. From an applied perspective, we focus on potential exit strategies, such as different changes to the early lockdown restrictions, age-based easing of the lockdown and basing the lockdown on local ICU capacity. We conclude that any route out of lockdown that does not involve pharmaceutical interventions (such as vaccination) has to be very slow and measured.	

First online: 17/06/2020	Leng, T., White, C., Hilton, J., Kucharski, A., Pellis, L., Stage, H., Davies, N., CMMID-Covid-19 WG, Keeling, M.J., Flasche, S.

Published: 29/03/2021	(2021) "The effectiveness of social bubbles as part of a Covid-19 lockdown exit strategy, a modelling study *Wellcome Open Res* **5**:213. https://doi.org/10.1268/wellcomeopenres.16164.2
Summary: Social bubbles have been proposed as a means of allowing extended contacts beyond the household while minimising the associated transmission risks. The concept is that members of one household are allowed to meet exclusively with members of one other household - while this increases the risk of transmission the premise is that the bubble remains relatively isolated. Our modelling work shows that social bubbles reduced cases and fatalities by 42% compared to an unclustered increase of contacts. Social bubbles may be extremely effective if targeted towards those small isolated households with the greatest need for additional social interactions and support.	

5. A summary of any articles you have written, interviews and/or evidence you have given.

First online: 16/09/2020 Published: 31/05/2021	Keeling, M. J., Tildesley, M. J., Atkins, B. D., Penman, B., Southall, E., Guyver-Fletcher, G., Holmes, A., McKimm, H., Gorsich, E., Hill, E. M., and Dyson, L. (2021). "The impact of school reopening on the spread of COVID-19 in England" *Phil. Trans. R. Soc. B*. **376** (1829): 20200261. https://doi.org/10.1098/rstb.2020.0261
Summary: We have used the Warwick COVID model for the UK to investigate potential scenarios for reopening schools in England. We consider different combinations of years returning to school, including the potential for teaching students in smaller classes which reduces infection risk. We find that, on its own, returning children to school is unlikely to lead to a second wave of infection, however there remains uncertainty if other measures are relaxed simultaneously. We conclude that even if R remained below one, any return of children to school will inevitably lead to some increase in transmission and therefore to an increase in cases, ICU admissions and, regrettably, deaths. We found that secondary school students returning led to higher increases than if only primary schools reopen, though in all scenarios the magnitude of changes depends upon the wider context in the community when the reopening of schools occurs. If transmission in the general community increases, this alone increases cases in all age-groups and exacerbates the increases seen in by school reopening (solid colours). The size of the increase due to schools returning is much smaller than the increase due directly to the increase in community transmission.	

First online: 24/09/2020 Published: 06/05/2021	Moore, S., Hill, E.M., Dyson, L., Tildesley, M., Keeling, M.J. (2021) "Modelling optimal vaccination strategy for SARS-CoV-2 in the UK" *PLoS Comp. Biol.* **17**(5): e1008849. https://doi.org/10.1371/journal.pcbi.1008849

Summary: In an early extension to the Warwick COVID model, we introduced a vaccinated class and a population with health conditions that are believed to have a significant impact on COVID-19 outcomes. At the time a number of different vaccine candidates were in development and the results from clinical trials were not fully available, leading to a large degree of uncertainty regarding the performance of these products. We therefore tested a range of efficacies (including reduced efficacy in the elderly) and three different types of vaccine each delivering a different level of protection. This paper highlighted the importance of prioritising vaccination towards the oldest and most vulnerable in the population, as this generates the maximum reduction in deaths and other severe outcomes.

First online: 29/09/2020 Published: 17/01/2022	Keeling, M.J., Dyson, L., Guyver-Fletcher, G., Holmes, A., Semple, M.G., ISASIC4C Investigators, Tildesley, M.J. & Hill, E.M. (2022) "Fitting to the UK COVID-19 outbreak, short-term forecasts and estimating the reproductive number" *Stat Methods Med Res.* https://doi.org/10.1177/09622802211070257
Summary: Fitting models to data is a key step in both understanding the current dynamics and generated projections of the short, medium or long-term. In this early paper we outline the basic fitting methods used by the Warwick model throughout the pandemic and consider the sensitivity to the ways the data is aggregated.	

5. A summary of any articles you have written, interviews and/or evidence you have given.

First online: 29/09/2020 Published: 20/07/2021	Parisi, A., Brand, S.P.C., Hilton, J., Aziza, R., Keeling, M.J. & Nokes, D.J. (2021) "Spatially resolved simulations of the spread of COVID-19 in three European countries", *PLoS Comp. Biol.* **17**(7): e1009090. https://doi.org/10.1371/journal.pcbi.1009090
Summary: In response to the pandemic, many governments issued measures aimed at containing the spatial spread of the virus and limiting the expected number of deaths. In this study, our goal was to use highly spatially resolved (5x5 km grid) stochastic transmission modelling calibrated to the observed spatial and temporal spread of the virus in Italy, Spain and the United Kingdom. We used a description of the population subdivided in age groups, high resolution population maps, and household structures: this allowed us to consider the measures imposed by governments and quantify their effectiveness.	

