Witness Name: Professor Michael Gravenor

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UK COVID-19 INQUIRY

WITNESS STATEMENT OF PROFESSOR MICHAEL GRAVENOR

I, Professor Michael Gravenor, will say as follows: -

Introduction: Background and establishment of Swansea Modelling Team

1. My whole academic career has been focused on infectious disease epidemiology or public health data analysis through mathematical modelling and statistics, starting with my DPhil on malaria (Oxford, 1991-1995). I was introduced to mathematical modelling of infectious diseases as an undergraduate, completing two projects on modelling measles in London with Professor Bryan Grenfell at Cambridge which set me on this path. In turn, as a post-doctoral researcher (Oxford followed by BBSRC Institute for Animal Health) then University academic (Swansea), I worked further on malaria, then scrapie, BSE (mad cow disease), avian influenza, HIV, MRSA, measles and dengue. Alongside this I have worked on

population-based mathematical and statistical studies of non-communicable diseases in particular diabetes, asthma, clinical trials, and coronary vascular disease and stroke. Prior to 2020 I had not completed any projects on coronaviruses. Coincidentally, in 2016, a PhD student from Saudi Arabia I was supervising (at Swansea) and I planned a project modelling the spread of the coronavirus MERS-CoV which had been identified in Saudi Arabia. I was familiar with the SARS-CoV-1 literature, and we discussed modelling the potential spill-over of a coronavirus from animal reservoirs to humans, but in the end I decided there was not enough data available to proceed and instead the project turned to modelling dengue virus spread associated with large movements of populations in Jeddah.

2. Being based most of my career in Medical Schools or applied research institutes, my projects have often been closely linked to public health responses, sometimes at very large scales. I therefore have professional experience in the practical (not just theoretical) application of mathematical models of infectious disease. The following are three large-scale policy-response examples.

3. First, for the disease scrapie, I worked for 4 years on the major UK BBSRC programme on the control of this disease in sheep. This had become a priority at the UK-level following the health concerns to humans of the BSE crisis. The programme linked mathematical modelling, laboratory work and genetic field studies, and provided the evidence base for the UK Scrapie Plan, and similar disease eradication programmes in Europe and the US.

4. Second, for BSE ('mad cow disease'), I was a member of the Scientific Panel on Biological Hazards of the European Commission (originally the European Food Standards Agency) for over 7 years. The panel produced a novel risk assessment for the geographical bovine spongiform encephalopathy (mad cow disease) risk (GBR) that was applied to every country in the world that exported animal products to the EU. The model was influential in driving policy action based on modelled risk factors, rather than surveillance-based data, an approach that was crucial for BSE for which the surveillance data was almost universally insufficient at the time. The results were used by the European Commission as the basis for trade legislation. The model was the primary tool for evaluating the potential global spread of BSE and resulted in the implementation of additional measures and management activities both to improve surveillance and to prevent transmission worldwide. Over 100 countries were assessed. I helped design the original model, and update it several times. I developed separate models for several specific food products and co-led the analysis of the following countries: USA, Canada, Norway, Australia, South Africa, Nicaragua, Botswana, Brazil, Uruguay, El Salvador, Panama, Costa Rica, New

Zealand, Swaziland, Paraguay, Namibia, Chile, Argentina, while contributing to the analysis of more than 20 others.

5. Third, I was a member of the Wales Measles and Rubella Elimination Task Force, that drafted the 2019-21 Measles Action Plan, with colleagues at Welsh Government (WG), NHS Wales and Public Health Wales (PHW). My focus in the immediate period before the pandemic was developing mathematical models at the local level for Wales to determine hotspots for outbreaks based on local vaccination coverage, and potential networks of low vaccination coverage along which an outbreak could spread.

6. My initial role in the early stages of the pandemic is described below. Here I outline how the Swansea Modelling Team was put together. In late March 2020, a Royal Society notice for the RAMP Initiative, calling for modelling support for the pandemic was circulated at Swansea University. Because I was already involved with pandemic projects using the SAIL public health databank, and was already engaged in modelling discussions with Public Health Wales (PHW, see paragraphs below on '**The early stages of the pandemic**') I notified colleagues I would not be involved with RAMP, but was keen on collaboration on my existing projects. I received a reply from Professor Biagio Lucini at the Mathematics Department on 30th March offering help. My initial impression had been that I could best help by providing support *interpreting* model output, rather than building new models. This was for two reasons, first there was a lot of modelling being published by large groups, such as Imperial and the London School of Hygiene and Tropical Medicine (LSHTM), many others and through SPI-M-O.

7. Second, strategic models can be built quite quickly, that offer general insights into epidemic behaviour, but more tactically focused 'policy' models can take some time to build. One of the central initial Imperial models, for example, that generated prominent scenarios of threats to the health service, had been in development for many years for influenza. Whilst it needed adapting to COVID-19, much of the basic disease processes and, crucially, the demographics and geography of the UK was already in place. However, as I built links with PHW it became more clear that this would be the type of model they were very keen on having close access to, and to use the model to ask Wales-specific questions.

8. This was made even more clear, when I was introduced to Brendan Collins and Craiger Solomons and their team, who were running the modelling interpretation for the Welsh Government, and were members of TAG (and regular attendees of SPI-M-O). I was introduced on 29th April, and we discussed their modelling requirements and the kind of

models I could deliver. Very quickly, I had several requests from an expanding group of colleagues at Welsh Government, Public Health Wales and the NHS for Wales-specific model interpretation, model building, model output discussion and quantitative epidemiological analyses.

9. I took this on board, and on May 5th I reported back to Biagio at Swansea, that we had been asked by PHW and Welsh Government if we could adapt the Imperial Model, any other model, or build models from scratch, so that the relevant data from Wales could be inputted, and scenarios could quickly be investigated using the models based on the specific questions PHW and Welsh Government wanted answering. Biagio and I met Welsh Government Colleagues on 5th May by Zoom. Although several large COVID models were available on GITHUB, there are still technical challenges to using them (these are on top of the expertise required to understand the model structure and interpretation), and the models at that stage were not fully accessible by Welsh Government.

10. Biagio demonstrated during the meeting that this would not be an obstacle at all for himself or his group, and at that moment I realised that as a team we could provide a lot more modelling support over short time periods than I had previously expected. However, being a very small group, we had to focus and Biagio and I discussed which models to build or develop.

11. Over the next 48 hours we ran the Imperial Model, the LSHTM model and several others. I suggested, on balance, to focus on the LSHTM model to provide the framework for our Wales model, based on a balance of demographic detail (allowing all 22 local authorities in Wales to be modelled), complex age structure (very important for COVID which has very different impact on different age groups), transparency, availability of stochastic outputs, and ease of use. At that point in time, it would have been impossible for us to complete a full evaluation of all the positive and negatives of the different model structure options in the period available.

12. The speed at which we were able to run and interpret the LSHTM model (it's transparency of structure and code) was the major positive driving our choice, along with my experience using models of similar structure (differential equations). We were able to open-up and annotate the code very quickly. This is important, as the model structure, assumptions and behaviour should be understood clearly before the model is used and especially if it was to be adapted and built upon. If we were to make changes to the model parameters, or assumptions, or make recommendations based on the model outputs we would need to

understand these, and we were able to do this with the model quite quickly. Thus, there was a combination of personal preference from my expertise in epidemiological modelling, familiarity with the methods that underpinned the model, ability to "open-up" the model code, plus the ability to easily run it in parallel on the Swansea HPC Supercomputing Wales computing hardware.

13. We decided that some of the available agent-based models would take too much time to adapt and re-work for the demographics of the whole of Wales (and the separate local authority components). We later compared model outputs to an agent-based model, with encouraging similarity in outputs, and there were subsequently many opportunities to compare and contrast independent modelling outputs, and choice of model structure, to those from other groups at SPI-M such as the Warwick, Scotland, or Public Health England groups. This comparison was informal, but frequent, as it could be based on the regular estimates of the current Rt value from the various models (presented weekly), the timing of turning points in the epidemic described by the models, the trajectory of medium term projections and the magnitude of specific scenarios that were being considered at different points of the epidemic. This model was therefore the basis, with development by the team and all subsequent interactions with TAG, WG and the modelling sub-group (including NHS and PHW colleagues), for the 'Swansea Model'.

