Witness Name: Neil Ferguson

Statement No. :1

Exhibits: 0

Dated: 8rd May 2023

UK COVID-19 INQUIRY

MODULE 1

WITNESS STATEMENT OF PROFESSOR NEIL FERGUSON

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1. I, Professor Neil Ferguson, Imperial College London, Exhibition Rd, South Kensington, London SW7 2BX , will say as follows:

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A. Introduction

2. I have structured this submission into sections. I initially provide background on my role, the research units I direct at Imperial College London and my involvement in providing scientific advice on infectious disease threats since 2001. I review my involvement in modelling and providing scientific advice for pandemic preparedness and in response to specific outbreaks (FMD [2001], SARS-1 [2003], H1N1 pandemic influenza [2009], MERS-CoV [2012-], Ebola [2014-] and Zika [2016]). I conclude with some reflections and suggestions for change relating to how the UK plans and responds to civil contingencies (focussing on infectious disease threats) and the role of scientific advice to policymakers in crises.

3. I note that the module 1 rule 9 request asks me to consider the period 11 June 2009 to 21 January 2020. However, I will consider the period 2001 to 2019 inclusive, since much of the research which informed pandemic preparedness planning in the UK occurred before 2009. In addition, the establishment of current structures to plan for and respond to civil contingencies (e.g. the National Risk Register (NRR)[1] and SAGE) predate 2009.

4. Parts of this witness statement repeat parts of my module 2 statement, notably sections D, E and L.

5. I do not describe our work on COVID-19 in this statement; my module 2 statement provides extensive details of that work and given only a very small proportion of COVID-19 work was undertaken prior to 21st January 2022, I felt it is more logical to present that work within a narrative describing the whole of our contribution to COVID-19 epidemiological analysis and modelling.

6. Superscripted numbers in the text are citations to documents listed in the bibliography (section N). All material referenced is in the public domain.

B. My role

7. I am a mathematical epidemiologist employed by Imperial College London, where I have been a Professor since 2001. My research focuses on using statistical and mathematical models to understand infectious disease dynamics and control. I have worked on emerging infectious disease outbreaks since 1995. Much of this work has involved national and international policymakers.

8. I hold the following research-focussed positions at Imperial College:

   a. Director of the MRC Centre for Global Infectious Disease Analysis (MRC GIDA): 2007-

   b. Head of the Department of Infectious Disease Epidemiology, School of Public Health: 2012-

   c. Director of the Health Protection Research Unit (HPRU) for Modelling and Health Economics: 2014-

   d. Director of the Abdul Latif Jameel Institute for Disease and Emergency Analytics (Jameel Institute): 2019-

   The MRC Centre, NIHR HPRU and Jameel Institute are discussed below.

9. I am an author on over 200 peer-reviewed scientific papers and am an elected fellow of the UK Academy of Medical Sciences and an elected international member of the US National Academy of Medicine.

10. I served on the predecessor of SAGE during the 2001 foot and mouth (FMD) epidemic and on every infectious disease related SAGE since (pandemic influenza 2009, Ebola 2014, Zika 2016, COVID-19 2020). I have also been a member of NERVTAG since its creation in 2014 and sat on its predecessor, SPI, from 2008 to 2011. I note there was a gap between the cessation of SPI and the creation of NERVTAG. I have also sat on SPI-M (the modelling subgroup of SPI and later NERVTAG) since its creation in 2008, and on the informal (modelling-focussed) scientific advisory group (SAG) which preceded SPI-M and SPI between 2005 and 2007. I participated in the UK Government Exercise Winter Willow in 2007 and Exercise Cygnus in 2014 in the role of an external scientist advising the government (note that while the largest scale parts of Exercise Cygnus took place in 2016, some initial aspects were undertaken in 2014). I have never received payment for any of these commitments, bar travel expenses.

11. As head of a large epidemiological research centre, my contribution to the groups and committees I participated in from 2007 onwards was as much as a representative of that centre as an individual scientist, in that much of my contribution was reporting or discussing the results of the research of the centre. In addition, I also provided more general scientific advice.

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C. MRC GIDA

12. I founded the MRC Centre for Outbreak Analysis and Modelling in 2007, with financial support from the Medical Research Council and Imperial College London. Funding was renewed in 2012, and then again in 2017 when the name of the Centre was changed to the MRC Centre for Global Infectious Disease Analysis (MRC GIDA).

13. At its founding, the MRC Centre consisted of approximately 7 tenured academic staff (*i.e.* lecturer and above) and some 50 people total (academic, research and professional staff plus PhD students). By 2020, the Centre had grown to 32 academic staff and over 150 staff and PhD students in total.

14. The Centre funding provided by MRC represents under 10% of our total research funding. Major funders include UKRI (project grants from multiple research councils), NIHR, the Wellcome Trust, the Bill and Melinda Gates foundation, the US National Institutes of Health, and Community Jameel (a philanthropy based in the Middle-East). The Director controls core Centre funding, but not the other research grants held by other principal investigators (i.e. the academic staff) within the Centre.

15. As Centre Director, I have been supported by four Associate Directors since 2017: Profs Christl Donnelly, Azra Ghani, Timothy (Tim) Hallett and Nicholas (Nick) Grassly.

16. In practice, and in common with most academic centres, decision-making within the Centre is typically collective and based on consensus. In particular, the Director does not have the authority to tell academic staff what to work on. Rather, the role is more focussed on strategically-drive coordination of activity and supporting the research (and career progression) of staff within the Centre.

17. The figure below illustrates the overall structure of the Centre. Since 2017, MRC GIDA has had 5 major research themes: (a) Outbreak Analysis and Modelling; (b) Global Health Analytics; (c) Vaccines; (d) Antimicrobial Resistance; (e) Methods and Tools. It conducts research on nearly all major human infectious diseases, most notably "emerging" infections (including COVID-19) and the high health burden globally endemic diseases of HIV, TB and malaria. Work spans epidemiological and genetic analysis together with statistical and mathematical modelling. We also conduct some field (epidemiological studies and clinical trials) and laboratory-based research. Most of our research is focussed outside the UK, principally

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involving low- and middle-income countries where the majority of the health burden from infectious diseases is now experienced.

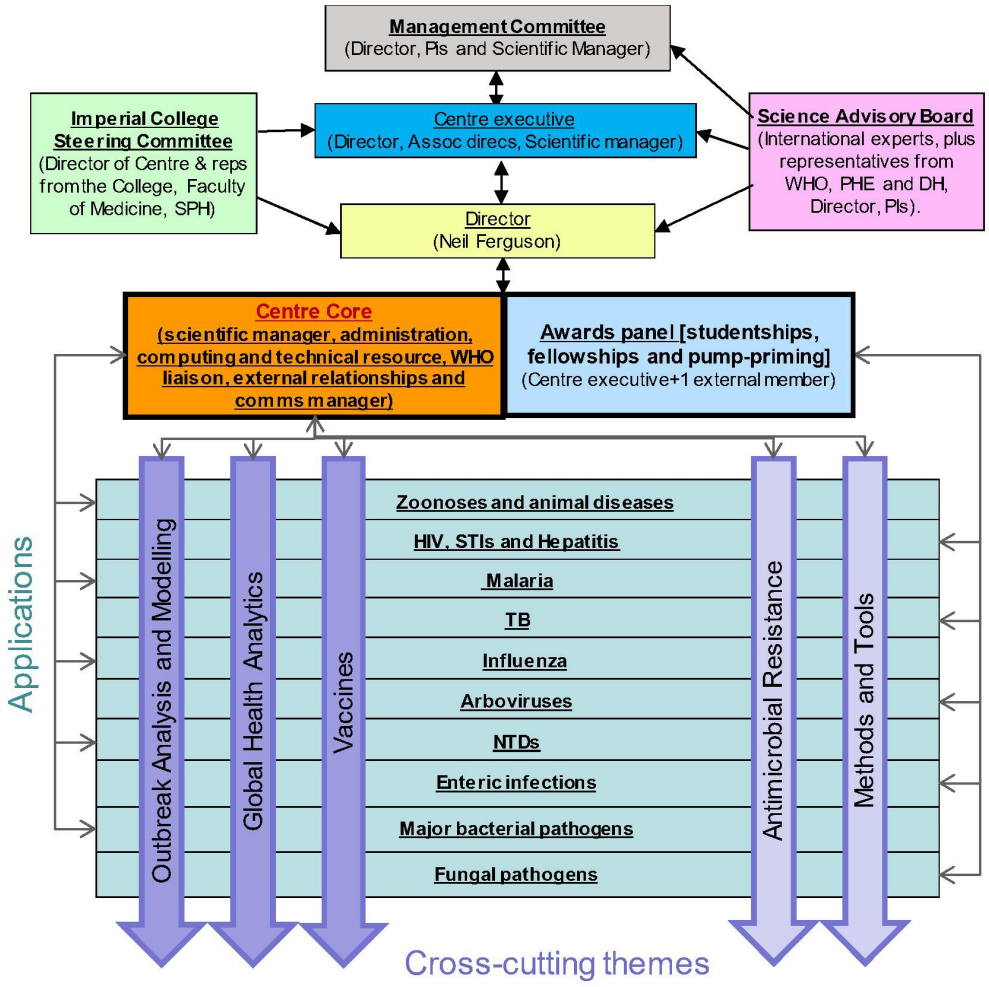

Figure: Structure of MRC GIDA. PI=Principal Investigator (*i.e.* academic staff of the Centre).

18. The mission of MRC GIDA is "*to be an international resource and centre of excellence for research and capacity building for the epidemiological analysis and modelling of infectious diseases*" and "*to undertake applied collaborative work with national and international agencies to support policy planning and response operations against infectious disease threats*".