First online: 14/10/2020 Published: 02/12/2021	Keeling, M.J., Guyver-Fletcher, G, Holmes, A., Dyson, L., Tildesley, M.J., Hill, E.M. and Medley, G.F. (2021) "Precautionary breaks: Planned, limited duration circuit breaks to control the prevalence of SARS-CoV-2 and the burden of COVID-19 disease" *Epidemics* https://doi.org/10.1016/j.epidem.2021.100526

Summary: Research undertaken in October 2020 examined the potential of a "Circuit Breaker" to contain a growing epidemic.
When cases of COVID-19 are rising exponentially, we consider the impact of a short 2-week period of intense control. Using two different modelling approaches we show that a short, sharp 2-week break leads to a decline in cases, with similar declines in hospitalisation and mortality over a short period - this could potentially reduce the acute load on the NHS enabling it to continue non-COVID care into the winter months. A precautionary break is not a lasting control measure, but effectively buys more time to put other controls in place; it takes us 'back to a time when cases were lower'. To save lives over longer time scales requires driving *R* below one, however the reduction in cases generated by a circuit breaker allows time for other measures to have an impact and could be beneficial when measures are resource limited (such as test-trace-and isolate).

5. A summary of any articles you have written, interviews and/or evidence you have given.

First online: 18/10/2020 Published: 29/06/2021	Hill, E.M., Atkins, B.D., Keeling, M.J., Tildesley, M., Dyson, L. (2021) "Modelling SARS-CoV-2 transmission in a UK university setting" *Epidemics* **36**: 100476. https://doi.org/10.1016/j.epidem.2021.100476

Summary: The higher education system in the United Kingdom comprises a large student population. Therefore, in the setting of the COVID-19 pandemic bringing together these student communities presents questions regarding the strength of interventions required to control transmission. We constructed a network-based model to capture the interactions of a student population in different settings within a university environment (housing, social and study) and ran an SEIR type epidemic process.
Our work shows high adherence to isolation guidance and effective contact tracing both curbed transmission and reduced the expected time an adhering student would spend in isolation. Irrespective of the adherence to isolation measures, on average a higher proportion of students resident on-campus became infected compared with students resident off-campus. Room isolation as an additional intervention generated minimal benefits. Finally, a one-off mass-testing instance would not drastically reduce the term long case load or end-of-term prevalence, but regular weekly or fortnightly testing could reduce both measures by more than 50% (compared to having no mass testing).

First online: 20/11/2020 Published: 16/06/2021	Hill, E.M., Atkins, B.D., Keeling, M.J., Dyson, L., Tildesley, M. (2021) "A network modelling approach to assess non-pharmaceutical disease controls in a worker population: An application to SARS CoV-2" *PLoS Comp. Biol.* **17**(6): e1009058. https://doi.org/10.1371/journal.pcbi.1009058

Summary: As part of a concerted pandemic response to protect public health, businesses can enact non-pharmaceutical controls to minimise exposure to pathogens in workplaces and premises open to the public. Amendments to working practices can lead to the amount, duration and/or proximity of interactions being changed, ultimately altering the dynamics of disease spread. We used an individual-based network model to analyse transmission of SARS-CoV-2 amongst a working population that was stratified into work sectors. Our study found the progress of an outbreak to be significantly hindered by instructing a significant proportion of the workforce to work from home. Furthermore, asynchronous work patterns may help to reduce infections when compared with scenarios where all workers work on the same days, particularly for longer working weeks. Finally, smaller work teams and a greater reduction in transmission risk led to a flatter temporal profile for both infections and the number of people isolating, and reduced the probability of large, long outbreaks.

5. A summary of any articles you have written, interviews and/or evidence you have given.

First online: 26/01/2021 Published: 18/03/2021	Moore, S., Hill, E.M., Tildesley, M., Dyson, L., Keeling, M.J. (2021) "Vaccination and non-pharmaceutical interventions for COVID-19: a mathematical modelling study" *Lancet Infectious Diseases.* **21**(6): 793-802. https://doi.org/10.1016/S1473-3099(21)00143-2
Summary: By combining models of vaccination with the methods of forwards projection, we considered the interaction between the relaxation of non-pharamaceutical interventions (NPIs) and the protection offered by the vaccine. This paper set the tone for unlocking the UK in 2021: Our modelled scenarios highlighted the risks associated with early or rapid relaxation of NPIs, stressing the need for slow release of control measures if large-scale waves of infection are to be avoided. We conclude that while the vaccines against SARS-CoV-2 offer a potential exit strategy for the pandemic, success is highly contingent on the precise vaccine properties and population uptake.	

First online: 17/02/2021 Published: 07/06/2021	Emma Southall, Alex Holmes, Edward M. Hill, Benjamin D. Atkins, Trystan Leng, Robin N. Thompson, Louise Dyson, Matt J. Keeling, Michael J. Tildesley (2021) "An analysis of school absences in England during the Covid-19 pandemic" *BMC Medicine*, **19** (137). https://doi.org/10.1186/s12916-021-01990-x
Summary: This paper analysed data on pupil and staff absences due to confirmed COVID 19 infection during September-December 2020. During this early phase there is no significant evidence to suggest that schools are playing a substantial role in driving spread in the community. We conclude that careful monitoring was required as schools re opened in 2021 to determine the effect upon community incidence.	