14. By 7th May, Biagio and his group were running the model in parallel on the Supercomputing Wales cluster. Although the model ran on desktops easily, to explore parameter space for model fitting or to explore different scenarios, often requires many hundreds of model simulations, and using the supercomputer at this stage was crucial. The Supercomputing Wales project was supported by the European Regional Development Fund. Outstanding computational facilities were made available across a consortia of Welsh universities. Key to the Supercomputing Wales project had been the creation of 'Research Software Engineer' (RSE) posts. Scientists familiar with state-of-the-art software engineering solutions, but also familiar with research projects and highly engaged in the scientific questions behind the software requirements. This enables a very strong link between the practical questions being posed, and the computational solutions, and ideal for the crisis situation. Two Supercomputing Wales RSEs were part of Biagio's group that had set up the models on high performance computers for investigation.

15. We formally requested a project on Supercomputing Wales on 17th May, entitled "Modelling COVID-19 Scenarios for Wales" with myself as Principal Investigator, Biagio as Technical Lead and a partnership with Swansea University and the Welsh Government Technical

Advisory Cell. On May 19th I met the RSEs on zoom, Dr Mark Dawson, and Dr Ed Bennett. Their contributions were invaluable, both their knowledge and ability to generate results rapidly. Without their involvement, and Supercomputing Wales support, our contributions would have been greatly reduced. Myself, Biagio, Mark and Ed were the start of the 'Swansea Team' and we shared details with Brendan Collins so that information could be shared within the group as they prepared any modelling advice. I was invited to join TAG on 20th May.

16. The established channels for requests to the Swansea Modelling Team were largely between myself, and either Brendan Collins' team at Welsh Government, or Dr Rob Orford (co-Chair of TAG). We were in very close contact, and I would likely get a quick reply no matter the time of day or night. There was an open channel of communication with PHW for requests, especially with Dr Chris Williams. In addition, there was the wider TAG group, the TAG Modelling Sub-Group and contact with stakeholders at the Welsh National Policy Modelling Forum (which involved many of the information officers at the Health Boards). To be clear, I do not consider the requests for work for most of the period "commissions". Until October 2021 (but backdated to 1st August 2021) all requests were informal and the Swansea Team simply tried their best to find the time to answer as many requests as possible, relying on stakeholders to set priorities.

17. From 1st August 2021, the work did become part of a formal commission from the Welsh Government to create a modelling team within the Technical Advisory Cell. This commission ran until 31st March 2022, then was extended to 31st July 2023 with a broader remit to cover RSV, influenza and (in response to the outbreak in summer 2022) monkeypox.

18. As a broad overview, the following summarises some of the projects we reported to TAG. These are reported roughly in chronological order. An overarching set of projects used the 'Swansea Model', this generated a wide range of 'policy scenarios for Wales', based on what-if assumptions for the interventions and changing patterns in the epidemic, such as introduction and removal of interventions and how they might potentially affect case numbers, hospitalisations and deaths, along with the changing characteristics of the virus (and vaccination). The use of this model carried on throughout the period and some specific examples are highlighted below. In addition to the main model, we often developed additional novel simpler models or mathematical / statistical analysis for specific questions.

19. From the earliest stages I worked with PHW to interpret Rt and how to best estimate from case/hospitalisation data in Wales, and on nowcasting methods for estimating the current state of the epidemic (since most recent data are affected by reporting lags). I also provided sessions for Health Board Information Officers to advise on interpretation of Rt and 'little r' (the growth rate of cases), the estimation of Rt, and help with the construction of their own models. Recall that Rt is the number of secondary infections typically caused by a single infection at a specific time point (t) in the epidemic, but 'little r' (r) is a subtly different parameter. Little r is the growth rate of the number of cases. It is relatively easily measured as the change in the number of cases over a defined time period. There is a mathematical relationship between little r and Rt, for example when the epidemic is growing, the value of r is positive, and the value of Rt is greater than 1. While when the epidemic is declining the value of r is negative and the value of Rt is less than 1 (but not negative).

20. Little r is very useful in calculating the expected doubling time of the numbers of infections or cases. This was often used to indicate the trajectory in which the COVID-19 pandemic was heading. Rt is a more complex parameter, because it includes more information on the characteristics of the virus, such as generation times, incubation period and infectious period. So, in general, little r (on its own) is a nice simple measure of the current status of the epidemic and how the case numbers will change over the very short time period (up or down), but Rt is a feature of the full process of how the virus spreads, and is more useful in providing information to help understand in detail the current status of the epidemic and also the potential future trends.

21. We modelled the capacity requirements for large plasmapheresis machines for PHW, based on combining demand from epidemic scenarios with machine production rates as well as plasma storage capacity.

22. We built a set of new models for the analysis of the test, trace and protect system (TTP). We periodically analysed the impact on the R value using the most recent information on the response times distributions and how this was affected by the number of cases at that time. This was used for the TTP system, but also to feed into parameter values used in the main policy model ('Swansea Model'). We modelled the impact of lateral flow devices on TTP. We identified key parameters of the efficiency of the system, and in July 2021, following the roadmap out of restrictions, we reported on the impact of removing the requirements for all contacts and all under18s to isolate. I understand Wales was the first to implement this policy in the devolved administrations.

23. With other colleagues at Swansea, led by Dr Kons Wells, we developed models to analyse the early geographical ('5 mile') movement rules and Welsh Government bubble policies.

24. With colleagues at the Swansea University SAIL databank, we conducted a statistical analysis of the impact of COVID on care home resident survival, the risk posed by hospital discharges into care homes and the risk posed by high community prevalence in the local area around care homes. We also analysed geographic spread at the LSOA level in Wales.

25. We provided a rolling set of Reasonable Worst Case and Most Likely Scenarios, as we tracked the evolution of COVID in Wales with the Swansea Model. These were regularly shared with TAG, the modelling sub-group, the National Modelling Forum, PHW, all NHS trusts, the Wales ambulance Service and periodically published. They were used for operational and long-term strategic planning of bed requirements and staff allocations.

26. We contributed modelling analysis to the design and assessment of the impact of the Wales firebreak. Modelling different lengths of firebreak, the anticipated impact on halting transmission given ranges of reductions in contacts, and the time taken before the epidemic returned to the pre-firebreak state (after the firebreak ended). For each scenario we generated models for the impact on number of cases, hospitalisations, intensive care usage and deaths.

27. Following the firebreak, we modelled the resurgence of COVID, and the impact of the more transmissible alpha variant. We modelled a range of interventions over the 20/21 period and their potential impact on transmission and hospital events.

28. In January 2021, we built the vaccination programme into the Swansea Model using daily data on doses received, and investigated the complex interaction between vaccination roll out and removal of NPIs (the 'road map'). On the one hand, the expanding coverage of vaccination would reduce the individual risk of people to the more harmful effects, and on the other hand, the removal of NPIs would expose a greater number of people, including those unvaccinated, to infection. The early focus of this was to model staggered school openings as the priority and first step in opening-up.

29. At several points, especially during the first half of 2021 we provided estimates to TAG of the number of individuals that remained susceptible to infection, and the 'population levels of immunity'. This included modelling scenarios of waning immunity and the impact of vaccination and boosters. These estimates were used to illustrate the considerable

potential that remained within the population despite being well into the epidemic and into the vaccination programme. This potential reduced over time with vaccination, however acting against this was the emergence of more transmissible variants.

30. In February 2021, following the extended second lockdown, prevalence levels were declining rapidly. However, due to the vaccine roll out, restrictions likely to be gradually lifted and a resurgence of some kind would be expected. At this point we were asked by Welsh Government to model scenarios for the prevalence of COVID at the time of the scheduled Welsh Senedd elections in early May so that it could be assessed whether a high prevalence would interrupt the smooth running of the election. Model scenarios suggested that levels would still be at relatively low levels at that point.

31. After school opening, we modelled the proposed Welsh Government road map out of restrictions from April onwards. As stated above, this was determined by the interaction of vaccination and increased transmission, but this was further complicated by the emergence of the highly transmissible delta variant. This means that a large number of cases would be expected after opening up, but they would potentially be focused in younger individuals, less susceptible to severe outcomes, and also a large percentage had by that time been exposed to natural infection and/or had received vaccines.

32. Following the removal of most restrictions by the summer of 2021, we modelled the expected 'delta wave' and the impact on younger populations in particular, as school terms began in the autumn. This included an analysis of when peak infections were expected, which would represent the first point in the epidemic in which Rt was brought below 1 by processes of cumulative infections and vaccination (levels of population immunity), rather than by NPIs. At a similar point in time we analysed the impact of the reported false negative Immensa laboratory errors in Wales, which may have increased transmission in certain areas for a short period as some infected individuals were mistakenly given a negative result.