19. Given our mission, we have established close working relationships with national and international public health bodies over the last 15 years:

    a. UKHSA (previously PHE): building on previous research collaborations, in 2014 Imperial College and PHE were awarded an NIHR grant to create the NIHR Health

Protection Research Unit (HPRU) for Modelling Methodology, a partnership between PHE and Imperial College London. In 2019 we were successful in a competitive bid to renew HPRU funding (this time for a unit titled the HPRU for Modelling and Health Economics), extending the HPRU partnership to include the London School of Hygiene and Tropical Medicine (LSHTM). The HPRU funds long term collaborative research between the partners and also provides "responsive mode" funding for short-term priorities. I have directed the HPRU since it was founded in 2014. In addition, I and other ICCRT staff contribute to two other NIHR HPRUs (again partnerships with UKHSA) hosted by Imperial College – in Respiratory Infections and in Healthcare Acquired Infections and Antimicrobial Resistance. We also have a number of staff with joint appointments between UKHSA and ICCRT (most notably Peter White, head of the modelling and economics unit at Colindale, and Steven Riley, now Director General for Data, Analytics and Surveillance for UKHSA), staff on long-term part-time secondments (Erik Volz), and a number of staff with honorary appointments at UKHSA.

b. The World Health Organization (WHO): in 2008, MRC GIDA was awarded WHO Collaborating Centre (WHO-CC) status as the first WHO-CC for Infectious Disease Modelling, building on the extensive links Centre staff had undertaken with WHO prior to the formation of the MRC Centre (e.g. on H5N1 avian influenza, SARS-1). WHO-CC status offers no funding but formalises a joint workplan across multiple areas of engagement and specifies the contexts under which WHO can call upon a CC for support. Since the formation of the CC, we have dramatically expanded our engagement with WHO, spanning not just work on epidemics and emerging infections, but also all major endemic disease threats (e.g. malaria, HIV, TB, dengue, yellow fever, hepatitis, polio, helminthic infections). In addition to work on COVID-19, in the past we have provided substantial analytical support to WHO during the 2009 H1N1 influenza pandemic (when I was an advisor on the WHO IHR Emergency Committee), during multiple Ebola outbreaks, and during the Zika epidemic in Latin America. Nearly all academic staff in MRC GIDA work with WHO, in many cases sitting on advisory panels.

c. Other international bodies: Over the last 15 years, we have developed close relationships with and have provided analytical support for most major international

public health organisations working on infectious diseases, including Gavi, the Global Fund, CEPI, PATH, the Bill and Melinda Gates Foundation (BMGF), the Wellcome Trust and the World Bank. Several of our staff and students have moved on to roles in those organisations.

d. Countries outside the UK: MRC GIDA researchers have research collaborations in approximately 80 countries world-wide, many low- or middle-income. Many of these links involve policymakers in those countries. Countries where there are particularly strong links (*i.e.* over many years, in multiple disease areas, or on largescale projects) include the USA, Singapore, Brazil, India, Zimbabwe, Malawi, Senegal, Colombia, Burkina Faso, Zambia and Indonesia.

20. The Jameel Institute at Imperial College was founded in 2019 with a substantial philanthropic donation (the majority used for capital investment in the new Imperial School of Public Health building) from Community Jameel, a large Middle Eastern philanthropy. Its remit is to use data analytics to address health emergencies, with a broader remit than MRC GIDA (*i.e.* including non-infectious disease health threats). The staff of the Jameel Institute overlap with those of MRC GIDA, and the work of the two bodies on the pandemic was entirely integrated. Hence much of the research on COVID-19 attributed to MRC GIDA in this document also benefitted from the financial support of the Jameel Institute and can also be attributed to the Institute.

D. Epidemiological analysis and modelling

Note: with the agreement of the Inquiry, this section was written with the assistance of Drs Charles Whittaker, Oliver Watson and Marc Baguelin. This section is duplicated in my module 2 statement.

Introduction

21. The aims of epidemiological analysis and modelling of infectious diseases are to understand the spread of pathogens and associated health burden on populations, and to inform public health strategies for control and elimination.

22. The distinction between epidemiological *analysis* and *modelling* is a not precise. Analysis (e.g. estimation of disease severity, or of vaccine effectiveness) makes use of sophisticated statistical models (e.g. linear regression, survival models) which embed assumptions (such as the linearity of relationships between variables) often just as much as dynamical

mathematical models of the type used to simulate epidemics. However, epidemic models attempt to represent more of the mechanistic process underlying disease transmission than purely statistical models, which focus on representing the correlations between variables.

23. All epidemiological models utilize data provided by surveillance systems and research studies to estimate epidemiological parameters, infer risk factors determining the spread or severity of the disease, and to give insight into the actual or potential effect of interventions. Outputs can support public health decision-makers, who use them to allocate resources, design and implement public health policies, and respond to outbreaks in real-time. Additionally, epidemiological analysis and modelling also provides insights into the long-term trends of infectious diseases, such as changes in disease burden and risk factors, and can help inform future prevention and control efforts.

24. The history of epidemiological modelling dates back to the 18th century, when the mathematician Daniel Bernoulli created a probabilistic model to assess the population benefit of the inoculation of smallpox. However, the history of modern epidemiological modelling is generally traced back to the early 20th century with the work of Ross (1911) and Kermack and McKendrick (1926-1927), who began studying the spread of transmissible diseases through populations over time. They developed mathematical models to better understand the dynamics of infectious diseases and the number and distribution of infections. Their work shared similarities with that of Lotka (one of the founders of theoretical ecology) and Volterra, who used mathematical models to study ecological systems such as predator-prey and host-parasite relationships. Since then, the discipline of epidemiological modelling has developed enormously, models have become hugely more sophisticated, but all current models still embed the core concepts included in those early models.

25. The very rapid growth in computing power seen over the last 40 years has driven the practical application of modelling to inform disease control, enabling models to incorporate much more detail (such as the structure of the human population). Perhaps even more importantly, that growth in computer power has allowed modern Bayesian statistical methods to be applied to epidemic models to allow rigorous estimation of epidemic model parameters by fitting models to epidemiological data.

26. Hence modelling has played an increasingly important role in informing public health responses to both major endemic pathogens (e.g. HIV, TB, malaria) and to emerging infectious

disease threat (e.g. SARS-1 in 2003, H1N1 pandemic influenza in 2009, Ebola, Zika, MERS-coronavirus). More specifically, real-time modelling can enhance situational awareness and support control policy planning.

27. In emerging infectious disease epidemics, such as COVID-19, early epidemiological analysis tries to address four questions:

    a. *How far has it got?*

       What's the true scale of the epidemic? What proportion of cases are being missed?

    b. *How fast is it spreading?*

       What is the epidemic growth rate, how fast is international spread?

    c. *How bad is it?*

       How severe is the infection? What health burden might an epidemic cause?

    d. *What can we do?*

       What are the policy options, what impact and costs might they have?

Model types

28. Infectious disease models can be broadly grouped into three categories:

    a. *Statistical models*, which do not explicitly model the mechanism of transmission, but instead aim to estimate either summary statistics (e.g. epidemic doubling time) or epidemiological parameters (e.g. incubation period, infection fatality ratio (IFR), vaccine effectiveness, excess deaths, properties of new variants). Because such models don't represent the transmission process, they are not well-suited to predicting medium or long-term epidemic trajectory, disease burden or the impact of interventions on transmission.

    b. *Mechanistic transmission models* (often called epidemic models), which explicitly account for the underlying mechanisms of disease transmission and aim to identify the drivers of transmissibility. They make more assumptions about disease dynamics and require transmission parameters to be estimated or assumed. Such models can be used to estimate epidemiological parameters such as the reproduction number (R), but their most useful application is examining the potential impact of interventions, especially on transmission.

    c. *Semi-mechanistic models*, which are a blend of both statistical and mechanistic models – they represent some aspects of transmission dynamics (mathematically, by representing

an epidemic via a renewal equation or branching process) but in a simpler way than full epidemic models. They are best suited to estimating epidemiological parameters such as R and making short-term epidemic projections.

29. Mechanistic transmission models can further be divided into two broad categories:

    a. *Individual-based models* (also called agent-based models or microsimulations), which explicitly represent every individual in a population, and can therefore be arbitrarily complex in how population structure (e.g. inclusion of households, schools and workplaces), disease transmission (e.g. inclusion of super-spreading) and progression (e.g. variation in time to or probability of hospitalisation) is represented. Individual-based models have the disadvantage of being relatively computationally costly, due to the computation required to track and evolve the states of millions of individuals.

    b. *Compartmental models*, which only track the number of individuals in the population in certain categories or states (e.g. susceptible, exposed, infectious and recovered – SEIR) and the flow of people between these states. While such models can stratify populations by characteristics such as age and/or region of residence, they represent the population (and therefore the transmission process) in a coarser-grained manner than individual-based models. However, compartmental models have the major advantage of being much less computationally complex to run, making them more suited to repeated real-time use in an epidemic. They also tend to have fewer parameters which need to be estimated or assumed than individual-based models.

30. While individual-based models always simulate an epidemic as a stochastic (*i.e.* random) process (meaning that no two simulations are precisely identical), compartmental models can be coded to be either deterministic (approximating epidemic spread as the average flow of people between states) or stochastic (representing the randomness of transmission and other processes). Stochastic models are more realistic, since transmission is a random process in reality, but are more computationally costly to run, especially given multiple model runs are typically needed to calculate average trends. Deterministic models provide a good approximation of disease dynamics when random fluctuations are small – *i.e.* when case numbers are high and a large population is being modelled.

31. Individual-based models allow for a more nuanced and detailed simulation of the spread of disease (including tracking disease spread from individual to individual), as well as more

precise representation of individual-level factors (such as households and workplaces that an individual spends their time within). As such, they are better suited to modelling non pharmaceutical interventions (NPIs) such as case isolation within the home, contact tracing or working from home.

32. Compartmental models do not capture the complexities and heterogeneity of individual behaviour, and so mostly have to represent all NPIs in the same way – as reductions in population contact rates or a change in R.

33. Epidemiological modelling is a far more multi-disciplinary exercise than might be expected; to develop and parameterise a transmission model, information is needed on:

    a. The natural history of infection – how infection progresses in a person, and how variable this is.

    b. Clinical severity and healthcare burden – the proportion of infected individuals who will be symptomatic, ill enough to require hospitalisation or ICU, the proportion who will go on to die – and information on the risk factors for severe outcomes (e.g. age).

    c. Transmission patterns – estimates of R from the epidemic itself, plus more detailed data on transmission derived from epidemiological studies (e.g. household studies, infection surveys).

    d. Demography – the age distribution of the population, population sizes locally, regionally or nationally (depending on the geographic scope of a model). For individual-based models, data on household composition, workplaces and schools are also needed.

    e. Population behaviour – most notably data on "who contacts who", typically derived from contact surveys. Data on population mobility (e.g. from mobile phones) can also be used as a proxy of overall contact rates. Behavioural surveys can provide information on the propensity to seek testing, wear masks or adhere to voluntary guidelines or mandatory measures.

    f. Intervention effectiveness – treatments, vaccines and NPIs. Randomised clinical trials provide the gold-standard estimates, but observational studies are equally important, especially for NPIs (given these have rarely been evaluated in randomised trials).

g. Immunology – to characterise the dynamics (e.g. duration) of infection- and vaccine-induced immunity and the level of protection provided against infection, mild disease, severe disease or death.

h. Viral genetics and evolution – new variants can have different properties, which need to be captured in models.

34. During the COVID-19 pandemic, we developed all three categories of models, including both deterministic and stochastic compartmental models (see module 2 statement).