First online: 21/02/2021 Published: 27/05/2022	Trystan Leng, Edward M Hill, Robin N Thompson, Michael J Tildesley, Matt J Keeling, Louise Dyson. (2022) "Assessing the impact of lateral flow testing strategies on within-school SARS-CoV-2 transmission and absences: A modelling study" *PLoS Comp. Biol.* **18**(5): e1010158. https://doi.org/10.1371/journal.pcbi.1010158
Summary: UK secondary schools have implemented a range of measures to control transmission within schools, including the isolation of close contacts of confirmed cases from September 2020 - July 2021, and twice weekly testing of staff and pupils since March 2021. We have developed an individual-based model to understand the impact of school control measures on pupil-to-pupil transmission, pupil absences and testing volume. Using an individual-based model of a secondary school implementing a bubbling strategy at the level of year-groups, and simulating infections over the course of a seven week half-term, we evaluated a range of strategies with differing isolation and rapid test strategies. In particular, we found that a policy of daily contact testing resulted in a similar reduction in transmission to an isolation of year-groups policy, but markedly reduced absences.	

5. A summary of any articles you have written, interviews and/or evidence you have given.

First online: 24/03/2021 Published: 01/09/2021	Hill, E.M., Keeling, M.J. (2021) "Comparison between one and two dose SARS-CoV-2 vaccine prioritization for a fixed number of vaccine doses" *Interface.* **18**(182): 20210214. https://doi.org/10.1098/rsif.2021.0214
Summary: Focusing on data from England, we investigated prioritisation of a one dose or two dose SARS-CoV-2 vaccination schedule given a fixed number of vaccine doses and with respect to a measure of maximising averted deaths. This work highlighted the advantage of a longer separation between first and second doses, as it enables more vulnerable people to be protected early in the epidemic, and therefore reduces hospital admissions and deaths from the pandemic.	

First online: 25/04/2021 Published: 10/08/2022	Tildesley, M.J., Vassall, A., Riley, S., Jit, M., Sandmann, F., Hill, E.M., Thompson, R.N., Atkins, B.D., Edmunds, J., Dyson, L. & Keeling, M.J. (2022) "Optimal health and economic impact of non-pharmaceutical intervention measures prior and post vaccination in England: a mathematical modelling study" *Roy. Soc. Open Science*. https://doi.org/10.1098/rsos.211746

Summary: Even with good progress on vaccination, SARS-CoV-2 infections in the UK may continue to impose a high burden of disease and therefore pose substantial challenges for health policy decision makers. Stringent government-mandated physical distancing measures (lockdown) have been demonstrated to be epidemiologically effective, but can have negative economic consequences. The duration and frequency of any intervention policy could, in theory, could be optimised to maximise economic benefits while achieving substantial reductions in disease. In this work we use a SARS-CoV-2 transmission model to assess the health and economic implications of different strengths of control through time in order to identify optimal approaches to non-pharmaceutical intervention stringency in the UK, considering the role of vaccination in reducing the need for future physical distancing measures. We find that the precise timing and intensity of interventions is highly dependent upon the objective of control. As intervention measures are relaxed, we predict a resurgence in cases, but the optimal intervention policy can be established dependent upon the willingness to pay (WTP) per QALY loss avoided. Our results show that establishing an optimal level of control can result in a reduction in net monetary loss of billions of pounds, dependent upon the precise WTP value. We therefore demonstrate how future health and non health harms associated with infectious disease outbreaks could be quantified, employing mechanistic infectious disease transmission models to establish optimal levels of control for the ongoing COVID-19 pandemic.

5. A summary of any articles you have written, interviews and/or evidence you have given.

First online: 07/06/2021 Published:	Robert Challen, Louise Dyson, Christopher E. Overton, Laura M. Guzmán-Rincón, Edward M. Hill, Helena B. Stage, Ellen Brooks Pollock, Lorenzo Pellis, Francesca Scarabel, David J. Pascall, Paula Blomquist, Michael Tildesley, Daniel Williamson, Stefan Siegert, Xiaoyu Xiong, Ben Youngman, Juniper, Jonathan M. Read, Julia R. Gog, Matthew J. Keeling, Leon Danon. (2021) "Early epidemiological signatures of novel SARS-CoV-2 variants: establishment of B. 1.617. 2 in England" (*medRxiv*) https://doi.org/10.1101/2021.06.05.21258365
Summary: Here we consider the early data on the Delta variant looking at its transmission advantage compared to the Alpha variant ' as seen in the transition from a declining epidemic to an increasing one. We use a variety of different methods to calculate real time growth estimates of S-gene positive (likely Delta) cases compared to S-gene negative (likely Alpha) cases and show a sustained, consistent advantage of Delta over Alpha in multiple regions of England. We use the normalisation of age distributions to argue that this transmission advantage is inherent to the Delta variant and is not a result of early higher transmission in specific subpopulations.	

First online: 10/06/2021	Louise Dyson, Edward M Hill , Sam Moore, Jacob Curran-Sebastian, Michael J Tildesley, Katrina A Lythgoe, Thomas

Published: 30/09/2021	House, Lorenzo Pellis, Matt J Keeling. (2021) "Possible future waves of SARS-CoV-2 infection generated by variants of concern with a range of characteristics" *Nature Communications* **12**: 5370. https://www.nature.com/articles/s41467-021-25915-7
Summary: We used three mathematical models to examine the potential drivers of SARS CoV-2 VOC epidemics in England. We found epidemiological trajectories for putative VOCs are wide-ranging and dependent on their transmissibility, immune escape capability, and the introduction timing of a postulated VOC-targeted vaccine. In particular, a variant that is less transmissible, but shows partial immune-escape, could provoke a wave of infection that would not be revealed until control measures are further relaxed.	