33. In December 2021, we analysed the emergence of omicron. The rate at which omicron displaced delta indicated a very high transmission advantage. We developed several models for interaction of delta and omicron variants, and it became clear that the number of infections over the new year period would be exceptionally high, much higher than at any previous point, despite the exposure of the population for nearly 2 years by that point. They key uncertainty at this point was the clinical impact of omicron, so that although very high numbers of infections were expected, the hospitalisation rate was likely much less

than previously (this was due to levels of population immunity from vaccination and previous exposure, in combination with variant characteristics). We developed a range of winter scenarios based on the assumed (it was unknown at this point) clinical impact, and then tracked these against the data. The tracking comparison of the model to the data was sufficient to rule out the higher severity scenarios by Christmas 2021, though considerable uncertainty remained. We then modelled various NPI addition and removal scenarios over the new year period.

34. Moving into 2022, thanks to the commissioned funding from the WG, we were able to provide formal weekly 'Medium Term Projections', from a fit of the model to the most up-to-date data, and a projection of the expected trajectory (and associated uncertainty) for up to 6 weeks. These projections are a representation of the potential future trends, assuming that no change over that period to key parameters such as contact patterns, or characteristics of the virus (variants). These were commissioned by Welsh Government and delivered weekly to colleagues in the NHS, PHW, Wales Ambulance Service, and UKHSA and used to monitor the recurrent waves of omicron. They continue to be delivered at the time of this statement and will likely continue into 2024.

35. I presented the work on many occasions directly to the TAG group for discussion, feedback and generation of new outputs. 'Modelling Update' or 'Policy Modelling' being a regular item on the agenda, often every week as a standing item during the key points in 2020 and 2021. The work featured in many consensus statements that were published by the Technical Advisory Cell, including the modelling updates and focused statements such as the Firebreak, winter NPIs and reasonable worst cases (see Appendix). As a regular member of TAG, I contributed to many additional circulated consensus statements.

36. From a professional perspective, the Swansea Modelling Team was initially myself, working with RSEs Dr Mark Dawson and Dr Ed Bennett, and Professor of Mathematics and Principal Investigator for Supercomputing Wales and Swansea, Biagio Lucini. Dr Dawson left the University in February 2021 and Dr Ben Thorpe took his role as RSE with primary responsibility for the project. Ben worked on the team until November 2021, when Dr Carla White, a mathematics post-doctoral researcher at Swansea University took the role. Carla has been supported by WG funding to continue the role to the present. The Team expanded with colleagues at Swansea to include Dr Alma Rahat, an Associate Professor of Computer Science who specialises in fitting models and preparing the Medium Term Projections; Dr Daniel Archambault, and Associate Professor of Computer Science specialising in visualising Projections and epidemic scenarios (now Professor at

University of Newcastle); Dr Noemi Picco, an Associate Professor of Mathematics who specialises in mathematical biology; and Dr Gibin Powathil a professor of Mathematics who specialises in mathematical biology.

37. At the start of the epidemic, before the Swansea Model was available, many scenarios produced using UK-level models were available to TAG. Even if they were not Wales-specific, scenarios for Wales could be generated by scaling the number events in a UK-level scenario down to the expected number of events in a population the size of Wales. This would often have been very useful, especially when the stages of the epidemic were synchronised. I think for most strategic purposes the adaptation of the SPI-M-O models in this manner would not have led to greater uncertainty in modelling outcomes for Wales in the early stages.

38. Despite the availability of SPI-M-O models, there are a number of reasons why TAG and PHW Wales requested a bespoke 'Wales Model'. First, there are some differences in Welsh demographics that could mean the effects could be different to other areas. Wales has a high proportion of the elderly, who are more susceptible to the severe effects of COVID for example, and these demographics need to be captured in the models. Second, due to different timings and durations of NPIs, Wales would not always be in synch with the average epidemic situation in the rest of the UK. There would be times in Wales where the R value would be below 1, while it was above 1 in England, and vice versa, hence the scaling of model outputs from the UK level to Wales would not always have been ideal. A key reason for the development of the Swansea Models for TAG was to enable a rapid interaction with stakeholders. Many of the SPI-M-O models did indeed include Wales specifically, and these increased over the period. On top of that, many SPI-M-O colleagues were very keen to provide expert advice and support answering Wales specific questions and generating scenarios for Wales. However, the amount of time anyone had for this was limited because of the overall work pressures. Because the Swansea Team was able to focus on Wales then we could prioritise and try and focus on Welsh scenarios. Perhaps most importantly we could quickly go back and forth between TAG/NHS/PHW colleagues so scenarios could be updated or tweaked if the original question changed, which was naturally a common occurrence and at time the epidemic situation changed rapidly.

39. It would have been good to have resources (financial support) made available over the summer period of 2020, and especially the period Autumn 2020 to August 2021. The team worked *pro bono* over that period, and had all our usual University roles to fulfil. These University roles were of course themselves complicated by the pandemic, so that, for

example, the teaching modules I delivered in the autumn semester of 2020 and spring of 2021 were delivered online and I had to prepare that material for the first time, then deliver the teaching, project supervision, the assessment and the student support. I also has considerable commitments to the management of the Medical School that I fulfilled, in particular, a lead role in the crucial Research Excellence Framework submission which was delivered in early 2021. Colleagues helped in many ways but ultimately this was only achievable by working exceptional hours. If even modest resources had been available to support the secondment of myself and a RSE at least, then we could have avoided the impact in human terms to the team and their families, devoted more time to the project, and produced more scenarios and analysis. If resources for any additional RSEs had been available we would have produced parallel model outputs by running at least one more model alongside the Swansea Model. The formal commission we received from 1st August 2021 was extremely welcome. I think an important consideration for future planning should be the accessibility of the large amount of expertise that exists in the University sector, across all aspects of the pandemic response. Inflation and rising costs (with income not keeping up) have put considerable financial strain on the University sector, meaning more demanding day-to-day roles, and therefore experts are less likely to be able to devote time to any emergency response without their University roles being to some formally backed-up and supported to an appropriate extent. Even considering the short time since the start of the pandemic, the changes and challenges that are clear in the university sector lead me to conclude I find it difficult to see how myself and other University colleagues could get involved to the same extent if it happened now. On the current trajectory, the situation will only get worse.

Infectious Disease Modelling: an overview

40. In the study of infectious disease epidemiology, the changes in the patterns of disease can be termed 'disease dynamics'. If *any* quantitative description is to be made of disease dynamics, then a mathematical framework is required, that is a 'mathematical model'. The shorthand for this mathematical framework is 'modelling'. A term I am not keen on. I am a professor of epidemiology, a specific field I work in is quantitative infectious disease epidemiology. This is a specialised field, distinct from public health epidemiology or virology. Mathematical and computer modelling is involved, and is indeed central, because there is no way to provide quantitative scenarios of epidemic spread, without using underpinning mathematical models. The aims are epidemiological, modelling is part of this. The use or emphasis of the term "modelling" can imply it is somehow different from epidemiology, but modelling is at the heart of the epidemiology if any quantitative questions

regarding disease spatial and temporal spread are to be asked. The separate use of the term 'modelling' can imply there is some alternative method for such quantitative epidemiological questions, and there simply is not.

41. An infectious disease (mathematical) model aims to capture the most important mechanisms of disease spread, so that there are some clear, explicit, assumptions made regarding how and why numbers of infected individuals change. The term 'statistical modelling' is also a mathematical description of infectious disease data, but in contrast it is usually a purely empirical description of the data. A statistical model can quantify the rate of spread of disease, for example, but it usually cannot explain it in mechanistic terms. If a disease is rapidly spreading, the rate can be estimated using a statistical model or an infectious disease model. However, only the latter will aim to explain the rate of spread in terms of real processes such as the availability of individuals that can be infected, the contact rate between those infected and those susceptible, and the transmissibility of the pathogen. The distinction can be said to be between mechanistic and empirical descriptive models. Statistical methods still play a crucial role in the use of mathematical models, for the fit of the models to data and the estimation of parameters (with quantified uncertainty). Statistical methods are always important parts of an epidemiology tool kit, and I use (and teach) statistic as a routine part of my work.

42. The model structure is chosen to reflect our understanding of how disease spreads in populations, and the 'parameters' of the model reflect real features of the pathogen and population, such as infectious period, transmissibility (for the pathogen) or contact rates and demographics (for the population). Policy decisions during an epidemic change key parameters of the disease dynamics. They might shorten the infectious period of a virus (by case isolation or contact tracing), or might reduce the number of people who could be infected per day (via reducing contacts with NPIs, or vaccination for example). Thus, the infectious disease model provides a framework in which an epidemiologist can manipulate the model parameters and use computer simulations or results from the model to see what effect these manipulations have on their model output.