Retrospective versus prospective modelling

35. Infectious disease models can be applied either retrospectively or prospectively:

a. *Retrospective modelling* involves fitting models to past data to analyse epidemic patterns, calculate epidemiological parameters such as the reproduction number, and evaluate the effect of prior interventions (e.g., determining the impact of non-pharmaceutical interventions).

b. *Prospective modelling* involves projecting future epidemic trends based on current information, often drawing on parameters and trends estimated using retrospective modelling.

36. There are two major types of prospective modelling:

a. *Prediction/forecasting* is a structured form of prospective modelling that involves making statistically rigorous predictions based on a set of assumptions, with the goal of making accurate forecasts. Typically forecasts for infectious diseases such as COVID-19 are only made over a time horizon of a few weeks, since epidemic trajectories (akin to the weather) are non-linear phenomena which tend to be poorly predictable over longer horizons due to, for example, changes in population behaviour, government interventions or even climate. Models used for forecasting can be mechanistic, semi-mechanistic or statistical.

b. *Scenario modelling* involves examining multiple medium- to long-term scenarios concerning the future of an epidemic, often exploring the potential outcomes of a menu of policy alternatives requested by policymakers. For example, scenario modelling was used in the COVID-19 pandemic by SPI-M-O to project how healthcare demand might be affected by proposed government interventions[2]. Mechanistic models are needed for scenario modelling.

37. The distinction between scenario modelling and forecasting is important and largely reflects the distinct types of questions that each approach is best suited for. Scenario modelling answers "What if" questions, such as "What would ICU admissions be if new NPIs were introduced next month?". Forecasting focuses on "What will" questions, such as "What will daily COVID-19 cases be in a week?". Scenario modelling should not be viewed as formal prediction; in reality, actual government policies rarely if ever precisely match what was modelled, and precise prediction of the impacts of policy and population behaviour changes is generally not possible.

38. Research spanning many application areas of modelling (beyond just infectious diseases) has demonstrated that more reliable short-term predictions are obtained by using an ensemble of multiple different models than any single model can typically provide. Such approaches were adopted by a number of countries in the COVID-19 pandemic to provide short to medium term forecasts or projections of trends in cases, hospitalisations and/or deaths (e.g. in the US[3]). This approach was used by SPI-M-O during the pandemic to generate R estimates and medium term (typically <4 week) projections. Ensemble approaches combine probabilistic estimates or projections made with multiple different models (for SPI-M-O, typically 8-12) in a statistically principled manner. SPI-M-O published an assessment of its approach to projections in December 2020[4]. Formal ensemble methods are less commonly used for scenario modelling, but more qualitative comparison of the results from multiple different models was standard practice for SPI-M-O throughout the pandemic when modelling intervention options or long-term scenarios.

Uncertainty, parameterisation, validation and verification

39. Uncertainty is inherent to epidemiological analysis and modelling. It is present across every aspect of the modelling process; from collection of the data used to calibrate the model, to design choices around model structure, to generation and interpretation of model outputs. Modellers must take into account numerous sources of uncertainty, including data limitations (*e.g.* case underreporting due to limited testing capacity), the uncertainty in epidemiological parameters arising from limited data (such as the basic reproduction number) and the inherent stochasticity in how pathogens spread through populations. These sources of uncertainty mean that modellers frequently make probabilistic projections which incorporate uncertainty in model parameters in a statistically principled manner. Where a full probabilistic analysis isn't feasible, sensitivity analysis can be used to show how model outputs vary

depending on the values assumed for key parameters (or sometimes structural assumptions) for which there is significant uncertainty. It should be emphasised that both approaches are ways of *presenting* model uncertainty; neither *reduces* uncertainty. Formal forecasting is now most commonly undertaken in a fully probabilistic framework (e.g. the SPI-M-O medium term projections), as this also allows results from different models to be more easily integrated into an ensemble forecast. Scenario modelling and other forms of illustrative modelling (e.g. to assess the potential effect of single policies such as bubbles) can make use of probabilistic methods (i.e. providing probability distributions for all model outputs, rather than single values), or use sensitivity analysis; both approaches were commonly used in SPI-M-O modelling throughout the pandemic.

40. As simplified representations of complex social and biological systems, epidemic models have intrinsic limitations. For instance, models typically represent human behaviour as constant over time, modified only by interventions. In reality, behaviour has changed over the pandemic in response to government policy, messaging and public perceptions of risk – often in unpredictable ways. Very few models attempt to predict such changes, largely because we don't have a good quantitative and predictive understanding of them.

41. Uncertainty is highest during the early stages of an epidemic, when data availability is most limited. This is particularly the case for novel pathogens such as SARS-CoV-2 where the absence of previous outbreaks in human populations precludes use of historical data. This leads to significant uncertainty in estimation of key parameters in epidemiological models, such as the basic reproductive number, the incubation period, and disease severity. However, as more data become available, epidemiological models can be refined and uncertainty reduced, allowing for more precise modelling and informed decision-making.

42. During an epidemic, major changes in interventions, population behaviour or the pathogen can introduce additional uncertainty. Examples include the implementation of new (previously untested) NPIs, external events that affect behaviour (such as the 2020 Euros football tournament leading to a surge in cases), new technologies (such as lateral flow testing or the Covid app), new therapeutics (such as vaccines), or changes in the biology of the pathogen (such as the emergence of a variant with distinct epidemiological characteristics).

43. Uncertainty in epidemiological modelling is typically larger for prospective modelling (looking forwards in time) than retrospective modelling (looking backwards). Prospective modelling

necessitates making assumptions about future events or trends which are inherently uncertain. It is also necessarily based on data from the past and therefore relies on an assumption that past dynamics are representative of expected future dynamics – an assumption that can be invalidated by new variants or major changes in policy or population behaviour.

44. Modellers try to reduce uncertainty by obtaining the most precise estimates of model parameters possible, using a wide range of data sources. These include behavioural data (describing population-level patterns of behaviour relevant to pathogen transmission such as the degree of adherence to control measures); demographic data (important for diseases like COVID-19 where severity varies with age); and data from epidemiological studies (e.g. on the incubation period). Where possible, parameters are estimated from such independent sources, but where this isn't possible, unknown parameters can be estimated by fitting epidemic models to surveillance data - this "tunes" parameters in a statistically principled way (e.g. using Bayesian methods) to find values which allow a model to best reproduce epidemic trends.

45. A particular challenge for epidemic modelling is that epidemics are only partially observed; recorded case counts only represent a fraction of total infections, since not everyone develops or recognises symptoms, or seeks testing. Data on infection *prevalence* is therefore particularly valuable – the proportion of the population who have been infected thus far in an epidemic (measured through serological surveys) or the proportion who are infected now, irrespective of symptoms (measured through studies such as the ONS or REACT infection surveys). Such data allow estimation of the degree to which recorded cases underascertain infections, allow tracking of the accumulation of immunity in the population, and allow reliable estimates of the IFR and IHR to be made.

46. Model verification is testing whether the code used to represent a model is formally correct (*i.e.* gives the correct solution to the equations used to specify the model). In reality, as is the case for most mathematical modelling in science, formal verification (in the computer science sense of the term) is rarely feasible for all but the simplest epidemic models. Therefore, a number of more heuristic approaches are used to check model implementations. One is to compare the outputs of different models when each is configured with the same parameters. A second is to examine model output for simplified "edge cases" where model output can be compared with analytical calculations or solutions of much simpler models. Another – for

models which are designed to be fitted (using Bayesian methods) to data – is to test the that model fitting code produces unbiased estimates using simulated data.

47. Moreover, the last 20 years have seen increasing professionalisation of research software development, assisted by version control, unit testing and the advent of tools such as GitHub – and coinciding with a trend towards teams rather than individuals developing code, open source development and code modularisation and reuse. ICCRT has a professional research software engineering (RSE) team of some 10 staff, many of whom contributed substantially to the development of the new COVID-19 models we created in response to the pandemic.

48. If time and resources permit, model code can also be reviewed by independent groups. However, this is uncommon, and rarely even forms part of peer-review of scientific papers making use of model (statistical or mechanistic) output. That said, the pandemic has seen an acceleration of pre-existing trends for journals to require that code and data are published with scientific papers to allow results to be reproduced. Except where prevented by data protection issues (associated with the analysis of individual-level data), ICCRT have followed this principle with our peer-reviewed journal articles on COVID-19 and the majority of our reports and preprints. All our COVID-19 epidemic models are open source.

49. Model validation is a less precisely defined term than verification, but is generally the process of checking that a model provides an "adequate" description of the system the model is designed to represent. Often this involves fitting a model to surveillance data (mentioned above). Model fitting is a statistical procedure involving exploring a large range of parameters to determine the sets of parameters that are most consistent with the observed data. The plausibility of the resulting parameter estimates and the model's ability to accurately capture the epidemiological patterns present in the data can then be assessed. Other methods of validation may include external validation, which involves the comparison of model outputs to independent data sources not involved in model fitting – so-called "out-of-sample" validation. In general, true out-of-sample predictive validation of epidemic models is challenging, since no two epidemics are identical (e.g. COVID-19 pandemic trajectories in different European countries), meaning some parameters always need to be re-estimated. However, for prospective analyses focussed on forecasting, assessment of past predictions from previous rounds of forecasting (but not scenario analysis) can be used for model selection and to refine models.

50. When modelling is being used to inform policy-making and model development is occurring under severe time pressure, an additional check on the robustness of model outputs or policy-relevant conclusions is to compare the outputs of independently developed models. This is the principal approach to model validation adopted by SPI-M-O. Throughout the pandemic, comparable modelling was requested from multiple academic groups; never less than two, and nearly always 3 or more.

Uses of statistical and semi-mechanistic models

51. Early in an emerging infectious disease epidemic, statistical models are used to estimate epidemiological parameters such as the incubation period, serial or generation interval, symptomatic fraction, the infection hospitalisation ratio (IHR), the case fatality ration (VFR), and the infection fatality ratio (IFR) – and to understand how those parameters vary over time and with risk factors such as age or pre-existing medical conditions.

52. Statistical or semi-mechanistic models are used to estimate epidemic growth rate (*i.e.* doubling time) and/or R.

53. In general, the choice of model utilised depends on a combination of the exact research question being asked and the data available.

54. An important distinction is whether available data is at the individual-level (i.e. data on every case) or aggregate (e.g. counts of cases per day). Individual-level data are essential for estimation of the incubation period, serial interval and other delay distributions. They are also important for evaluating differences between groups of cases – such as assessing how disease severity varies with age, sex, ethnicity, vaccination history or the variant of virus causing the infection.

55. Individual-level data is also essential for analyses which rely on data linkage – for instance, evaluation of how disease severity (IHR and IFR) varies by virus variant, or estimation of vaccination effectiveness (VE). In the COVID-19 epidemic, many UKHSA and SPI-M-O analyses relied on (anonymous) linkage of multiple large databases of COVID-19 testing records, hospital episode records, vaccination records, deaths and viral genetic sequences.