5. A summary of any articles you have written, interviews and/or evidence you have given.

First online: 20/06/2021 Published: 07/10/2021	Samuel P.C. Brand, John Ojal, Rabia Aziza, Vincent Were, Emelda A. Okiro, Ivy K. Kombe, Caroline Mburu, Morris Ogero, Ambrose Agweyu, Edwine Barasa *et al.* (2021) "COVID-19 Transmission Dynamics Underlying Epidemic Waves in Kenya" *Science* **374**, 989- 994 DOI: 10.1126/science.abk0414
Summary: It has been recognised around the globe that the socio-economic status (SES) of individuals is a critical determining factor in their risk of SARS-CoV-2 infection, and developing severe COVID-19 disease. In this study, we integrate data from Google mobility data, longitudinal serological surveys and the laboratory PCR data into a mathematical model aimed at investigating the evidence for differential SES risk in Kenya. We found evidence that in urbanised regions of Kenya, characterised by high-density informal settlement, the risk of infection during the first wave in Kenya was extremely high among people in lower SES groups with very low ascertainment of infection by PCR testing. Subsequent waves in Kenya are explained by the delayed infection of people among higher SES groups who could maintain higher levels of social distancing for longer, and the introduction of highly transmissible variants of concern: Alpha, Beta and, more recently, Delta variants.	

First online: 16/07/2021 Published: 01/03/2022	Trystan Leng, Edward M Hill, Alex Holmes, Emma Southall, Robin N Thompson, Michael J Tildesley, Matt J Keeling, Louise Dyson. (2021) "Quantifying within-school SARS-CoV-2 transmission and the impact of lateral flow testing in secondary schools in England" *Nature Communications* **13**, 1106. https://doi.org/10.1038/s41467-022- 28731-9

Summary: Here, we incorporated various data into the individual-based model of secondary schools in order to quantify SARS-CoV-2 transmission between secondary school pupils in England. We have used community swab testing data to inform community prevalence for schools according to their local area and to inform a school's level of participation in lateral flow testing; we have used secondary school absences data to inform the size of group a school isolates upon identification of a positive case; and we have fitted this model to community swab testing data in 11-16 year olds and secondary school absences data. With this fitted model, we simulated outbreaks from 31st Aug 2020 - 21st May 2021 to quantify SARS-CoV-2 transmission in secondary schools in England. Doing so, we evaluated the impact of twice weekly lateral flow testing (LFT) of pupils on transmission, finding that twice weekly mass testing likely played an important role in controlling pupil-to-pupil transmission in secondary schools in England. We also considered the counterfactual impact of alternative strategies, finding that strategies involving mass testing have the potential to control within-school transmission while substantially reducing absences.

5. A summary of any articles you have written, interviews and/or evidence you have given.

First online: 09/11/2021 Published: 27/06/2022	Leng, T., Hill, E.M., Keeling, M.J., Tildesley, M.J. and Thompson R.N. (2022) "The effect of notification window length on the epidemiological impact of COVID-19 contact tracing mobile applications" *Communications Medicine* **2**:74. DOI: 10.1038/s43856- 022-00143-2

Summary: The reduction in SARS-CoV-2 transmission from contact tracing applications (apps) depends both on the number of contacts notified and on the probability that those contacts quarantine after notification. Referring to the number of days preceding a positive test that contacts are notified as an app's *notification window*, we use an epidemiological model of SARS-CoV-2 transmission that captures the profile of infection to consider the trade-off between notification window length and active app-usage. We focus on 5-day and 2-day windows, the lengths used by the NHS COVID-19 app in England and Wales before and after 2nd August 2021, respectively. Short windows can be more effective at reducing transmission if they are associated with higher levels of active app usage and adherence to isolation upon notification, demonstrating the importance of understanding adherence to control measures when setting notification windows for COVID-19 apps.

First online: 10/11/2021 Published:	Keeling, M.J., Thomas, A., Hill, E.M., Thompson, R.N., Dyson, L., Tildesley, M.J., Moore, S. (2021) "Waning, Boosting and a Path to Endemicity for SARS-CoV-2" *medRxiv.* https://doi.org/10.1101/2021.11.05.21265977

Summary: In many countries, an extensive vaccination programme has substantially reduced the public-health impact of SARS-CoV-2, limiting the number of hospital admissions and deaths compared to an unmitigated epidemic. The observed waning of vaccine efficacy over time suggests that booster doses may be required to maintain population immunity especially in the most vulnerable groups. Here, using data and models for England, we consider the dynamics of COVID-19 over a two-year time-frame, and the role that booster vaccinations can play in mitigating the worst effects. Although formulated for the Delta variant, this paper has key implications for Omicron.

First online: 30/12/2021 Published:	Matt J Keeling, Ellen Brooks-Pollock, Robert J Challen, Leon Danon, Louise Dyson, Julia R Gog, Laura Guzman-Rincon, Edward M Hill, Lorenzo M Pellis, Jonathan M Read, Michael J Tildesley. (2021) "Short-term Projections based on Early Omicron Variant Dynamics in England" *medRxiv.* https://doi.org/10.1101/2021.12.30.21268307
Summary: The Omicron variant (B.1.1.529) was first reported to the WHO by South Africa on 24 November 2021 and was declared a variant of concern by the WHO on 26 November 2021. The variant was first detected in the UK on 27 November 2021 and has since been reported in a number of countries globally where it is frequently associated with rapid increase in cases. We present analyses of UK data showing the earliest signatures of the Omicron variant and mathematical modelling that uses the UK data to simulate the potential impact of this variant in the UK. To account for the uncertainty at the time of writing (December 2021), we include a sensitivity analysis to assess the impact of variant characteristics (transmission advantage, vaccine escape and severity) on future risk.	