43. If policy decisions can be framed as changes to the model parameters, then the effect of the policy can be 'tested' by the model. The validity of this exercise, of course, depends on the posing of a plausible mathematical model in the first place, and the ability to correctly link the impact of a policy to the manipulation of the model parameters. I think it is important to stress that if *any* quantitative assessment of any proposed change to disease dynamics is to be made, this can only be done within a mathematical model framework of some kind.

An aim of the academic field of infectious disease modelling is to try and provide the best available framework to allow these kinds of questions to be posed, and to gain expertise in the link between data and the model.

44. The terms 'modeller' and especially 'modelling' are shorthand. All science has underpinning models, not always explicitly mathematical, but often so. I am a professor of epidemiology, not 'modelling', but I have a focus on understanding infectious disease dynamics, and this requires a mathematical modelling framework. The goal is to understand the epidemiology of infectious disease dynamics, but to do that one usually must have an understanding of the mathematical models.

45. There are a few common, and well established, frameworks for mathematical epidemic models. Compartmental models classify populations into distinct groups, such as those 'infected' and those 'susceptible' to infection. Within a compartment, individuals are considered homogenous with the same characteristics (although there can be very many compartments to distinguish characteristics). Often, ordinary differential equations are used to model the changes in the numbers within each compartment, and how compartments interact. The classic framework is the "SIR" framework, with a susceptible population, S, an infected population, I, and a recovered population, R. The equations are used to model how the numbers of infected change based on the size of the infected population, the availability of susceptibles to infect, and the contact rates between these groups. This basic framework is expanded upon by adding equations to describe more realistic details of disease spread such as demographics, and characteristics of the virus and the development of immunity.

46. An alternative to the compartmental approach is to use 'individual-based' models or 'agent-based' models, in which every individual in the population is modelled separately as they interact with one another and spread disease between individuals. Models can also be deterministic or stochastic. A deterministic modelling approach generates a fixed output for any set of assumptions. This represents the 'average' output of an interacting population. A stochastic modelling approach uses the expected randomness from probabilities, so that the model generates a potentially different output every time it is used. For example, if the average number of cases produced per day in a deterministic model is 2, then 2 cases will be produced every time the model is run. If a stochastic version of the model is used, then *on average* 2 cases will be produced, but on some days it could be 0 or 1 or 3 or any number from a chosen probability distribution. A stochastic model (and often an individual-based model) can usually be considered 'more realistic' to a deterministic (and

compartmental) however in computational terms they can often take a lot more time for a computer to generate the results. In addition, the outputs from a stochastic model tend to be more similar to the deterministic version when the aim is to describe disease spread in a large population. So a typical modelling approach might be to use a stochastic model for small populations, for which a high variability might be expected, and use the (quicker) deterministic version for a large population where the mean behaviour is sufficiently representative. The model will never capture everything that is happening in reality, and if it did it would be unwieldy, and we would not know what parameter values to use (there would be so many of them). So expertise is required to choose a model that balances a good representation of the system under study, while being practically useful.

47. The Swansea Model was based on a standard compartmental approach, with a large number of age compartments, and model code shared by the London School of Hygiene and Tropical Medicine. We used a deterministic and stochastic version of the compartmental model, but in practice almost all results presented used the deterministic formulation. The Swansea model used a standard SEIR framework, but also considered an asymptomatic infectious compartment, which is useful for COVID.

48. Using information on the characteristics of the SARS-CoV2 virus we used computer simulations to model how the virus would spread within the population of Wales. We modelled spread within each of the 22 Welsh local authorities separately, with links between the authorities which represented spread between areas. This was the 'transmission' component of the model, but most of the policy decisions are not based on number of infections (which cannot be observed easily), but rather on the impact of those infections such as the number of recorded clinical cases, the number of those cases that have to go to hospital or intensive care units, how long they occupy a bed (and therefore the total number of beds occupied), and the number of deaths.

49. The model linked the number of infections to a 'clinical event model' that counted the number of these events expected each day. To run the model, one would require an input of the model transmission parameters (the key assumptions on how the virus spreads) and the model clinical parameters (for example the infection case, hospitalisation, and death rate, and the length of stay of a case in hospital or ICU). The model would then produce as output a trajectory of expected infections and clinical outcomes per day calculated under those scenario assumptions.

50. In practice, for the model to be useful, it requires sufficient 'calibration', which is a set of reasonable choices for the model parameter values. Sometimes these are available from the literature, and these had to be updated whenever new information became available. Other parameters had to be estimated from emerging data in Wales using the model. For example, the reproduction number, R, which is the average number of new infections produced by a single infection. For a value of R above 1, the epidemic will grow, and for a value below 1 the epidemic will decline. R varies across an epidemic naturally: it will decline as more people become infected and susceptibles are 'used up', though it could increase again if there is rapid waning immunity or through virus mutation. R will also be impacted by policy interventions, for example reducing contacts between individuals will reduce R.

51. In order to generate any forecasts or policy scenarios one must understand the current value of R, how it has changed (along with other parameters). This value must ideally be obtained for the population of interest. We used the model to estimate the value of R in Wales by comparing the model output to the observed data in Wales and 'choosing' the value of R in the model for which the model output looks most like the data that has been collected up to that point (a statistical process called model fitting). We fitted the model initially (May 2020) to the trends in deaths in Wales, because they were the most reliable observations.

52. This was followed by fitting the model to hospital admissions data provided by PHW (from June 2020). In August, we started fitting the model to case data as well as it became more consistent following the expansion of testing availability. From autumn 2020 onwards we fitted to deaths, cases, hospital admissions, intensive care admissions, total hospital bed occupancy and intensive bed occupancy as this data became regularly available (updated several times per week by PHW).

53. The process of model calibration / model fitting is important preparation for generating model scenarios or forecasts. A real-time forecast can be made by fitting the model to data up to the current point in time, and then using the model to generate the expected future trajectory of all outputs of interest under the assumption, for example, that population behaviours will remain the same. We would only make this kind of forecast over a short period of 2-6 weeks, because of this assumption. The term 'projection' is often used for this kind of model use, because the current behaviours are being *projected* forward for a short time. Another use of the model is to generate a 'scenario', based on future changes to the system. This requires more detailed assumptions on how the population behaviour

will change in the future or how a future intervention will impact the virus spread. For example, how much will the contact rates reduce after the NPI, in comparison to typical contact rates before the pandemic. The Model can be useful for such a 'what-if' exercise, because the assumptions have to be formally (mathematically) defined. Making these assumptions clear is a strength of modelling.

54. It is very important to evaluate model assumptions, and these can be encapsulated in the parameter values used to generate a scenario. Thus, in a scenario exercise, one might pose the question of what would happen if, in say 2 months time, an intervention was put in place that would halve the contact rates between individuals. The model would be set up by fitting to the current disease trend data, then the model would be run on the computer to see what trajectory would be expected if nothing changed for 2 months, and then the model parameters would be changed to reflect the proposed reduction in contact rates; the model run would continue and the output would be used to see what kind of impact that would have on disease spread in the scenario. Many different scenarios could be combined, so that scenarios could be explored whereby contact rates were reduced due to movement restrictions for a certain time, and then increased again as restrictions were removed. At the same time the scenarios could include reductions in the typical effective infectious period that could reflect more rapid test and trace capacity, or reduction in the numbers of susceptible people through vaccination, or increase in the transmissibility of the virus through a new variant emerging.

55. Over the course of the epidemic the Swansea Model was extended to include the impact of different variants, vaccination (including differing protective effects of vaccine on infection, hospitalisation, intensive care and death), boosters and waning immunity. Separate models were developed for competing variants, and for assessing the test and trace system specifically. The data sources relied upon were provided as weekly (3 times per week at critical times) emails from Public Health Wales Colleagues on cases, hospital admissions, intensive care admissions and deaths. For occupancy data, separate data was provided by weekly (daily at critical times) Welsh Government StatsWales data. Because the model generates output that reflect all these data sources the model can be 'jointly fitted' to the data, so the parameter values are chosen for which the model output best matches the combined patterns in all the data sources. If there were gaps in the data, a reduced number of data sources could be used so the model was not reliant on having all data sources available at all times.

56. Uncertainty in the models can come from numerous sources. It can be structural, so that if different assumptions are used to build the model then the output can be different (for example a compartmental vs individual based formulation). My experience was there was very little time to test different model formulations and I picked the structure based on experience, expected ease of use, it was a 'standard' and well used and understood framework by those familiar with quantitative epidemiological dynamics; there was considerable age-structure (crucial for COVID-19, which has such a different impact on different ages), and some geographic consideration (22 local authorities), the structure was transparent, so easy (in principle not in time) to reproduce. As mentioned, we occasionally used a stochastic formulation which aims to mimic some of the natural uncertainty in disease dynamics. However, in practice we did not find relevant differences in scenarios produced using the stochastic formulation and relied mainly on the deterministic outputs.