Mechanistic epidemic models for respiratory viruses

56. Mechanistic transmission models for respiratory viruses such as COVID-19, influenza, respiratory syncytial virus (RSV) and measles typically have the same basic structure. These

models aim to describe the spread of the disease in a population by tracking the infection and disease states of either groups of individuals in a population (in the case of compartmental models) or individuals (in the case of individual-based models).

57. In all respiratory virus models, transmission of the pathogen is driven by a combination of the rate at which individuals make contact with one another, the probability of successful transmission upon contact and duration for which individuals remain infectious.

58. Because the transmission route is the same for all respiratory viruses, the same population contact rate data (on social contacts) is used to parameterise influenza, measles and COVID-19 models. Transmission models do not represent the physics of transmission, and hence do not distinguish between, for instance, droplet versus aerosol transmission. However, models of diseases with very different transmission routes (e.g. sexually-transmitted or water-borne) do differ in structure from respiratory disease models.

59. Hence the fundamental approach to modelling different respiratory viruses is largely the same, with the differences between models of different pathogens primarily being in how a model is parameterized – with R_0, the incubation period, infectious period, infection hospitalisation ratio (IHR) and infection fatality ratio (IFR) being key parameters, plus how some of these parameters (e.g. susceptibility, symptomatic proportion, IHR and IFR) vary with age and by other population characteristics. Hence a model coded to model COVID-19 can be repurposed to model the next influenza pandemic, so long as parameter values are appropriately updated. The converse is also true.

60. Respiratory virus models are parameterised to represent contact patterns (and sometimes networks) relevant for respiratory virus transmission. Contact patterns refer to the frequency and duration of interactions between individuals, while networks describe the relationships between individuals in a population. Understanding these is essential for predicting the potential spread of a virus and for informing effective control measures. Models that take into account the specific ways in which individuals interact, can potentially (if they can be parametrised) provide more accurate predictions of transmission patterns and the effects of NPIs than those which more crudely capture overall contact rates.

61. When designing models, choices are often required about the level of granularity to include. These decisions are often based on the specific questions a modeller is aiming to answer and the availability of data. For example, if the goal is to forecast hospital demand, a model may

need to include explicit information about the passage of COVID-19 patients admitted to hospitals and the time spent in different types of facilities (*e.g.* general ward versus ICU). The availability of data to parameterize models also plays a role in determining the level of granularity, with the absence of data often limiting the complexity of models that can be reasonably justified. For example, extending models to differentiate droplet versus aerosol transmission (or transmission associated with indoor versus outdoor contacts) would introduce additional model parameters that currently are unable to be reliably estimated from available data. In such cases, it is often better to use simpler models with more coarse-grained representations of contact processes for which data are available.

62. Population heterogeneity (*i.e.* differences between people) is the type of granularity most frequently considered by modellers. Appropriately representing heterogeneity is important for accurately representing transmission and disease risk. Models can represent person-to-person variation in characteristics such as contact rates, infectiousness, susceptibility, and severity. Nearly all respiratory virus epidemic models allow model parameters to vary by age, given age is a predictor of both contact rates and clinical outcome. Compartmental models are limited in their ability to represent heterogeneity (though regional variation is often included), while individual-based models have fewer constraints. A type of heterogeneity which was important early in the pandemic was variation in the number of secondary infections an infected person generated (so-called super-spreading), and a range of individual-based models were developed to examine the implications of this for control (*e.g.* [5,6]).

63. In a long-running epidemic, it is common to extend and update models to incorporate new evidence as it becomes available. For example, while we were aware that reinfection occurs with endemic (and antigenically diverse) human coronaviruses typically every two years, the expectation that infection would generate good protective immunity for at least a year meant that early models did not include the waning of immunity. As data became available on the duration of immunity induced by COVID-19 infection in late 2020, models were updated to account for this. Additionally, models may need to be extended to be able to model the effect of new interventions, such as vaccines and novel therapeutics. Furthermore, the emergence of new variants of a virus with distinct epidemiological properties requires models to be extended to model more than one variant at once circulating in the population, each with sometimes subtly different epidemiological parameters. All such extensions increase model complexity and the computational cost associated with running models.

64. Models for endemic diseases (such as seasonal influenza or measles) differ from those used to model the initial epidemic of a new virus. At the start of the pandemic, there was no immunity in the human population, meaning spread occurred between individuals of all ages. At the opposite extreme, measles only infects young children because everyone else has (lifelong) immunity. Thus, to model measles, it is essential for models to include births (and deaths), given it is newly born children who renew the susceptible population the virus can then infect. This type of dynamics has not yet been important for COVID-19, so few COVID-19 models include new births into the population (or other demographic processes such as migration). I would also comment that endemicity for COVID-19 will be more complex than for measles, given the rate of viral evolution and that immunity wanes over time.

The reproduction number, R

65. The basic reproduction number, R_0, is a metric that quantifies the average number of new cases generated by a single infected individual in an uninfected (entirely susceptible) population (i.e. at the start of an epidemic). It is determined by the combination of the rate at which individuals contact one another; the length of time individuals remain infectious, and the probability of pathogen transmission per contact event. It determines the potential for an epidemic to occur, as a spread will only continue and grow in a self-sustaining way if R_0 is greater than 1 and will diminish if R_0 is less than 1.

66. As immunity builds up in a population (due to infection or vaccination) and/or control measures (e.g. social distancing) are implemented, transmission intensity is reduced and we quantify this by the so-called time-varying reproduction number, R (also labelled R_t or R(t), where t is time) – the average number of new infections generated by a single infected individual at that stage of the epidemic. If R is above 1, the epidemic will be growing, while if it is below 1, daily case numbers will be declining. By tracking the changes in R, public health officials can monitor the effectiveness of control measures and make informed decisions on how to respond to potential surges in cases.

67. If the aim of policy is to suppress transmission and hence cause daily case numbers to decline, interventions need to reduce R to below 1. This means that R_0 also determines the control effort required for suppression. For example, if R_0 is 2, 50% of transmission needs to be blocked to get R to 1, while if R_0 is 4, a 75% reduction in transmission is required.

68. R solely quantifies epidemic growth rate; it says nothing about incidence measures such as the number of daily new cases or hospital admissions.

69. R can be estimated in a variety of ways, but most commonly using methods that analyse trends over time in disease indicators – such as incidence (reported confirmed cases, hospitalisations, or deaths) or prevalence (as measured by the ONS and REACT infection surveys). Estimation is complicated by several challenges during an epidemic. These include reporting delays (which make recent case counts appear lower than the true value and lead to erroneous conclusions of epidemic decline unless corrected for), and changes in testing capacity and propensity to test over time (which alters the fraction of infections being captured by surveillance systems over time and which can therefore present erroneous pictures of epidemic growth). Furthermore, in the case of an emerging infection such as SARS-CoV-2, the natural history of the pathogen is often not well understood at the start of the epidemic, which adds to the uncertainty in estimates of R. This is because estimating R requires good estimates of a parameter called the *generation interval*, which measures the distribution of time between when cases become infected and when they transmit to others.

70. R can only be estimated retrospectively; COVID-19 cases recorded today were likely infected a week or more ago, and new admissions to hospital were likely infected even longer ago. Hence estimates of R based on current data reflect transmission in the past. Given the range of data sources used by SPI-M-O groups to estimate R during the pandemic, and the 3-4 days it took for new R estimates to be signed-off, most of the weekly official R estimates released by the UK government actually quantified transmission trends 2-3 weeks earlier.

E. The role of epidemiological analysis and modelling in pandemic preparedness

Note: This section largely repeats a matching section in my module 2 statement.

71. I have 20 years of experience researching interventions to control the spread of respiratory and other viruses. This includes work on SARS-1[7], 1918 "Spanish" Influenza[8], H5N1 "bird flu" and related preparedness research[9,10,11], Ebola[12], MERS-CoV[13] and, most recently, COVID-19. In addition, I have also worked on livestock pathogens, notable BSE[14] and foot-and-mouth disease (FMD)[15,16].

72. Modelling can inform pandemic preparedness planning in three key ways:

a. Characterising past pandemics

b. Assessing the likely impact of interventions

c. Modelling of future pandemic scenarios and associated intervention options

73. Interventions deployed in an epidemic fall into three broad categories:

a. Vaccines – to prevent infection or illness.

b. Therapeutics (e.g. antiviral drugs) – to treat illness and/or reduce infectiousness.

c. Non-pharmaceutical interventions (NPIs) – measures to reduce infectious contacts between infected and uninfected individuals.

74. NPIs span a wide range of measures which can also be divided into three classes by the population groups targeted:

a. *Border controls* – targeting people entering a region (usually a country). Testing and quarantine of international visitors was introduced by most countries during the COVID-19 pandemic, with varying levels of effectiveness.

b. *Case-focussed measures* – targeting suspected or confirmed cases of infection. Isolation of suspected or confirmed cases (in quarantine units or at home) is the most obvious measure and was introduced by most countries during the pandemic. The next step is to isolate contacts of cases – identified either through group membership (*e.g.* members of the same household, school class or workplace group) or via explicit contact tracing. Most countries introduced such measures, again with varying levels of effectiveness.

c. *Community-focussed measures* – these measures aim to reduce (infectious) contacts between all individuals, on the basis that not all infected individuals can necessarily be identified rapidly enough for purely case-focussed measures to achieve sufficient control of transmission. Most of the social-distancing measures adopted by different countries during the pandemic fall into this category (*e.g.* working from home, stay at home orders, closing schools and universities, closing hospitality venues, closing non-essential retail, limiting gatherings of people from different households, recommending minimum physical separation distances), as do mask-wearing mandates.

75. Randomised clinical trials (RCTs) represent the gold standard for gaining evidence about the effectiveness of interventions. However, RCT results are lacking for nearly all NPIs, due to the difficulties of running such studies and the relatively rare situations such interventions are deployed. Face masks are the one exception, but prior to the pandemic only one RCT of face mask use in a community setting had been conducted, to my knowledge (all others being in clinical settings). I had worked with an Australian clinical colleague on that one study, which examined the effectiveness of mask use at preventing influenza transmission in households[17].

76. Despite the lack of RCT evidence, considerable effort was invested in the analysis of observational datasets to assess the likely effectiveness of NPIs as part of pandemic planning following the 2003 SARS-1 outbreak and the re-emergence of H5N1 in South East Asia in 2005. I was heavily involved in much of this work via my then involvement in the US NIH-funded MIDAS network[18].