5. A summary of any articles you have written, interviews and/or evidence you have given.

First online: 27/01/2022 Published: -/11/2022	Sam Moore, Edward M. Hill, Louise Dyson, Michael J. Tildesley, Matt J. Keeling (2021) The impacts of increased global vaccine sharing on the COVID-19 pandemic; a retrospective modelling study *medRxiv* DOI: 10.1101/2022.01.26.22269877 (to appear in *Nature Medicine*)

Summary: We use an age-structured model of SARS-CoV-2 dynamics, matched to national data from 152 countries, to investigate the global impact of different vaccine sharing protocols during 2021. We assume a direct relationship between the emergence of variants with increased transmissibility and the cumulative amount of global infection, such that lower global prevalence leads to a lower reproductive number within each country. We compare five vaccine sharing scenarios, from the current situation, through sharing once a particular within-country threshold is reached (e.g. all over 40s have received 2 doses), to full sharing where all countries achieve equal age-dependent vaccine deployment.
Compared to the observed distribution of vaccine uptake, we estimate full vaccine sharing would have generated a 1.5% (PI -0.1 - 4.5%) reduction in infections and a 11.3% (PI 0.6 - 23.2%) reduction in mortality globally by January 2022. The greatest benefit of vaccine sharing would have been experienced by low and middle income countries, who see an average 5.2% (PI 2.5% - 10.4%) infection reduction and 26.8% (PI 24.1% - 31.3%) mortality reduction. Many high income countries, that have had high vaccine uptake (most notably Canada, Chile, UK and USA), suffer increased infections and mortality under most of the sharing protocols investigated, assuming no other counter measures had been taken. However, if reductions in vaccine supply in these countries had been offset by prolonged use of non-pharmaceutical intervention measures, we predict far greater reductions in global infection and mortality of 64.5% (PI 62.6% - 65.4%) and 62.8% (PI 44.0% - 76.3%), respectively.

First online: 18/03/2022 Published: 22/08/2022	Keeling, M.J., Dyson, L., Tildesley, M.J. Hill, E.M. & Moore, S. (2022) "Comparison of the 2021 COVID-19 roadmap projections against public health data in England" *Nature Communications* **13**: 4924. https://doi.org/10.1038/s41467-022-31991-0
Summary: Here we present a retrospective analysis of our six Roadmap documents generated in 2021 to assess the likely impacts of future relaxation steps in England. In each case we directly compare results generated at the time with more recent public health data (primarily hospital admissions, but also hospital occupancy and death) to understand discrepancies and potential improvements. We conclude that, in general, the model projections generated a reliable estimation of medium-term hospital admission trends, with the data points up to September 2021 generally lying within our 95% projection intervals. The greatest uncertainties in the modelled scenarios came from estimates of vaccine efficacy, hampered by the lack of data in the early stages of the Alpha and Delta variant waves, and from assumptions about human behaviour in the face of changing restrictions and changing risk.	

5. A summary of any articles you have written, interviews and/or evidence you have given.

First online: 13/06/2022 Published:	Keeling, M.J. (2022) Patterns of Reported Infection and Reinfection of SARS-CoV-2 in England. *medRxiv* https://doi.org/10.1101/2022.06.13.22276316

Summary: Here we investigate reported SARS-CoV-2 cases in England, partitioning the data into four main waves, and consider the pattern of first and second reports of infection. We conclude that there is considerable heterogeneity in risk of reporting reinfection by wave, age-group and location. The high levels of reinfection in the Omicron wave (we estimate that 18% of all Omicron cases had been previously infected, although not necessarily previously reported infection) point to reinfection events dominating future COVID-19 dynamics.

First online: 13/06/2022 Published:	Guzmán-Rincón, L.M., Hill, E.M., Dyson, L., Tildesley, M.J. & Keeling, M.J. (2022) Bayesian Estimation of real-time Epidemic Growth Rates using Gaussian Processes: local dynamics of SARS-CoV-2 in England. *medRxiv* https://doi.org/10.1101/2022.01.01.21268131

Summary: Here, we calculate the exponential growth rate, *r*, using a Bayesian hierarchical model to fit a Gaussian process to the epidemiological data. We show how the method can be employed when only case data from positive tests are available, and the improvement gained by including the total number of tests as a measure of heterogeneous testing effort. Although the methods are generic, we apply them to SARS CoV-2 cases and testing in England, making use of the available high-resolution spatio temporal data to determine long-term patterns of national growth, highlight regional growth and spatial heterogeneity.

First online: 22/08/2022 Published:	Keeling, M.J., Penman, B., Hill, E.M & Moore S. (2022) The Impact of SARS-CoV-2 Vaccine Dose Separation and Dose Targeting on Hospital Admissions and Deaths from COVID-19 in England. *medRxiv* https://doi.org/10.1101/2022.08.22.22278973

Summary: In late 2020, the JCVI made two important recommendations for the initial roll out of the COVID-19 vaccine. The first was that vaccines should be targeted to the elderly and vulnerable; the second was to increase the interval between first and second doses for 3 to 12-weeks. Here, using the latest data on vaccine efficacy we re-examine these recommendations through a mathematical model and show that targeting the most vulnerable had the biggest immediate impact. The 12-week delay was also highly beneficial, estimated to have averted between 32-72 thousand hospital admissions and 4- 9 thousand deaths over the first ten months of the campaign (December 2020 - September 2021).