57. Although greatly constrained by time, the team did investigate the structural uncertainty briefly with some comparison to a published agent-based model (Open ABM, maintained at Oxford). We ran simulations with the same parameter input (as far as possible, given different models have different parameters) and found outputs appeared similar enough for us to make the decision to focus on the Swansea Model. We would have used both if we had time. If different models can be run in parallel then this would help address structural uncertainty more formally. This was part of the importance of SPI-M-O, at which different modelling groups (including ourselves) independently generated model output for specific (or similar) scenarios and the results could be compared.

58. A second source of uncertainty for any model is the input values used for the parameters. Sometimes these can be obtained formally by fitting the model to data (thereby obtaining an estimate of the parameter value and an estimate of uncertainty in the value, which then can be used to define ranges of parameters for use in the model). Other parameter values can be obtained from the literature, or from expert opinion. The latter might be especially important for generating parameter values for future scenarios. If a policy is proposed then a decision must be made on how that will change a model parameter. Rarely will a precise value be known, so uncertainty needs to be taken into account. The approach of the Swansea Team would usually be discuss parameter values with the TAC modelling subgroup and chose plausible values across a range of uncertainty. For example, when modelling the rise of a new variant one could consider 'high', 'medium', or 'low' ranges for transmissibility. The model outputs would then represent our uncertainty according to these assumptions. It would be very rare not to consider wide ranges of uncertainty in scenarios.

59. Model validation usually rests on a retrospective analysis of model conclusions. One can consider whether the model fits the existing data closely, and whether certain conclusions from use of the model were realised.

60. The Swansea Model was quite useful for analysis of the first wave (retrospectively conducted as soon as the model was up and running in May). During the first wave there was very limited data. Due to lack of testing, case data was unreliable, and there was no data on the total numbers infected. The model could be fitted to the deaths-only data, but the output used to infer the actual number of infections. These values were important for later assessments of 'herd immunity' which is the process by which the rate of spread of infection declines as more individuals have been exposed to the virus and have developed some immunity, so that there are fewer fully susceptible individuals that can come into contact with a case.

61. Since the number who had been infected during the first wave was not directly measured, the model could be used to provide an estimate. This was useful in preparing the reasonable worst case for winter 2020, which was based on the calculations that there were sufficient fully susceptible individuals remaining to generate a large wave.

62. Similar arguments were used in the summer of 2021 for the delta wave. The fit of the model could also be used to 'back calculate' the initial exposure of the Welsh population, ie the number of cases brought into Wales in early 2020 to 'seed' the epidemic. This is a value required to run any simulation with the model, and hence had to be estimated. The initial seeding of the population was estimated as the total introductions, and their geographical dates, that generated the best model fit to the first wave of deaths. Thus, the models are useful for inferring several processes that cannot be directly observed during the early stages of the outbreak of a novel virus, making good use of limited data.

63. A key parameter that derived from infectious disease modelling and was used throughout the pandemic is the reproduction number, R. On average, a single infected individual causes R new infections. The value of R changes over time, because it is determined by the interaction of infectious and susceptible individuals, so at any point in time in an epidemic, the subscript t is used to define the reproduction number at that point in time: R 'at time t' or 'Rt'.

64. If Rt is greater than one the number of new infections is increasing. Because this is a compound process, the increase in infections can be very rapid or "exponential" with

numbers doubling over potentially short time periods. Hence control efforts can be focused on bringing the Rt value below 1 (when the numbers of infections will decline) or if this is not realistic bring it closer to 1 so that the doubling time is long (which give a longer warning and preparation time for the increase in cases and hospitalisations).

65. Infectious disease models are useful for determining which parameters of disease spread can be changed to have the biggest impact on reducing Rt, such as reducing contact rates or removing infectious individuals quickly via test and trace. Rt is usually calculated by fitting models to data on the rate of change of confirmed cases (since the numbers of new infections cannot easily be observed). In any estimation of a parameter from a data set, if the data set has smaller number of observations, there will tend to be greater uncertainty in the estimate of the parameter.

66. For this reason, the Rt estimate in Wales was naturally less certain than for larger populations in Scotland or England. This does not mean that strong conclusions could not be made on the Welsh Rt value at many points. However, at some points there would have been greater uncertainty. An example of this would be 'troughs' in case numbers following strong interventions, such as summer 2020. At this point there were very small numbers of cases per day in Wales meaning that the uncertainty in the estimate of Rt was high, and it would be difficult to detect the precise period at which the Rt value returned to above 1 (as would be expected following the removal of interventions). This would gradually become apparent as the signal of doubling of case numbers emerged.

67. Rt in Wales was calculated by several groups at SPI-M-O, and published on dashboards (for example by Imperial and London School of Hygiene and Tropical Medicine). A composite, combined, estimate of Rt in Wales was produced weekly by SPI-M-O at which the different model estimates were discussed and a consensus reached for publication. (Note that this addresses some of the structural model uncertainty discussed above, plus some of the data uncertainty since different models used different sources of data (cases, hospitalisations, deaths)). Outputs from composite models were particularly useful for addressing the uncertainty, since this would become apparent in any discrepancies between SPI-M-O model estimates, for example if one team's model had R below one and another R above one. This could be indicative of a turning point of some kind in the Welsh epidemic.

68. Within Wales, I advised colleagues at Public Health Wales on how to estimate Rt using standard statistical software. These estimates were then produced weekly by PHW. The

Swansea Model also generated an estimate of Rt, although this was not usually a weekly process (statistical software estimates are much quicker to produce and the Swansea Model was largely used for generating retrospective analysis or longer term scenarios).

69. If quantitative forecasts of any kind are to be made, a mathematical model is a necessity. However, this does not mean that the forecast is accurate. The accuracy depends on the posing of a reasonable model framework, and the availability of good data to use as inputs for the model parameters. In my view, the model framework used at SPI-M-O were generally robust (and further strengthened by the complimentary approaches made by different teams).

70. There is a very strong literature on mathematical epidemiology going back over 100 years, and outstanding expertise in epidemiology at SPI-M-O. I also think in general that the data available for estimating model parameters was at most times very detailed. The provision of sometimes daily data on cases, admissions, and clinical events was unprecedented. However, there is a further step in making a forecast: how will parameter values *change* in the future? This is exceptionally difficult to predict.

71. For this reason, I stressed every time that I presented model output the term '*scenario*' rather than 'forecast' or 'prediction'. The co-chair of SPI-M, Professor Medley, was a great advocate for the importance of this, such that it became a mantra for people working on the modelling. We cannot make long term forecasts because we just do not know how parameters will change. For example, if a set of restrictions are introduced, what will be the effective reduction in contact rates (which would generate a scenario), and how long exactly would those reductions last? We might have evidence from previous NPIs, but would the same effect manifest if they were introduced another time? Would people adhere to restrictions to the same extent for the whole period, or would there be a relaxation of behaviour? For this reason we often included different levels of assumed adherence in scenarios.

72. Another example would be the impact of vaccinations. At the early stages there was limited data on the long term effect, so a scenario would have to be generated based on different scenarios for the waning protection on infection or clinical events. I like to use the term 'what-if' for our model scenarios. The models are useful (and are the only way) of generating quantitative scenarios on well-defined *assumptions* on future events, and then how they would combine to impact the epidemiology. This meant that, in practice, when I used the model, most of the time was spent in discussing, justifying and preparing those

assumptions for a model scenario run. I found several colleagues at the TAG Modelling Sub-Group to be extremely helpful for this. Expertise could be brought in from different areas of epidemiology and used to try and pin down useful assumptions for the model inputs. The TAG sub-group was very collegiate, but also very challenging through a wide range of expertise, so that model inputs and outputs were often criticized and the aim was to come to as good a consensus as we could within the time period, to update the model if necessary and also to focus on an appropriate range of parameters (since the exact values would not be known) to generate useful model scenarios. Again, the emphasis was on 'what-if' scenarios rather than saying these were forecasts of exactly what would happen. If I were faced with a similar situation again, I would definitely want involvement of the TAG modelling sub-group. It is to the benefit of the modelling exercise to have sceptical challenges, experts in related domains, and those directly involved in the planning decisions to ask the most important questions.

73. Probabilities of certain future events were not generated as model outputs. In many cases this would be an inappropriate use of the modelling. The mathematics in the models is essential, but it is important to stress that the quantitative/mathematical nature of the modelling does not by itself lend the models a false sense of precision. I presented a great deal of scenarios to TAG, but they did not assign probabilities to future events directly. They were considered by other members, discussed and a consensus summary of the evidence would be generated and circulated for final adoption. In that way, the models would be combined with other evidence and expert opinion to generate a consensus on likelihood for events similar to PHIA yardsticks, which uses terms such as 'highly likely', 'remote' or 'almost certain'.