77. My preparedness research in the period 2004-2008 had two streams:

    a. Estimating the effectiveness of NPIs from historical data. This spanned evaluation of the effectiveness of border measures[19], analysing data from the 1918 influenza pandemic on mortality and the timing of NPI use in different US cities to estimate the effectiveness of the NPIs (mostly social distancing measures such as closure of schools, bars and churches) used then[8], and analysis of seasonal influenza data from France to estimate the potential impact of school closure as an NPI to limit pandemic influenza transmission[20].

    b. Using simulation modelling to examine different strategies for NPI, antiviral and pre-pandemic vaccine use in a future lethal influenza pandemic. I first examined the feasibility of containing (*i.e.* eliminating) a nascent pandemic in its source location[9] – which concluded elimination was only likely feasible if the outbreak was detected at a very early stage and intensive NPIs were deployed. I then examined the layered use of NPIs (border, case and community-focussed) and stockpiled antivirals to mitigate the health impacts of an influenza pandemic[9]. This work informed pandemic planning in the US[21] and UK (*e.g.* page 41 of the 2011 UK Pandemic Preparedness Strategy[22]) . The research made use of the large-scale individual-based simulation model which was later adapted to model NPI strategies for COVID-19[23].

78. Given the lethality of a future pandemic virus is unknown, I did not model healthcare demand or mortality when simulating potential future pandemic influenza scenarios in the work

described above[9]. My analysis solely focussed on the impact of interventions on the potential total number of infections or symptomatic cases.

79. In UK pandemic preparedness planning up to 2018, DHSC analysts (at that time led by Dr Peter Grove) translated symptomatic case numbers into predicted health-care demand and mortality using agreed UK government RWC assumptions for an influenza pandemic. I believe there was considerable work examining the implications of these planning scenarios for the NHS (*e.g.* emergency triage protocols, resource implications such as refrigeration capacity, body bags, PPE), but I was not personally involved in that work.

80. Richard Hatchett, now CEO of CEPI, but then a member of the White House Homeland Security team can give a policy-focussed perspective on much of the US pandemic preparedness planning regarding NPI use undertaken between 2005 and 2009.

81. The past work on pandemic mitigation described above did not model long-term large-scale use of intense community-focussed NPIs to suppress (*i.e.* achieve R<1) influenza transmission for many months; rather, the focus was on the extent to which "feasible" NPIs (case isolation, household quarantine, time-limited closure of schools only after cases are detected in them, limited reactive closure of a minority workplaces with outbreaks, border restrictions) together with antiviral use might mitigate a pandemic wave – *i.e.* reduce numbers infected and/or flatten and delay the peak of the pandemic in an affected country.

82. I cannot recall any discussion of the potential use of long-term suppression policies (outside the containment at source context) in meetings with public health policymakers in either the UK or US prior to 2020. The goal of the pandemic preparedness planning I was involved in prior to 2020 was to minimise the health impact of a pandemic while still allowing society to function as close to normally as possible, thus limiting economic and social disruption.

83. Containment/suppression was only viewed as a viable option for outbreaks of high severity pathogens which were limited in size and geographic scope and where the elimination of the virus from the human population therefore seemed feasible. Real-life examples include SARS-1 and the West Africa and DRC Ebola epidemics – where control achieved elimination of those epidemics largely via case-focussed measures (case isolation and contact tracing).

84. Thus the decision by the UK and many other countries in March 2020 to adopt long-term use of NPIs to suppress (*i.e.* reduce R to below 1) COVID-19 transmission until vaccines were available was a paradigm shift in the global response to a pandemic. Such an approach was

never anticipated in prior UK pandemic preparedness planning, which at most had considered transient NPI use to mitigate (but not stop) a pandemic wave. In addition, none of the previous infectious disease crises I detail approached the COVID-19 pandemic in terms of their health, economic or societal impact, or their duration. Also, none required a policy paradigm shift of the magnitude that the COVID-19 pandemic required.

F. 2001: the UK FMD epidemic and 9/11

85. I will not review the history of the Foot and Mouth Disease (FMD) epidemic here; the UK response to this livestock epidemic was reviewed by the Andersen inquiry[24], and the scientific response by a Royal Society report[25].

86. At its start, MAFF (the Ministry of Agriculture, Fisheries and Food) had sole responsibility for both the operational and technical/scientific response to the epidemic. However, approximately one month after the detection of the first case, the then GCSA David King (after an intervention by the then chair of the Food Standard Agency, John Krebs) created a relatively small (approximately 15 individuals) emergency scientific advisory group involving both MAFF scientists and veterinarians and external scientists (including myself). This group, via the GCSA, provided scientific advice to COBR.

87. Mathematical modelling of the epidemic played a central role in informing the policy response to the outbreak. Modelling on the FMD emergency advisory group was principally provided by three groups: Imperial College (Roy Anderson, Christl Donnelly and myself), Warwick/Cambridge/Edinburgh (Bryan Grenfell, Matt Keeling and Mark Woolhouse) and by a Veterinary Laboratory Agency (VLA) team. None of these teams received significant additional financial support for their work on the epidemic; the only funding Imperial received was a small amount to purchase an additional PC.

88. One of the Andersen Inquiry recommendations (which was adopted) was that "DEFRA's Chief Scientist should maintain a properly constituted standing committee ready to advise in an emergency on scientific aspects of disease control".

89. The GCSA (and government more widely) also recognised the value of a senior scientific advisory group reporting to the GCSA (and relevant departmental CSA) at times when COBR was stood up.

90. The events of 9/11 in 2001 and the anthrax attacks in the US beginning a week later also highlighted the need for increased readiness to respond to civil contingency events which might require a scientific input into response efforts, especially in context where data were limited and uncertainty was high. In the UK, these considerations motivated the creation of the Cabinet Office Civil Contingencies Secretariat under Bruce Mann and the development of the National Risk Register[1]. David King and Bruce Mann are well-placed to give insight into how the UK refined its planning for civil contingencies at around that time.

91. As a result of events in 2001 and discussions within the UK government about civil contingency planning, David King created and ad hoc advisory group called SAPER – the scientific advisory panel of emergency response. I believe it was existence from 2002 to 2009, but given a substantial part of its remit was to consider terrorism-related threats (as well as "natural" contingencies), much of the panel's work was classified, meaning its membership, activities and start and end dates are not in the public domain. I was not a member of SAPER, though I contributed to some of the horizon-scanning activities it oversaw and to a related (classified) Home Office advisory group.

92. SAPER largely if not entirely acted as an advisory group on civil contingency preparedness (including some aspects of threat assessment/horizon scanning). I am not aware of whether it ever acted in the emergency role SAGE later adopted (e.g. during the SARS-1 crisis in 2003 or when COBR was called after the 7th July 2005 London bombings).

93. I believe SAPER was dissolved in 2008 or 2009 during John Beddington's tenure as GCSA.

G. 2003/4: SARS-1

94. The Imperial group, then led by Roy Anderson, played a significant role in epidemiological analysis and modelling of the SARS-1 outbreak[26,27], initially largely focussed on supporting the response of the Hong Kong government. Roy Anderson and I also provided largely informal advice to David King on occasion during the crisis. I am not aware of any SAGE-like group being stood up at that time.

95. Again, I will not review the SARS-1 epidemic here or our work on it. However, SARS-1 highlighted how quickly novel viral infections could spread globally, and triggered substantial research (at Imperial and many other groups) to improve models of global spread of emerging infections, and of epidemic mitigation and containment.

96. SARS-1 was able to be eliminated from the human population due to the highly severe disease it caused (which allowed nearly all infected individuals to be identified and isolated) and because viral shedding was low in early infection – meaning quarantining of pre-symptomatic contacts of cases was effective at breaking chains of transmission. In addition, the generation interval (time between one person being infected and that person infecting someone else) was relatively long (approximately 8 days on average), making the practicalities of contact tracing and quarantining easier. Nevertheless, the eventual containment of the outbreak in mainland China required an enormous country-wide effort.

97. Following the epidemic, many of the heavily affected countries, perhaps most notably China, invested substantially in improving surveillance for respiratory pathogens, in virological laboratory capacity and in public health systems and infrastructure. The impetus for such investment was further strengthened by later outbreaks of avian influenza (notably H5N1 – see below), and, in the case of South Korea, MERS-CoV. The net result was that China and multiple SE Asian countries were in a relatively strong position to scale up surveillance and testing at the start of the COVID-19 pandemic.

H. 2004-8: Pandemic preparedness in the UK

98. In the summer of 2003, highly pathogenic H5N1 avian influenza was detected in a number of countries in SE Asia, including China, South Korea and Thailand. In 2004, large outbreaks were seen in poultry populations in Thailand and Vietnam, with some human infections detected (of whom over half were lethal). Prior to 2004, the largest outbreak of H5N1 had been in Hong Kong in 1997. This was controlled by mass culling of the poultry population of Hong Kong, following detection of 18 human infections (6 of whom died). Vietnam and Thailand likewise initially responded to the outbreak with culling of poultry flocks, together with enhancements in biosecurity and, later, vaccination of poultry.

99. The emergence of an avian influenza strain which was highly transmissible between poultry and was able to directly (if inefficiently) infect humans and which caused very severe illness in most human cases rang alarm bells globally, particularly in the aftermath of the SARS epidemic. It led to major government investments in pandemic preparedness and influenza research in many high-income countries, including the UK and US.

100. My work on pandemic preparedness began in late 2003, when I started participating in a US NIH-funded MIDAS[18] consortium (led by a Johns Hopkins university group) and the EU Framework 6 funded INFTRANS project. The MIDAS network quickly became well-connected with the US policy community (CDC, ASPR and the Homeland Security Council) and much of the work I undertook between 2004-7 had as much of a US as a UK focus.

101. As part of MIDAS, I also worked with the staff and leadership of the Biomedical Advanced Research and Development Authority (BARDA[28]) in the first few years after its creation in 2006. BARDA lies within the Administration for Strategic Preparedness and response (ASPR), part of the US Department of Health and Human Service (DHHS). In my view, BARDA was responsible for strategically important and farsighted investments in pandemic vaccine research and development, including novel manufacturing platforms.

102. I became involved in UK policy-focussed pandemic preparedness modelling in early 2005, initially feeding into ad-hoc meetings held by the Department of Health, and then into a scientific advisory group on pandemic influenza (SAG) chaired by David Harper. Other key participants were John Edmunds (initially when he was still at HPA Colindale), Steven Leach (HPA Porton Down) and Peter Grove (head of DH's operational modelling team).

103. A key early UK government decision informed by the work of SAG was the purchase of 14.6 million courses of Tamiflu, the influenza antiviral drug – sufficient to treat 25% of the population.