5. A summary of any articles you have written, interviews and/or evidence you have given.

Other Publications

Thompson, RN et al. (2020) Key questions for modelling COVID-19 exit strategies *PROCEEDINGS OF THE ROYAL SOCIETY B-BIOLOGICAL SCIENCES* **287** 20201405

https://www.doi.org/10.1098/rspb.2020.1405

Brooks-Pollock, E; Read, JM; House, T; Medley, GF; Keeling, MJ; Danon, L (2021) The population attributable fraction of cases due to gatherings and groups with relevance to COVID-19 mitigation strategies *PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES* **376** 20200273 https://www.doi.org/10.1098/rstb.2020.0273

Brooks-Pollock, E; Read, JM; McLean, AR; Keeling, MJ; Danon, L (2021) Mapping social distancing measures to the reproduction number for COVID-19 *PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B-BIOLOGICAL SCIENCES* **376** 20200276 https://www.doi.org/10.1098/rstb.2020.0276

Danon, L; Brooks-Pollock, E; Bailey, M; Keeling, M (2021) A spatial model of COVID-19 transmission in England and Wales: early spread, peak timing and the impact of seasonality *PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B-BIOLOGICAL SCIENCES* **376** 20200272 https://www.doi.org/10.1098/rstb.2020.0272

Cavallaro, M; Moiz, H; Keeling, MJ; McCarthy, ND (2021) Contrasting factors associated with COVID-19-related ICU admission and death outcomes in hospitalised patients by means of Shapley values *PLOS COMPUTATIONAL BIOLOGY* **17** e1009121 https://www.doi.org/10.1371/journal.pcbi.1009121

Aliee, M; Castano, S; Davis, CN; Patel, S; Miaka, EM; Spencer, SEF; Keeling, MJ; Chitnis, N; Rock, KS (2021) Predicting the impact of COVID-19 interruptions on transmission of gambiense human African trypanosomiasis in two health zones of the Democratic Republic of Congo *TRANSACTIONS OF THE ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE* **115** 245-252 https://www.doi.org/10.1093/trstmh/trab019

Mateen, BA; Wilde, H; Dennis, JM; Duncan, A; Thomas, N; McGovern, A; Denaxas, S; Keeling, M; Vollmer, S (2021) Hospital bed capacity and usage across secondary healthcare providers in England during the first wave of the COVID-19 pandemic: a descriptive analysis *BMJ OPEN* **11** e042945 https://www.doi.org/10.1136/bmjopen-2020-042945

Orangi, S et al. (2022) Epidemiological impact and cost-effectiveness analysis of COVID-19 vaccination in Kenya *BMJ GLOBAL HEALTH* **7** e009430 https://www.doi.org/10.1136/bmjgh 2022-009430

5. A summary of any articles you have written, interviews and/or evidence you have given.

Media

14/10/2020 Science Media Centre on Circuit Breakers

21/01/2021 Science Media Centre on Vaccination and NPIs
15/06/2021 Science Media Centre on Roadmap modelling
13/07/2021 Science Media Centre on Roadmap modelling
15/12/2020 Plus Magazine article, https://plus.maths.org/content/covid-19-vaccines your-questions-answered
01/04/2021 Plus Magazine article, https://plus.maths.org/content/vaccination-where-do we-stand-and-where-are-we-going
12/05/2021 Plus Magazine article, https://plus.maths.org/content/shining-light-covid modelling
13/05/2022 Plus Magazine interview, https://plus.maths.org/content/mathematical frontline-matt-keeling

Evidence

02/06/2020 Lords Select Committee
10/06/2020 Science and Technology Committee. UK Science, Research and Technology Capability and Influence in Global Disease Outbreaks
2021 various WHO SAGE on vaccination
08/04/2021 Commission on Human Medicine on vaccination
20/12/2021 Anthony Fauci on the result of Omicron modelling
01/03/2022 All Party Parliamentary Group on COVID-19

Question 6. Whether groups succeeded in their aims.

This is mainly going to reflect my experience with the SPI-M-O subgroup, but will also bring in my occasional participation in the SAGE meetings and my membership of JCVI.

On the whole, I feel the way the academic community became involved in the COVID-19 pandemic – giving their time, energy and expertise for free – has been a fantastic achievement. There are some things that I feel could have been handled differently, but given the immediate time pressures, SAGE and its subgroups performed remarkably well.

The composition of SPI-M-O was wide and diverse, with modelling expertise from across the UK. This expertise became wider as the pandemic progressed as more individuals with different skill-sets became involved. It was good to see many early career researchers and less-senior academics as part of SPI-M-O, which is ideal training and preparation for future situations.

In the very early stages of the pandemic, modelling activities were dominated by Imperial College and the London School of Hygiene and Tropical Medicine (LSHTM) who had representatives on SAGE, and therefore by-passed SPI-M-O. As the epidemic progressed, and certainly by April/May 2020, the entire SPI-M-O committee was being asked to produce results and feed into the weekly consensus document. Warwick was in a fortunate position relatively early in the pandemic, of having a sufficiently large group (PhD students, post-doctoral researchers and academic staff) that were prepared to give their time to synthesize the available knowledge, analyse data and generate results. When the JUNIPER consortium formed in November 2020, this additional funding and organisational capacity redressed the earlier imbalance and meant that many institutions from around the UK could contribute far more.