74. Therefore, I do not believe there was an over reliance on modelling. Without the mathematical framework there would have simply been no framework for the trajectory of the epidemic, nor the impact of introducing or removing interventions. That framework however was not an end point, it was a *starting point* for discussions which would involve considering the model uncertainties, and the many factors outside the scope of the model.

75. In addition, the model also provides a framework for considering several such additional factors. We incorporate economic costs and QALYs into the model at quite an early stage (Autumn 2020) such that, in theory, the costs of interventions (economic, QALYs) could be calculated alongside the benefits (reduced deaths, reduced cases, reduced periods of mild or severe illness, reduced hospital admissions and lengths of stay, reduced intensive care costs). [A QALY is a "quality-adjusted life year"; a measure of the quality and quantity of

life lived (or lost) that is used to assess the impact of any medical intervention. 1 year lived in ideal health conditions is equal to 1 QALY, and the value of the QALY is reduced dependent on the level of poor health experienced by a patient during the year].

76. Typically, an intervention is considered cost-effective if the cost per QALY saved is below a defined threshold. In England and Wales, the National Institute for Health and Care Excellence (NICE) provides guidelines for this. For example, an intervention is typically considered cost effective if the cost of the intervention is less than £30,000 for each QALY saved (this can be higher for some life extending interventions). Health burdens of a disease on a population through deaths, and illnesses of certain durations can be evaluated, if data is available, by health economists by assigning QALY values (hence costs) to these events, and then these costs can be compared to costs of interventions to investigate the balance of an intervention against the costs of the impact of the disease. Every run of the Swansea Model can produce these outputs, however reliable values for enough of the inputs were not readily available for the generation of robust outputs which could be used in practice.

77. While data on the epidemiology and typical hospital costs and disease burdens was generally available, data on indirect effects was not, and that modelling could not be well developed at that time. This was frustrating, because the potential for indirect effects of NPI interventions was recognised absolutely immediately, and discussed on many occasions at TAG, including economic, social, educational and medical (through cessation of regular services) with the recognition that these could be long term. However, the quantitative data to consider these factors formally, within any model framework was unavailable. I find it somewhat ironic that one aspect of the epidemic analysis that very quickly did produce a rigorous framework to analyse the pandemic: quantitative infectious disease epidemiology has been given the blanket term 'modelling' and attracted some criticism of over-reliance and for not including factors relating to certain harms, when a formal framework for understanding those harms quantitatively simply did not exist, was not generated during the early pandemic and largely still does not exist today. Further, when these factors can be properly understood they will then inevitably be brought within a 'modelling' framework alongside the epidemiology if the costs/benefit analysis of any intervention is to be properly understood. One cannot understand the pandemic without 'modelling'. At this point the modelling aspects that are best understood are probably still the infectious disease dynamics.

TAG and its Subgroups

78. I was a member of TAG, the TAG modelling sub-group and SPI-M-O. There were several other members of all three groups, in particular Brendan Collins, Craiger Solomons, Laura Andrews amongst others. All were excellent at asking regular Wales-focused questions and I felt that Wales was well represented at SPI-M-O.

79. I think the discussion of advice within TAG and the communication of advice between TAG and ministers was good and rapid. I think I was in a good position to see this in practice, given how often modelling scenarios were requested and how there was often a quick 'back and forth' if further scenarios were needed or different ranges in underlying assumptions needed to be explored. I was confident in the ability of the TAG communicators to represent the model outputs (for example stressing the 'scenario' rather than 'forecast' aspect). But there were also occasions where I was invited to meetings to directly explain the modelling process, model scenarios and their interpretations to ministers (for example to the Cabinet on 12th April 2021, the new Health Minister on 8th June 2021, to special advisors 24th June 2021, Ministerial Briefings meeting 9th September 2021).

80. There was a standing item on many TAG meetings where the international perspective was reviewed. I always found this interesting and learned a lot from it.

81. The commissioning of my scientific advice as far as my experience was concerned was informal. Over most of the period considered in the inquiry we were not 'commissioned', and not paid in any way directly or indirectly through support grant funding. We were simply in a position to have expertise in the field of infectious disease dynamics modelling and on hand to provide as much support as we could. As soon as it became apparent we had skills in this field and could deliver rapid outputs we were asked continuously for modelling output. Most of the work was done by myself, alongside my regular university roles (including adapting teaching to online) and one research software engineer from the university (who was released from some Supercomputing Wales commitments). Three RSEs filled this role sequentially. Thus, the advice generated was underpinned by the University, Supercomputing Wales, and largely by our own time given for free. Later, the Swansea Team received formal commissions from October 2021 (backdated to August 2021) which freed myself from most University commitments and allowed the team to expand by formally supporting the RSE position. It would have been exceptionally difficult to have kept working *pro bono* for any longer.

82. The questions posed by the informal requests were almost always relevant, and well chosen by TAG, in particular led by Dr Brendan Collins (chair of the modelling sub-group) and his team; by Dr Rob Orford (co-chair of TAG); Dr Chris Williams and other colleagues at PHW; Dr Jenny Morgan from NHS Wales Delivery Unit. At the TAG modelling Sub Group a large number of colleagues contributed and kept the focus on relevant and important questions, in particular Dr John Watkins from PHW, Hugh Bennett and James Cooke from the NHS Wales Ambulance Trust, Andrew Nelson from Cwm Taf Morgannwg University Health Board on the bed planning side, and other important contributors. Because the commissioning was informal, I was not limited by the framing. Almost all modelling outputs were generated by a back-and-forth discussion process which allowed feedback and questions to be refined.

83. Several members of TAG sat on SAGE and the SAGE sub-groups. This was very useful in bringing the latest news and events rapidly to TAG. I believe that TAG had a good and challenging voice within SAGE, through both co-chairs. For the modelling work I did not encounter any unequal access to information across the 4 nations, since I had access to the SPI-M-O documentation which always considered the devolved administrations and contained some of the most detailed DA-level comparative analysis.

84. There was a good range of experience across TAG, though of course experience with actual pandemics within the UK was limited. There was considerable influenza (including pandemic influenza) experience. Behavioural scientists were well represented and vocal (for example running very good seminars to discuss emerging evidence). There was extensive clinical expertise. I believe there was a clear definition of roles, and an open collegiate environment. Divergence of opinion within TAG was addressed during the many meetings, and then a summary of the consensus would be circulated by e-mail for final comments. The support teams around the TAG groups were excellent. Focusing on the modelling aspects, support provided by the TAG modelling team led by Brendan Collins and Craiger Solomons, including Laura Andrews, Sean White, Aimee North, Emma Ng and others were excellent. I also witnessed the excellent support provided by Public Health Wales colleagues in providing regular data updates, and NHS informatics / Delivery Unity colleagues. I did not participate in any WhatsApp groups with policy makers, advisors, or civil servants concerning the Welsh Government's response to the pandemic.

85. Regarding the TAG structures, personally I did not find there was much time to stop and think much about the organisation itself while it was running. I felt that the key people were there with whom I wanted to share results and scenarios, and also frame questions for my

Team. After that, I was just too busy getting on with as much modelling and analysis as could be provided, while teaching and performing other University duties.

The early Stages of the pandemic

86. I first became aware of COVID-19 from the news, around mid-January. Given my academic background I obviously took interest and followed the story closely. I have a lot of colleagues in the infectious disease modelling community. I knew Neil Ferguson at Oxford Zoology Department when I was a PhD student (and Neil was a post doc), so paid close attention to output from his group at Imperial and his interviews in early February, which pointed very much to a concerning situation. I discussed with colleagues at the Medical School that the scenario of very large numbers of infections in 2020 would be likely, and I expected some considerable interventions would be very unlikely to be avoided and would happen soon. I took the opportunity to discuss this with a colleague from PHW on 13th and 14th February, when we were teaching together (epidemiology to medical students). I offered analysis help to PHW if they needed it and it was obvious he would be exceptionally busy over the next few weeks. On 4th March 2020, following some of the publication of modelling from Imperial and LSHTM, I reached out again saying that I was available if any specific modelling strategies relevant to Wales that need looking into or interpretation needed. I was particularly interested in analysing the effectiveness of contact tracing strategies at that time and suggested that as a starting point.