104. In March 2007, the UK government published a new national framework for responding to influenza pandemics[29]. This was very substantially informed by SAG discussions and work over the previous 2 years and also highlighted the role for scientific evidence and advice in pandemic preparedness and response. The framework envisaged extensive use of antivirals and (when available) and limited use of NPIs, most notably case isolation in the home (throughout the pandemic) and time-limited school closure in heavily affected areas. Measures such as internal travel restrictions were viewed to be likely ineffective. Mask-wearing was discussed; while definitive guidance wasn't given, the report suggested that the planning presumption should be that large-scale mask use would not be recommended. Surge capacity planning in the NHS is also discussed. Emphasis was placed on the need for pandemic response measures to maintain business continuity (and public order). Overall, the emphasis was on the adoption of policies and countermeasures to slow pandemic spread and mitigated

its impacts. As already mentioned in section D, suppression measures (driving R to below 1 with use of intensive NPIs) was not mentioned in the 2007 framework document, nor had it been discussed as a policy option on SAG in 2005 and 2006, except in relation to containing a potential pandemic at source.

105. US pandemic planning guidelines also issued in 2007[21] were relatively consistent with the UK framework, albeit with greater emphasis on the US of NPIs, and less emphasis on antiviral use. The differences reflect the longer historical tradition of NPI use in the US, and that the UK order a proportionately much large antiviral stockpile than the US. Richard Hatchett (now CEO of CEPI) was heavily involved in US government pandemic preparedness (including as a consumer of modelling) at the time and is therefore well-placed to give much more detail and context to US thinking at that time.

106. I note that high-level thinking around the goals of UK pandemic planning and the use of countermeasures did not change substantially between 2007 and 2020.

I. 2009: the H1N1 pandemic

107. I will not review the epidemiology of the 2009 H1N1 pandemic here, or the details of the scientific advice the Imperial group (then called the MRC Centre for Outbreak Analysis and Modelling) provided to the UK government. The independent review of the response to the H1N1 pandemic led by Deirdre Hine[30] provides extensive detail on the history of the pandemic, the policy response and the role of SAGE and other groups.

108. However, I note that the 2009 H1N1 pandemic was the first time that the SAGE and SPI-M-O system operated in a similar way to what occurred in 2020. There were some differences in the operation and constitution of SAGE and SPI-M in the two pandemics:

a. The GCSA (John Beddington) chaired SAGE alone in 2009. The CMO (Liam Donaldson) did not attend, chaired his own Pandemic Influenza Group (PIG). This reduced coherence of scientific/medical advice to COBR, as noted in the independent review of the response to the H1N1 pandemic led by Deirdre Hine[30]. SAGE participants represented a wide range of disciplines, including virology, respiratory medicine, public health, social science, modelling and immunology.

b. SPI-M-O was much smaller in 2009 than in 2020. HPA was the lead provider of epidemiological analysis and modelling, with Imperial (led by me), LSHTM (John Edmunds) and Warwick (Matt Keeling) providing "second opinion" analyses and additional modelling. SPI-M-O was chaired by a DHSC civil servant at that time (Peter Grove) and was a more informal group in its operation.

109. In addition to participating in SAGE during the H1N1 pandemic, I also acted as an advisor to the WHO Emergency Committee, was a member of the US CDC "Red Team" pandemic advisory group, and advised the US National Security Council. All our work on the pandemic was funded by our existing funding (notably our MRC Centre grant and NIH MIDAS grant).

110. Some UK lessons from H1N1 were not learned for COVID-19. In both pandemics:

a. The initial UK government response (not discussed with SAGE) was "containment" – testing focussed on travellers returning from affected areas, notably (in 2009) Mexico. This was despite the independent modelling groups contributing to SPI-M-O all saying this policy would likely have a minimal effect.

b. It took too long to establish systematic sentinel surveillance in healthcare settings in the UK. Unlike during the COVID-19 pandemic, universal testing (even in hospitals) was never adopted in the H1N1 influenza pandemic; rather sentinel surveillance in GPs and hospitals was used.

c. There was a substantial delay between self-sustained local transmission starting in the country and government acceptance that it was happening. This was due to the delays in establishing systematic surveillance and the initially limited sensitivity of that surveillance. Rather than adopting the precautionary principle and assuming that the detection of substantial numbers of cases in travellers meant that it was highly likely local transmission had begun, in both pandemics the government moved out of the containment phase of the response only when there was overwhelming evidence of local transmission.

111. In the 2009 pandemic, it took several months (until August 2009) to reliably estimate severity (as quantified by the infection fatality ratio, IFR), though upper bounds on severity were estimated by us and other groups within the first month. Developing methods and surveillance structures which would allow more rapid estimation of severity was an important technical lesson from the H1N1 pandemic[31] which did contribute to the more rapid generation

of reliable IFR estimates for COVID-19 – though the higher severity of COVID-19 also made estimating IFR somewhat easier.

112. The low severity (final IFR estimate of approximately 0.01%) of the H1N1 pandemic virus meant that there was limited discussion of the use of NPIs by SAGE in 2009. Hence the policy response to the H1N1 pandemic rarely deviated from pre-existing plans. The use of influenza antivirals for treatment of symptomatic cases was, after considerable debate, recommended by SAGE and was adopted as policy by COBR.

113. As expected (given the timescale of influenza vaccine production), substantial stocks of H1N1 pandemic vaccine only became available in late 2009, initially targeted at clinically vulnerable groups. Since the first wave of the pandemic was largely over by the time vaccine was rolled out, the net impact of vaccination in reducing disease and mortality was limited, especially since vaccination uptake in vulnerable groups was low.

114. After the pandemic, there were some criticisms of the large investments in vaccines and antivirals, given the low mortality attributed to it (annual influenza mortality was lower than average in 2009). However, at the time decisions regarding ordering of vaccines and deployment of antivirals had to be made, estimates of IFR were still relatively uncertain (upper bound on estimates of approximately 0.1%).

J. MERS-CoV (2012-), West African Ebola epidemic (2014) and Zika (2016)

115. I had some concerns that the low severity of the H1N1 pandemic would reduce government focus on pandemic preparedness. However, this concern proved largely unfounded. In part this was because a lethal influenza pandemic remained at the top of the National Risk Register[1], in part because of the efforts of the new CMO (Sally Davies) and the GCSA (John Beddington and then Mark Walport), and in part because of a sequence of new emerging infectious disease threats that occurred between 2012 and 2016.

116. The first such threat to be recognised was Middle Eastern Respiratory Syndrome coronavirus (MERS-CoV), with initial human cases detected in Saudi Arabia in 2012. Limited human-to-human transmission in the community has been observed, but transmission in hospital settings led to a large outbreak in Saudi Arabia in 2014 which spanned multiple

regions and hospitals, and a smaller but still disruptive multi-hospital outbreak in South Korea in 2015.

117. MERS-CoV is a zoonosis, with most human exposure thought to occur from dromedary camels, in which the virus circulates endemically across North Africa and the Arabian peninsula[32]. Bats have been hypothesised to be the original source of the virus, though the epidemiological and virological evidence is not definitive,

118. Since 2013, MRC GIDA team at Imperial has been one of the leading groups worldwide undertaking research on the epidemiology of MERS-CoV, including an intensive period of work in 2014 assisting the Saudi Arabian government in the response to the large outbreak that country was then experiencing.

119. SAGE was not stood up as a result of MERS-CoV, though it was discussed in a number of DHSC and PHE advisory meetings I attended, including at SPI-M and NERVTAG.

120. The second major emerging infectious disease outbreak during this period was the unprecedented West Africa Ebola epidemic of 2014-16. After initially offering assistance to WHO in late April 2014, MRC GIDA began working with WHO colleagues on the epidemic in the summer of 2014, prior to the epidemic being designated a Public Health Emergency of International Concern (PHEIC) by WHO. The delay between our initial offer of assistance and starting work reflects the very limited data available prior to July 2014 and the unfortunate initial delays in organising and resourcing a systematic regional and global response to that epidemic.

121. In addition to supporting WHO, we also provided analysis and modelling to the UK government in support of its response to the Ebola epidemic in the autumn of 2014 – most notably to DfID, via its then chief scientific advisor, Chris Whitty, a specifically formed Ebola Modelling Group (co-organised by DHSC and DfiD and with a small membership similar to SPI-M) and three SAGE meetings[33] (note that there is an error in the attendance list of the October 2014 meeting in omitting my name).

122. The operation of SAGE and the Ebola Modelling Group in 2014 largely mirrored how SAGE and SPI-M-O operated in 2009, albeit with a slightly slower cadence of meetings and considerably less input from PHE and NHSE. A similar range of disciplines were represented on SAGE in 2014 as in 2009, albeit with a greater emphasis on global health expertise.

123. Our principle contribution to analysis of the Ebola epidemic was in estimating and tracking key epidemiological parameters (R, the infection fatality ratio, incubation period, secondary attack rates, exposure routes) and undertaking some modelling of likely bed capacity needs for Ebola Treatment Centres.

124. MRC GIDA also provided assistance to WHO in the modelling and analysis of the 2018 Ebola outbreaks in the Democratic Republic of Congo, the second of which (in North Kivu province) took over a year to bring under control and ended up as the second largest Ebola outbreak after the 2014 West African epidemic.

125. The third major emerging infectious disease event in this period was the Latin America Zika epidemic of 2016. Zika is a flavivirus first detected in humans in Uganda in 1952. However, the virus was not detected outside Africa until 2007, and likely only entered the Americas in 2015. While Zika infection is typically mild and self-limiting, concern grew in 2016 around the association of Zika infection in pregnant women with an increased incidence of birth abnormalities, notably microcephaly – termed congenital Zika syndrome.

126. I felt that aspects of the regional and global response to Zika were disproportionate, if understandable. There is still considerable uncertainty about the overall burden of disease caused by the Latin America epidemic, but the relatively high rates of microcephaly reported for some areas of Brazil were not replicated in most other countries in the continent (though all countries saw some increase in incidence). Furthermore, experience from dengue (a closely related virus) suggested that control measures (insecticide spraying) would have limited effectiveness, and I was concerned that the epidemic would be largely over (due to herd immunity) by the time vaccine trials were able to start[34].

127. The UK response to the Zika epidemic was largely limited to enhancing surveillance in travellers and investments in research and vaccines. I contributed to the last of six SAGE meetings[35] organised to review Zika science and research priorities.

128. We did not receive additional emergency funding for our work on MERS-CoV, Ebola or Zika; all our research was funded from existing resources, notably the MRC Centre grant.

K. UK preparedness planning 2010-2019

129. The net effect of multiple MERS-CoV and Ebola outbreaks and the Latin American Zika epidemic was to maintain a high level of both scientific and policy engagement in preparedness for emerging infectious epidemics and pandemics.