The support from the SPI-M-O secretariat was amazing – they were highly responsive to requests for help and advice, and worked tirelessly to enable the academics to meet deadlines. From November 2020, the JUNIPER consortium (Bristol, Cambridge, Exeter, Lancaster, Manchester, Oxford and Warwick) won funds from UKRI to support post doctoral researchers working on COVID-19; this was hugely transformative, but there is a danger that the step-change in methods that was required by the pandemic will be lost without further support.

In general, the advice given to government was of the highest quality, and UK researchers are seen internationally as world leaders. However, I think there was often a failure to effectively communicate these ideas beyond the immediate decision makers. Mathematical modelling was one of the few elements of advice that was open to detailed and deep public scrutiny, and hence has faced substantial criticism by those that have opposed the government approach to the pandemic. In contrast, the economic modelling, the estimates of vaccine efficacy, the projected deployment rate of the vaccine etc were never available for this level of public consideration.

If I had to find one fault with the operation of SAGE and its subgroups, it would be the level of between-group communication. I think there were 3 problems with the adopted approach: 1) There was limited direct communication between the SAGE subgroups. While each of the subgroups presented work and findings to SAGE, there was not an easy route for all that information to feed into other committees. Occasional (monthly) meetings between sub-group members might have helped generate greater

interdisciplinary interaction and insights.

Similarly, I feel that there should have been much closer links between JCVI and SPI-M-O. I was the sole modeller on JCVI, and while I attempted to convey both my own results as well as the findings of other groups, greater involvement between JCVI and SPI-M-O, especially in terms of being able to ask for modelling support could be vital in the future.

2) The information chain from academics to SPI-M-O to SAGE to policy makers was often very slow. During 2021 and the decisions about the Roadmap Steps, I was generating results on Monday/Tuesday to be written up Tuesday evening for presentation to the SPI-M-O meeting on the Wednesday. These would then be presented to SAGE on Thursday, and finally presented to policy makers on Saturday or Sunday, for a policy announcement on Monday. While typographical corrections occurred between Thursday and Sunday, updates to the modelling to reflect the latest data were not encouraged as they would not have been scrutinised by SPI-M-O and SAGE. Fortunately, the week of additional data never produced a major qualitative change in the projections; but the delay is nevertheless a concern.
3) SPI-M-O generated a weekly consensus that was presented the next day at SAGE, and then became publicly accessible via the SAGE webpage. This worked extremely well with the two excellent chairs (Prof Medley & McLean) and the very knowledgeable secretariat, and was the only way to cope with the compressed timescales of meetings. However, this form of consensus document does not readily convey the degree of scrutiny, peer-review and discussion that occurred during the meetings

While these communication issues are items that could ideally be addressed before a future pandemic, it is my firm view that they did not significantly affect the advice that was provided by SAGE and its sub-groups during the COVID-19 pandemic.

Question 7. Lessons Learned

Here I will outline the issues that caused potential problems early in the COVID-19 pandemic, many of these were slowly resolved as the outbreak progressed but many have resurfaced in the Monkeypox outbreak. I¶d raise five issues as key lessons to be learned

1) As mentioned in Question 6, I feel that better lines of direct communication between the subgroups, that did not have be fed through SAGE, may be of great help in future pandemics. I think more informal meetings between subgroups could be highly beneficial and provide all groups with a more holistic understanding of future outbreaks. We are now seeing a similar situation with Monkeypox, in which the modellers, the clinicians and the behavioural experts are somewhat siloed.
I¶d also state that continuing to have meetings on-line is a definite improvement especially for the majority of academics that live outside London. There is no way I could have generated the output that I did for the COVID-19 pandemic if I also had to attend meetings in person with the associated travel times.

2) Models are only as good as the data that feeds into them, and modern models are often data-hungry. UKHSA (formally PHE) and NHS control access to much of this data. I fully appreciate the ethics of data confidentiality, but often there were substantial bottle-necks that could have impacted what was achieved. While UKHSA/PHE held a large database of reported infection episodes, modellers only had access to partial information that was passed to us on a regular basis. For example, for the majority of 2020 and 2021, the modellers were only told about the first time an individual tested positive ± so any subsequent positive tests were ignored. While there were good reasons for this in the early outbreak (not counting people testing multiple times in succession), later in the outbreak it could have been biasing the modelling results. Even when this was resolved, tests within 90 days were ignored ± again there were reasons for this, but the reinfections within 90 days helps to explain some of the patterns observed just after 90 days. Another continuing issue with the data is the disconnect between case and death data, which was highly detailed and hospital admission data that was aggregated at a relatively course scale. Again, we all appreciate the confidential nature of hospital data, but the differences between data sets seems excessive. In addition, there were often changes to the way that hospital data was counted, meaning that modellers were often fitting to the counting rather than the underlying processes.
Finally, I¶d flag the vast differences in data quality and formatting between the four nations, with different countries providing different data in very different formats. After the initial phase of the epidemic DSTL and later UKHSA did an excellent job of bringing this data into a unified document, but differences in the ways data is reported and recorded caused multiple problems throughout the pandemic.
I had hoped that many of these difficulties would have been resolved for the Monkeypox outbreak, but if anything, the data access issues are worse. Admittedly SAGE and SPI-M are not directly involved in Monkeypox modelling, but the academic community has still been asked for its help. With Monkeypox, the UK data is only available to UKHSA affiliated staff with a UKHSA laptop, and is again siloed so that the entirety of the data sets are not available to all users.
As we move to a new protocol in working with large data sources, it is important that the public-health academic interface matches these innovations. Either academic institutions need to be trusted with large volumes of data, such that the power of university computer systems can be used to analyse the dynamics, or data access needs to be provided in

secure environments with plenty of flexibility and processing power such that the same analyses can be performed.