87. I received a reply on 26th March and was put in touch with Dr Chris Williams who was leading in this area, and with whom I got later to work very closely with. I immediately emailed Chris, and offered my services, suggesting interpretation of the models coming out of Imperial and other large groups at the time, as I did not think that new Wales-specific models could be developed so quickly with the resources available. I had an immediate reply from Chris that insight into the models would be useful, but also Chris pushed the idea of building Wales specific models. This was my first indication that Welsh models would be very welcome. I knew this would be a lot of working from a standing start, so started thinking about different approaches. Over the next few days, we discussed an All-Wales model, and by the end of March, Professor Biagio Lucini had been in touch with me and told me support with software engineering might possibly become available. This set us on the path to build the Swansea Models.

88. Throughout April, I prepared some simple models for fitting the Welsh local authority epidemic curves, and met colleagues at the SAIL databank in my department at Swansea University to discuss initiation of projects that could monitor the health outcomes of the Wales population as rapidly as possible throughout the crisis. SAIL is a databank of linked health records that can be accessed as a trusted research environment so that individual events can be linked and analysed anonymously. This is exceptionally important system for the monitoring of populations over time in the health service and assessing the spread and burden of disease and hospital activities. SAIL provided timely reports to the Welsh Government on many aspects of the impact of COVID in Wales throughout the pandemic.

89. Meanwhile, in mid to late April, I was introduced to more colleagues from Public Health Wales and had zoom meetings to advise on the calculation and interpretation of Rt, helping with software methods and preparing the code. This project ran through the duration of the pandemic, with weekly reports on the R value at the national and local level.

90. In January and February, I did not provide advice to core-decision makers within the Welsh Government (or other governments). Although I had started my correspondence with PHW before, I believe my first contact with Welsh Government was when I was introduced to Brendan Collins at TAC, by Chris Williams, via an email on 29th April.

91. In January and February, I liased informally with UK counterparts in Edinburgh University, Professor Rowland Kao, a colleague in the field I had known for a long time. I had similar contacts with long standing colleagues in Microsoft in Seattle (Professor Simon Frost) and North Carolina (Professor Alun Lloyd, who provided expert support on many occasions over the whole period). I had no discussions with PHW or Welsh Government regarding the major gatherings in Cardiff in March 2020 such as the Stereophonics Concert or Wales vs Scotland Match.

The timing of the first national lockdown

92. It is clear that once the situation of late February/ early March was reached, a first national lockdown was necessary. By this point there had been thousands of 'seedings' of COVID throughout Wales, and a non-linear rapid increase in cases. Even given the very large reduction in contact rates that occurred leading up to – and at the time of the full lockdown, and the subsequent great reduction in transmission rates, the inevitable wave that had

already built up caused extremely high hospitalisations, stress within the health services and a high death toll. Having the interventions arrive later, or be less stringent would simply have generated a higher peak in all clinical measures. It is clear that there remained enormous potential for infection left in the population. It is also clear that an earlier lockdown would have generated fewer severe clinical events, fewer deaths and less of an impact on the health service over the first wave period. The practical impact of R is dependent on the prevalence at the time, since if R is close to 1, a similar prevalence would continue to be maintained. Hence even if measure short of full lock down reduced R to close to 1, or even just below 1, then the high prevalence and clinical impact that was already in existence, would still be maintained for a long period, rather than be suppressed.

93. I did not provide any advice to core decision makers or PHW regarding the first national lockdown. The delay in lockdown, in my opinion, is likely due to the unprecedented circumstances that were being faced, with very little experience to draw upon. Clearly, a lockdown would generate economic and social difficulties, and everyone recognised these issues, but the extent of their importance was not quantified against the costs of any alternative (there was not the evidence base for this at the time, and today the evidence remains limited).

94. In retrospect, the national lockdown should have come sooner. This would clearly have reduced the impact of the first wave. We analysed this in July 2020 (paper presented and discussed initially at TAG on 24th July 2020 and shared with NHS). [**MG/32 - INQ000228473**]. It is likely that even a week earlier would have made a significant impact on the first wave, approximately halving all clinical events and hospital occupancy. This is not surprising given the doubling time at that point. Thus, even a few days would likely have made a notable difference. If lockdown was moved 2 weeks earlier the effect would have likely been compounded, resulting in approximately a quarter of the clinical events, and so on.

95. Similarly, we estimated a delay by a week may have led to a very large (close to doubling) increase in all clinical events over that observed. Clearly, lives would have been saved and hospital burden reduced significantly by earlier lockdowns over that time period. Note that by 'lockdown' here I do not refer to a single event, but the combined NPIs that significantly reduced contact rates at that time, including advisory and mandated NPIs and reductions in contacts in the days preceding the full lockdown. In our what-if analyses, we considered these NPI contact-rate changes as a whole and modelled the effect of moving the whole period of contact changes earlier or later in the year. Our conclusions were echoed by a

number of independent analyses of the timing of the UK lockdown reported around the same time. It is very difficult to assess the differing components of the lockdown, given how closely in time they were enacted, and their unique nature.

96. The impact of earlier lockdown on the subsequent stages of the epidemic are not nearly so clear. There is a possibility that later waves might have been larger or would have to have been dealt with sooner. However, there was such a steep learning curve to managing the first wave that it is self-evident that it would have been better for this learning to take place under a lower stress than the situation that was faced in late March, April and May. It is also clear how difficult it would have been to manage the period at a higher prevalence that would have been so likely without such stringent measures.

97. During this time there were advances in the understanding of treatment, therapy, individual protective measures, PPE availability, test and trace and general epidemiology. Thus, even if subsequent waves had the potential to be larger (following an earlier lockdown) they would likely have been met with such improved tools, and the baseline impact of the pandemic in Wales from the first wave, and likely overall, would have been less. Further, a key difference between the first wave and second wave was the greater shut down in non-covid services at the first lockdown, to provide the required capacity for cases of COVID. During the second lockdown, more of the routine services were still active. It is plausible that an earlier lockdown, with a much lower general burden of COVID would have allowed more elective treatments in the health services at that time, reducing the delays that were experienced and long-term consequences. Finally, one must consider the huge impact within care homes, despite the knowledge they were at high risk. Evidence suggests that efforts available at the time to keep COVID out of care homes could not overcome the extensive exposure when communities had such a high prevalence of infection. An earlier lockdown, which would have lowered community prevalence in April, would likely have reduced the exposure in the high-risk care home population that was ongoing at that time.

April 2020 onwards

98. I do not have expertise in understanding 'behavioural fatigue'. The topic was discussed on many occasions at TAG and I understand that there was generally very good adherence to rules throughout, and especially during the first 12 months, so that behavioural fatigue

at that point was not a major factor. At most points of NPI introduction there were clear reductions in transmission, suggesting the reduction in contacts were occurring as expected. At several points we were asked to include 'what-if' levels of adherence in model scenarios, to try and cover the possibilities that the effect of an NPI later in the epidemic might not be as high as early on. However, I do not think it is easy to disentangle the different effects at different stages of the epidemic, such as test and trace, NPIs, general awareness, to isolate the effects of any behavioural fatigue.

99. To my knowledge, TAG was not consulted on the effects of 'Eat out to help out'. The policy was introduced on August 3rd to August 31st. At this point it was already clear that, due to relatively low cumulative number of infections and low level of 'population immunity', that the recent removal of NPIs would result in Rt soon rising above 1 and a resurgence in cases. In Wales, cases gradually declined from June into July, but the subsequent plateau was indicative of an R value very close to 1 (as mixing increased). The pattern of increased cases in Wales is indicative of R becoming greater than 1 around early to mid August, and hence it was likely from that point that the high growth rate in cases and hospitalisations would follow. It is likely that many changes to behaviour across July and August contributed to increased mixing and transmission, but any policy that explicitly encouraged the mixing of people indoors, such as 'eat out to help out', would obviously contribute to increasing the R value and the growth rate. This sped up the arrival of the second wave and gave less time to prepare. Clearly, a financial investment would have far better been spent on encouraging outdoor activities which could have had a lesser impact on effective contact rates, especially at that time of year.

100. The TAC circuit breakers were a useful indicator of early warning of rising case or hospitalisation rates. Having a range of these factors, from R values to case incidence, to hospital admissions, was important because of the natural lag in the system, whereby changes in transmission patterns have an immediate effect on infections, but these are not manifest in clinically confirmed cases for several days, then these cases are not usually manifest in hospitalisation until another delay of several days and so on to ICU and deaths. These lags caused difficulty in interpreting data and communicating epidemiological trends throughout.