130. Accelerating vaccine development became a particular national and international priority after the 2014 West Africa Ebola epidemic, partially stimulated by the success of the real-time trial of Ebola vaccine started in Guinea that year. Chris Whitty, then DfiD CSA, founded the UK Vaccine Network (which I am a member of) in 2015, to coordinate government investment in vaccine research and development for pandemic threats. In 2017 the Coalition for Epidemic Preparedness Innovations (CEPI) was launched, initially funded by Wellcome Trust, the Gates Foundation and the governments of Norway, Germany and Japan. CEPI[36] aims to accelerate vaccine development and production for pandemic threats, with an emphasis on ensuring globally equitable access to vaccines. These initiatives were relatively well integrated with other international initiatives, such as the WHO R&D Blueprint process for pandemic vaccines[37] and ongoing pandemic vaccine investments by BARDA (in the US). It is my view that this combined focus on pandemic vaccines (starting with BARDA investments prior to 2009) contributed substantially to the rapid development of effective SARS-CoV-2 vaccines during the COVID-19 pandemic.

131. The aftermath of the 2009 H1N1 influenza pandemic saw relatively few changes to other aspects of UK pandemic planning, which largely remained focussed on the risk from influenza pandemics. The UK Pandemic Influenza Preparedness Strategy[22] published by DHSC in 2011 included only one page of relatively minor lessons learned from the 2009 pandemic, but did not substantially deviate from the 2007 national framework[29]. Following the launch of the Preparedness strategy, both PHE[38] and NHS[39,40] published pandemic response plans. Both detailed how responses would develop according to the detection, assessment, treatment, escalation and recovery phases of the national strategy.

132. In this time period, beyond the scientific advisory input listed above, I had limited involvement in UK government pandemic preparedness activities. In particular, I was not involved in advising on PHE and NHS operational planning for a pandemic. However, in retrospect, I would note how brief the NHS pandemic operating framework documents

published in 2013[39] and 2017[40] were; the 2013 document only mentions PPE once, in a single table.

133. The 2014 PHE plan[38] is more detailed and in relation to surveillance specifically, sets out clear and appropriate priorities which did take account of the lesson from 2009 that more rapid severity assessment was a priority in future. However, that plan did not anticipate the adoption of very large-scale or universal testing in healthcare settings seen during the COVID-19 pandemic.

134. More generally, neither the PHE or NHS plans state anything about the resources (*e.g.* financial, personnel, laboratory, stockpile sizes) required to effectively deliver the activities anticipated. In retrospect, this suggests lack of sufficiently robust planning around resource requirements, especially in light of the challenges in PPE procurement faced by the NHS in 2020.

L. The UK science-policy interface during infectious disease crises

Note: This section is an edited version of a matching section in my module 2 statement.

Introduction

135. The COVID-19 pandemic highlighted a number of key limitations in how the UK government plans for and responds to contingencies. I detail these limitations below and suggest some possible actions to address them. I also note that I understand that much (but perhaps not all) of what I recommend in relation to UKHSA already forms part of current plans; the notable exception might be the creation of a substantive, rigorous and quantitative policy analysis and assessment capability.

The UK model for planning for and responding to civil contingencies

136. While the COBR mechanism to respond to civil contingencies has been in existence since the 1970s, SAGE as a formal structure for gathering real-time scientific advice to inform COBR decision-making emerged out of the experience of the 2001 Foot-and-Mouth Disease (FMD) epidemic in UK livestock (see section F). It is of note that the 2001 advisory group often considered operational aspects of policy in some detail, contrary to the later operation of SAGE.

137. It is also notable that reviewing epidemiological analysis and modelling made up a substantial part of SAGE activities during the 2009 Influenza pandemic, the 2014 West African Ebola epidemic as well as the COVID-19 pandemic. In this, SAGE followed the pattern set by David King's FMD scientific advisory group.

138. It was only when the ad-hoc structures used in 2001 evolved into the formal SAGE mechanism that a clear division was made between scientific advice (the responsibility of SAGE) and policy-making, operational planning and implementation (the responsibility of COBR, lead departments and technical agencies). While I understand the rationale for it, trying to maintain this division of responsibilities has been a tension ever since.

139. I think this issue is symptomatic of broader issues in the UK's governmental mechanisms for responding to certain types of crises. So rather than just focussing on SAGE, I feel the UK needs to reassess its response to crises overall, and then plan advisory structures in that broader context.

140. I will therefore discuss the broader context of how the UK's approach to risk assessment and crisis response has evolved in the last 20+ years and the weaknesses revealed by the pandemic.

141. I am not an expert in civil contingency planning, decision analysis or risk assessment. However, I have sat on SAGE and its predecessor during multiple different infectious disease crises over more than 20 years, and have had significant interaction with civil servants in multiple government departments on risk assessment, preparedness and response over that time.

142. The creation of the Cabinet Office Civil Contingencies Secretariat (CCS) in the aftermath of FMD and 9/11 presaged a more systematic approach to crisis preparedness in the UK government.

143. In the years after its creation, the CCS spearheaded a review of major risks and the creation of the National Risk Register (NRR[1]), an assessment of the major potentially significant risks facing the UK. This was initially a classified assessment, but from 2008 a public facing version was published.

144. I was involved in discussions around the methods used to quantify risks in the NRR on a number of occasions since 2001, and advised specifically on a number of the key risks identified.

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145. The NRR quantifies risk within a two-dimensional "likelihood"/"impact" matrix. Impacts are assessed in a cross-sectoral manner, spanning mortality, the economy, essential services and population displacement.

146. Risks are assessed and located on the matrix on a Reasonable Worst Case (RWC) basis. This is reasonable but perhaps not optimal in terms of planning policy responses, as I'll discuss in more detail below.

147. Risks identified in the NRR are the topic of cross-government risk mitigation planning, typically with a lead department coordinating planning for each risk. Mitigation is focussed on preparedness and response planning to reduce impact, though sometimes reducing likelihood is also a focus.

148. In general, I think the UK has been ahead of many countries in this quantitative and relatively rigorous approach to risk assessment and management.

149. For many (if not all) of the risks identified, a "playbook" of policy responses has been formulated. There has also been an emphasis – accelerated by the COVID-19 pandemic – on better understanding of cross-sector network ("domino") effects, and on real-time data capture to inform situational awareness (e.g. real-time dashboards presenting key indicators).

Lessons from COVID-19 for policy planning

150. However, I think the COVID-19 pandemic (and before that, the 2009 Influenza pandemic) have highlighted some limitations of the current approach to contingency/extreme event planning and response in the UK.

151. I believe that the focus on RWC scenarios is overly restrictive, and risks leading to tunnel-vision – both in only planning for "very bad" scenarios, but also in perhaps giving officials and policy-makers the sense that reality is unlikely to be as bad as the RWC. In addition, the definition of "reasonable" has always been subjective.

152. A related challenge is that for certain risks on the NRR (particularly pandemics, but also some other), it is not at all straightforward to assess the (potential) impact of an event immediately. Indeed, it is often not obvious that the relevant event *has* started; *e.g.* that a potentially concerning infectious disease outbreak in another country really poses a risk to the UK.

153. Focussing specifically on epidemic/pandemic risks, as an outbreak unfolds, there will always be a need to iteratively reassess the costs and benefits of policy actions or *inaction* in a context of likely high levels of uncertainty.

154. While the judgement of what constitutes an "appropriate" policy response (as compared with over-reaction or under-reaction) will always be a political one, I think the government can do much better than it has in the past in prospectively mapping out potential epidemic scenarios and policy responses for each.

155. This will require moving beyond viewing risks through the lens of the RWC, but instead assessing the range of impacts a novel infectious disease threat (which might or might not cause a pandemic) could generate. This would probably best be done as a set of scenarios, spanning expected ranges of transmissibility, severity, but also more categorical variables (e.g. mode of transmission, risk profile across age groups). Then for each scenario, an evidence-based menu of policy responses can be generated, spanning a range of risk appetites from the precautionary "escalate first, de-escalate if needed" approach to the "never cry wolf" end of the spectrum.

156. Critical to such an approach is a detailed consideration of how to balance the scale of potential impacts of both the disease (i.e. deaths) and the policy response (i.e. economic and social disruption) and the uncertainty in the assessment of those impacts existing at a point in time.

157. Both SAGE and UKHSA use a sensible semi-quantitative system for evaluating the confidence they have in particular pieces of evidence (e.g. an estimate of the IFR), particularly within formal risk assessments. This involves a categorical scale which spans the range from very low confidence (meaning highly uncertain or depending on a single evidence source) to very high confidence (multiple convergent streams of high quality evidence).

158. In my view, much more thought needs to be given to how those assessments of uncertainty/confidence influence decision-making, especially in the context where the "central" estimate points towards a very high impact event. The default policy response to the high levels of uncertainty we saw early in the COVID-19 pandemic was to prioritise collecting more data, to update RWC scenarios, but in other respects to wait and see.

159. Much of the work I propose above can be done now. Research should be commissioned to systematically compare the health and economic costs of waiting too long to act against

those of over-reacting early and then needing to de-escalate. This can draw upon the enormous amount of data which has been collected on the health, social and economic impacts of the pandemic, and on the effectiveness and socioeconomic impacts of NPIs.

160. A key factor for such research to consider is the *time horizon* over which policy and disease impacts are assessed. In my view, a critical failing in the UK policy response to COVID-19 in 2020 – particularly between May and December – was the overly short time horizon over which the impacts of NPIs on the economy (and the epidemic, to a lesser extent) were being evaluated. Adopting a strategy where NPIs were only intensified when the NHS capacity (locally or nationally) was at risk of being overwhelmed was intended to minimise the imposition of economically (and socially/politically) costly measures. However, delaying intensification of NPIs just led to more hospitalisations and deaths without any economic savings, given that measures did eventually need to be escalated, and then kept in place for at least as long (if not longer) than they would have been had action occurred earlier.

161. Of course, being willing to make decisions on the basis of projected costs and benefits evaluated over a, say, 6-12 month time horizon requires policy-makers to trust (and be able to explain) the modelling underpinning those assessments. By comparison, decisions made late can be justified by pointing to recent numbers of hospitalisations and deaths – which was generally what ministers, the GCSA and CMO emphasised when announcing and justifying intensification of NPIs during the pandemic. This speaks to a more general and complex issue – namely that, the longer the time horizon used, the higher will be the uncertainty in evaluating costs and benefits.

162. Nevertheless, even accepting that politicians will vary in their appetite to accept modelled projections versus recent data trends, I feel the formal analysis and presentation of the potential costs and benefits of policy options over a range of time horizons would be of value in clarifying the trade-offs associated with different approaches to interventions.