3) The epidemiological models and projections that fed into SPI-M-O and SAGE are only one part of a holistic decision-making process; economics and social impacts are needed to form a balance. While I fully understand the principle that SAGE is only involved in the science, from a mathematical modelling perspective the economics and other factors are required if we are to produce optimal solutions. Many of us requested to be more joined up with the economic forecasts, but this never occurred. In early 2021, myself and a group of other academics investigated the potential of combined epidemiological and economic modelling (Optimal health and economic impact of non-pharmaceutical intervention measures prior and post vaccination in England: a mathematical modelling study" *Roy. Soc. Open Science*. https://doi.org/10.1098/rsos.211746) ± this work showed how the optimal pattern of controls changed as the economic value placed on a single year of healthy life varied. I feel this shows the power of what could be achieved by more integrated thinking between scientists and economists ± our economic assessment based on the drop in DGP during the first lockdown was very pessimistic compared to the much smaller drops observed in November 2020 and January 2021.

4) The academic community worked wonders with incredibly tight deadlines and on very limited resources. Many groups managed to secure some extra funds to support additional research staff, through research council grants (UKRI hosted specific schemes) and funds from other organisations (such as the RAMP initiative from the Royal Society) ± although the time needed to apply for such funds is time taken away from active research into the pandemic. In addition, many universities were responsive to demands placed on these researchers and reduced their teaching or administrative loads. However, there was little direct government funding for those performing activities for the multiple subgroups, and many academics would not have been able to provide the scientific input they did without the support from UKRI and host institutions. Moreover, we are now in the situation where major innovations that were generated during the pandemic, and which have placed the UK as a scientific world-leader, are likely to be lost without continued broad investment in the research field.

5) During the pandemic, communication of scientific findings to the public and other interested parties was sometimes disjoint and patchy ± despite the best efforts of organisations such as the Science Media Centre. It is vitally important that the public understands the scientific evidence and other inputs if they are to have any confidence in the final policy decisions, which will in turn increase the level of compliance. Unfortunately, the dialogue during the pandemic, and since, has often been dominated by those who have not been part of generating the advice, have not seen the processes in action, do not understand the logistical constraints and often have little experience in the field. Two false narratives have persisted that may undermine future scientific advice and the response to any future public-health emergency:
i) There are multiple false narratives concerning lockdowns. Firstly that ³*lRckdRZnV dRn¶W work´* ± yet all the evidence shows that the three UK lockdowns have each led to a dramatic decline in cases shortly after introduction. Each of the lockdowns was applied at a time when cases and hospital admissions were rising so quickly that resources were in danger of being overwhelmed. Secondly that ³*lockdowns have caused NHS backlogs´*, whereas the majority of pressures on the health services have arisen due to the vast number of COVID-19 patients that have required treatment, generally in isolation. Thirdly

that ³*lockdowns have had a devastating effect on the economy´*, while this was undoubtedly true for the uncertainty surrounding the early pandemic and first UK lockdown, the subsequent lockdowns in November 2020 and January 2021 had a much smaller impact (as measured by GDP).
ii) The models used to make projections of potential pandemic trajectories have also been

the subject of intense criticism. For example, it is often claimed that ³*models have been shown to be wildly incRUUecW´*, yet there are a number of detailed scientific papers, generated by the groups involved and fully peer-reviewed, that show the agreement between model projections and data in retrospective comparisons. Obviously, models cannot be perfect, they were making long-term projections in a highly uncertain world often from relatively early data; yet models remain our only means of extrapolating from the current situation to explore potential future dynamics. It is also stated that ³*models were extraordinarily pessimistic´*, yet analysis of results shows that models also underestimated outbreaks, while reasonable worst-case scenarios are expected to be pessimistic so that organisations can plan for the worst. Finally, it is often said that ³*Omicron models overstated the threat´*. There were a large number of model projections presented to SPI M-O and SAGE in December 2021 and early January 2022; these explored a range of scenarios, were based on discussions with international scientists (especially those with direct knowledge of the wave in South Africa), and became increasingly refined as more UK data became available, closely projecting the scale of the first Omicron wave.

It is unclear how we could have better countered such misinformation, or better explained our findings to the general public. The article from the CSA (https://www.gov.uk/government/speeches/its-not-true-covid-19-modellers-look-only-at worst-outcomes) was an excellent explanation of the facts but unfortunately has done little to change the general narrative. Such undermining of expert advice may have long-lasting repercussions for how this country responds to future emergencies and how scientific advice is used.

Question 8.

Throughout the pandemic I have accumulated a large number of files (over 400GB) which are primarily epidemiological data, model code, model output, presentations, documents (as summarised in Question 4) and manuscripts (as summarised in Question 5).