163. A related critical issue is what the strategic goals of policy (and policy-makers) are. This was less clear than it might have been for much of 2020, and less clear then that it was in previous crises (FMD, H1N1 pandemic influenza, Ebola). However, I would note that none of the previous infectious disease crises during which I advised government approached the scale of health, economic and societal impacts caused by COVID-19, nor did any of those previous crises last over than a year. Thus I think particular attention should be paid to the

challenges of achieving evidence-based policy during complex, extended, multisectoral crises where there are multiple, often competing policy objectives.

164. In my view, one of the lessons to learn from that experience is to have technical science advice inform operational policy formulation to a greater extent than happened in 2020. SAGE and SPI-M-O were not prospectively asked for input into or assessment of a number of key policy initiatives, most notably the March 2020 COVID-19 Action plan, the May 2020 Alert level system, the October 2020 local tier system (including the precise criteria for escalating local tiers), and border measures throughout the pandemic. This led to flaws in all of these policy measures, in my view. While I am not arguing that all policy initiative should have been "approved" by SAGE, a rapid scientific and epidemiological assessment of the likely effects of all of them could have been undertaken before they were introduced. Optimally, such assessments would have been undertaken by UKHSA rather than SAGE directly, but it would be important for them to have been transparent (i.e. published).

Governance of science inputs into government in epidemics

165. Even exhaustive scenario planning will not precisely anticipate the exact characteristics of the next infectious disease threat the UK faces. There will always be a need for real-time and continuous assessment of the actual threat and similarly agile updating of policy playbooks (the "menu" of options). In my view, doing this well is not aided by the current "Chinese wall" between SAGE (scientific advice) and COBR/government (policy planning). Nor can high level committees such as SAGE and COBR necessarily give the level of detailed consideration that are needed to such assessments.

166. I think that technical assessments of risk (including current uncertainty) and of the potential impacts of policy options in mitigating that risk should be the proper responsibility of the relevant lead government technical agency. In the case of infectious disease risks, this is UKHSA. That did not happen in the first 3-6 months of the COVID-19 pandemic in the UK, where PHE did not have the capability to provide the scale and depth of analysis required and SAGE therefore largely took on that role.

167. Placing primary responsibility for scientific inputs (including policy assessment) into government during a pandemic onto UKHSA mirrors systems in place in many northern European countries (Netherlands, Norway, Denmark, Finland and Sweden).

168. As I detail in my Module 2 statement, I strongly feel that UKHSA (and for other NRR risks, other technical agencies) should be proactive in forming long-term partnerships with academic and commercial partners and draw upon the additional capacity those partnerships provide in crisis situations. It will also be key for UKHSA and NHSE to work seamlessly together, particularly in surge capacity planning (and in determining, at an early stage, what the limits are on surge capacity).

169. In the case of a potential pandemic threat, impacts of both the event and policy responses will go well beyond just the health sector, so it would be beneficial for a cross-governmental taskforce with executive authority (determined by COBR) and significant analytical and technical capacity to be convened at an early stage. Akin to "Gold command" used for terrorist threats and other risks on the NRR, but configured for a potentially much longer duration event. I did not have good visibility of these types of structures within government during the pandemic, but from what I did glean, they were weak in the first 3-4 months and strengthened notably thereafter.

A revised role for SAGE

170. With such a system in place, the need for SAGE should be substantially reduced, but not eliminated. The majority of scientific data which went into SAGE (sometimes for "approval") during the COVID-19 pandemic would better be fed into UKHSA and/or the operational "Gold command" structures. This would leave SAGE with more of a challenge and feedback function; identifying weaknesses and gaps in the evidence base being generated by UKHSA and others, challenging assumptions and even paradigms, and highlighting research priorities or other evidence needs.

171. In doing so, thought should be given to the potential value of SAGE taking on some responsibility for "red teaming" activities[41], particularly in relation to gap analysis ("what have we missed?"). This role could be adopted by a parallel group, but this might pose challenges in terms of establishing hierarchy and clear lines of responsibility. If red-teaming is to be part of SAGE's function, then its mode of operation and chairing may need to be reassessed. I also note that red-teaming is perhaps difficult if SAGE retains the role it had in the COVID-19 pandemic as the definitive source of scientific evidence for government. It is more compatible with a challenge and feedback role.

172. Red-teaming could also (or alternatively) play a greater role within the more technical advisory structures operated by UKHSA. However, to be fair, my experience of a number of UKHSA technical advisory groups in the last two years is that they have already encouraged a high level of constructive challenge.

173. The disciplinary scope of SAGE should be reconsidered; in particular, I see no reason why the remit of SAGE should not extend to economics and the social sciences more generally. In choosing economists to participate in SAGE, thought should be given to ensuring linkage with Treasury and Bank of England advisory structures.

174. While the role of SAGE is to provide high-level scientific advice to COBR, it is not clear to me that it is always optimal for that advice to be filtered solely through the GCSA and CMO. This is not an implied criticism of either Patrick Vallance or Chris Whitty, but I see risks associated with having just one or two individuals (plus a civil service secretariat) be solely responsible for communicating complex, policy-sensitive syntheses of scientific knowledge to ministers and senior civil servants.

175. In that context, while the primary distinction between advising on and advocating for a policy should be retained (i.e. "advisers advise, ministers decide"), removing the somewhat arbitrary distinction between strategic/scientific advice and operational/technical advice would be beneficial. This would also allow something of a lowering of the Chinese wall between SAGE and COBR. Occasional joint meetings of participants in both groups might be considered, where SAGE as a committee can discuss scientific assessments with ministers and be questioned on them.

176. That said, I do not have a perfect model of SAGE in mind. However, I think there would be value in evaluating the range of approaches taken across European countries. Ideas to consider include:

a. Having SAGE chaired by one or two independent scientists, while retaining the role of the GCSA (and CMO) in determining the priority list of topics SAGE is tasked with addressing. This may be particularly valuable for red-teaming activities. It would also align SAGE with the practice of statutory committees such as JCVI, ACDP and NERVTAG, all of which have independent chairs.

b. Offering more opportunity for extended scientific discussion within SAGE. Compared with 2009 and 2014, SAGE-COVID was much larger, and run in a considerably more formal

manner, particularly as time went on. Much of its activity was reviewing and approving documents, with limited associated discussion. This made brain-storming/horizon-scanning discussions more difficult, which I believe is the main reason why Patrick Vallance organised informal small group discussions on various occasions in 2020-21.

c. Reviewing the role of SAGE participants. "Participant" and "member" perhaps imply different things, especially in relation to collective responsibility and the level of commitment required. In addition, while perhaps unavoidable to a degree, the extent to which scientists on SAGE are providers versus reviewers of scientific evidence should be considered.

d. Introducing detailed minuting of plenary SAGE meetings, in addition to the summaries currently produced. It is a policy decision as to whether these are published at the time, but overall I believe detailed minuting will aid transparency, give more insight into areas where there is less consensus between SAGE participants, and allow Inquiries such as yours to better understand deliberations retrospectively.

177. I think the expansion of SAGE to include multiple sub-groups and task-and-finish groups should be resisted in future long-duration crises. SAGE became a significant "operationalised" government structure in its own right during the COVID-19 pandemic, almost being viewed as the normative source of scientific input into government. I am aware that Patrick Vallance tried to resist this trend, and that an increasing number of those functions were moved to UKHSA in late 2021. However, my view is that UKHSA – supported by a network of university partners – represents a more sustainable and appropriate source of scientific input into government for an infectious disease threat of potentially multi-year duration. SAGE requests for additional evidence would be better addressed by UKHSA than by SAGE setting up parallel structures itself.

178. This is not to say that I think that government will not benefit from the input of university scientists just as much in the next pandemic as occurred during the COVID-19 pandemic. Rather, I think the vast majority of engagement between government and the academic community should be via UKHSA, with SAGE having the lighter-weight, more challenge-oriented function detailed above.

179. UKHSA will need to be adequately resourced to deliver this function. In particular, I don't think resourcing of pandemic preparedness and decision analysis/policy evaluation is

currently adequate. In addition, while there have been significant organisational improvements with the transition from PHE to UKHSA, some unhelpful aspects of past culture remain. Among these is the contain/delay/mitigate "playbook" for handling the earliest stages of a new infectious disease threat which relies too much on measures for while the evidence base is weak.

Specific policy recommendations for future preparedness

180. *Border measures*: I think research needs to be commissioned to critically evaluate what the measures adopted at various stages of the pandemic achieved. This should be followed by development of a more evidenced-based strategy for border surveillance and controls for future infectious disease threats. We should never again use the term "containment" to describe a set of measures that are palpably unfit to achieve the goal implied by that term. At the end of the day, some policies with a weak evidence base may still be adopted, but this limitation should be transparent to everyone. I note that this was an issue for both the 2009 H1N1 pandemic and the COVID-19 pandemic.

181. *Surveillance and testing*: government should not assume that sustained person to person transmission of a new infectious disease threat isn't occurring in the UK just because it hasn't been detected. Again this was an issue for both the 2009 H1N1 pandemic and the COVID-19 pandemic. In the absence of data to say otherwise, the default assumption should be that it *is* occurring. Surveillance should be rapidly put in place to detect cases unlinked to travel with a certain level of sensitivity, and public statements interpreting the detection (or not) of "sporadic" cases should be couched with reference to the sensitivity of the surveillance system in place. In my view, NHS hospital testing capacity should be maintained at a level which allows rapid (~7 days) initiation of comprehensive hospital-based surveillance for any new infectious disease threat.

182. *Policy red lines*: From my perspective, it seemed to take until March 13th 2020 for the UK government to decide it was not prepared to allow NHS surge capacity to be overwhelmed (and to determine precisely what that surge capacity was). In the future, it would be highly advantageous for policy planning (and science advice informing that) for such "red lines" to be clearly defined at the earliest possible stage. Furthermore, early definition of strategic policy objectives (*e.g.* minimising economic impact, minimising mortality, keeping schools

open) for the response would also be beneficial, accepting that these might not all be achievable and will likely evolve over time.

183. *Healthcare capacity*: The NHS is run at substantially higher normal levels of bed occupancy and has fewer hospital beds per capita than seen in most (if not all) comparable European countries. For instance, France has twice as many hospital beds per capita as the UK[42]. In my view, it is plausible that this difference – together with the higher peak number of hospital admissions in the first COVID-19 wave seen in England compared with France – largely explains why France experienced a two-fold lower IFR in first wave of the pandemic than did the UK[43]. Clearly, any decision to expand hospital capacity needs to consider much more than just NHS resilience to pandemic-related surges in demand, but I still think the topic requires careful consideration by the Inquiry.

M. Statement of Truth

184. I believe that the facts stated in this witness statement are true. I understand that proceedings may be brought against anyone who makes, or causes to be made, a false statement in a document verified by a statement of truth without an honest belief of its truth.

Signed: Personal Data

Dated: 11/05/2023

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