101. For example, after periods of epidemic growth, if an intervention reduced transmission and R was brought below 1, hospitalisations could continue to rise for a substantial time because this was an inevitable (sometimes the term 'baked-in' was used) consequence of infections that happened *before* the intervention, but the individuals were yet to be

admitted to hospital. The modelling was very useful in illustrating these lags, and I was asked on many occasions to explain and provide an illustration of this. I thought it was a good idea to include separate practical factors for circuit breakers, such as ICU occupancy levels, because whatever the transmission indicators are, there are constraints within the health service (such as bed capacity) that must be monitored. I think a retrospective analysis of the data stream that gave the earliest warning indication would be useful. In practice I think after the first wave, the case, Rt and hospitalisation (and occupancy) were sufficient and used most often.

102. By September 11th 2020, it was very clear R was above 1, cases were in the 100s per day while there had occasionally been single figures in early August. At this time a TAC report referenced the SAGE R number for Wales at between 0.7 and 1.0 and stated that the current R number was higher than this suggests. This is because the SAGE published estimates of R, indeed any estimate of R using case or hospitalisation data, represents a lagged estimate. There are two components to this, one is that the data itself has reporting delays, so that an estimate on a given day would use data up until a few days prior to that. The second is that trends in cases are a lagged indicator of trends in infections. It takes about a week for trends in infections to be manifest in case data, so that if there was a sudden increase in infections today, that would be seen in the case data in about 1 weeks' time. The lag is even greater if a model uses hospitalisations or deaths to estimate R. When these effects are combined (and the preparation of the model estimate plus its publication adds two further delays) it means that an R value published on a particular day typically represents the transmission situation roughly 2 weeks prior. This means educated assumptions can be made, so that in the example, if R was estimated at 0.7-1.0 and in the intervening 2 weeks contacts were known or expected to have increased, one could expect the given R value to be an underestimate.

103. The reason for the increase in R was the increased contact rates across the summer following the removal of NPIs. By this time, we had prepared a new model Reasonable Worst Case, which showed potential for a large second wave, and we were also asked to investigate application of more stringent restrictions. While school opening and closing factors (as well as the contact rates usually associated with school activities taken from epidemiological surveys) were explicitly considered as part of the model, we did not explicitly model the effect of returning students to university. We could, however, include a scenario with increased contact rates in these age groups at that time.

104. TAC advice on 11th, 18th and 25th September and 2nd October tracked the worsening situation. I believe the conclusion that NPIs would likely be needed to bring R below 1 if incidence and hospital admissions were not to exceed planning levels was taken very seriously by the Welsh Government, evidence by the plans that were then implemented for the firebreak. We were first asked to model specific firebreak scenarios of 2 or 3 weeks on Sunday 11th October. Over the next week we considered 'what-if' scenarios for the duration of a firebreak (2-4 weeks), it's likely impact on R (whether it had the same impact or less compared to the first lockdown) and the post-firebreak assumed R value with scenarios for it to return to exactly as before, be a little less (if for example TTP was able to have a greater effect) or for it to rebound and be higher (as we were heading deeper into the winter and there might be seasonal effects). Under each scenario we calculated the model estimates for the potential reductions in cases, hospitalisations and deaths over various timelines, and the expected time before the epidemic returned to the pre-firebreak point.

105. In retrospect, the timing of the firebreak does appear reasonable, at a time when the trajectory was clearly concerning (and trajectory inevitable), but before it was overwhelming. In retrospect, a longer firebreak would have been very useful. The effect on R in Wales at the time was very significant, driving transmission rates down to levels similar to the first lockdown, and R well below 1. If it had lasted only another week or 2, then it is likely that the additional suppression of transmission would have meant that the rebound afterwards, the return to pre-firebreak levels, would have been delayed by several weeks, pushing it deep into December. This would have meant that Wales would have faced the period of high winter transmission, plus the emergence of the alpha variant, from the starting point of a much lower community prevalence than it had to face in December 2020. It is highly likely another lockdown would have still been needed when the potential of alpha (both transmission and severity) became clear, but the subsequent peak would, again, likely have been significantly lower (as measures were sufficient to bring the R value of alpha well below one). The emergence of alpha and the exact characteristic of winter spread were not possible to predict. Hence, given the information at the time, the firebreak length could be considered reasonable, because a key aim was not to prolong a lockdown. Nevertheless, the period was short, and if it could have been longer then more time could have been bought during this difficult period, and overall community levels could have been kept lower. It is clear that without any intervention, over the time period of the firebreak (subsequent period) the burden of cases, hospitalisations and deaths in Wales would have been far higher.

106. Following the firebreak, the return to the pre-firebreak situation fitted well with the model scenarios. The R value returned above 1, as would be expected with the relaxation of NPIs, and the value was initially returned to pre-firebreak levels. The question then became how long until hospital admissions again would exceed planning levels and another set of NPIs might be required. Model scenarios for these were prepared. As this point approached (into December), this was further complicated by the emergence of the alpha variant. This resulted in the rapid implementation of the third lockdown in December. In retrospect, given the knowledge we have of the timing of the emergence of the alpha variant, an earlier implementation of the third lockdown would have been useful to reduce the peak and impact of the second major wave.

107. In terms of other NPIs, the model used a contact matrix that described the typical number of contacts per day between different age groups. The starting point for this matrix was epidemiological surveys such as POLYMOD or COMIX which provide estimates for the typical number of such contacts per day (in pre-pandemic times, and during the pandemic) and also assign them to activities such as work, school, home or leisure. In order to model an NPI, a proportion of these contacts could be 'removed' from the model to simulate the intervention and its subsequent effect on the transmission rates of the virus. In practice, we did not specifically model working from home, or the use of face coverings. This is partly because the changes to the effective contact rates would be unknown but also because we regularly fitted the model to current situation in Wales, so that the model represented the overall contact levels in Wales *at that time* (essentially captured in the Rt value, which would be influenced by all NPIs in tandem). We made more explicit analyses of school openings and closures, as they were easier to clearly defined.

108. Half-terms and holiday periods were explicitly included in all model scenarios. We focused on this question in greatest detail in early 2021 when were asked to provide evidence to inform school openings after the third lockdown. In terms of relaxing the stringency of restrictions, this was the priority, so we modelled a range of staggered school opening scenarios as the first opening up, while other NPIs were kept in place.

109. We spent a very limited time analysing local and regional restrictions and border controls as these were not generally a focus when we became involved. I think this would be a useful area to explore retrospectively, as it was clear at times that there was considerable variation across Wales due to north-south geography (and its links to different urban centres in England) and rural-urban contrasts. I would aim for a Wales model to have these explicitly included in future.

110. For self-isolation requirements, we developed a separate model, that was used for estimating the impact of test trace and protect. We used data provided by the Wales TTP team on the likely ascertainment of cases, the time since infection, and the time taken to trace contacts to generate an estimate of the likely R value in the absence of TTP hence its impact (and how this could change with changes to the ascertainment or trace times). We later used this model to estimate the impact of removing isolation requirements of contacts (before they were confirmed positive) and for all the u18s. This was implemented in August 2021.

Communication of Scientific Advice

111. I believe the advice of TAG and its subgroups was sufficiently transparent. I was really impressed by the efforts made by the TAG teams to write documents and make them available to the public so quickly. It was difficult enough for them to process the information coming in, and pass that on to policy makers with meetings and presentations. I was genuinely surprised (positively) that on top of that the published summaries of the advice were always kept at such high priority. I think it really would have been quite difficult (involving a lot more resources) for them to have presented more data, statistics and decision-making supporting information.

112. I don't think I ever recall the term 'following the science' being discussed. In my experience the scientists had enough on their hands to try and understand what was going on, and presenting that to TAG and the other groups. I had a clear understanding that once our scientific outputs were set out, then the policy decision discussions were separate. On most occasions, once a set of results had been delivered from a request, I moved straight on to working on the next set, while colleagues at Welsh Government collated the material, worked on their other evidence and shared with policy makers.

Lessons Learned

113. TAG was exceptionally well chaired, as was the TAG Modelling Sub-group. The sub-group structures seemed to work well. The amount of people who gave their time for so many TAG meetings was notable. As a large group, there was reasonable diversity and I

believe this improved as time went on. I felt that there was great collegiality, support, and that our voices were being heard. As highlighted in paragraph 39 I have serious concerns over the reliance on expertise from the University sector for prolonged periods without providing support for their day-to-day activities that they had to maintain, and do not think this could easily be drawn upon again. Also, on reflection, a formal public-engagement sub-group would have been really useful. A lot of time was spent speculating on public perceptions, with the absence of supporting data (because no one had been through a crisis like this before). A more formal way of collecting some of those opinions and information would have been helpful in many of the sub-groups, the modelling included. It would have been very useful to share the modelling process via public engagement, especially given the profile for the modelling that emerged rapidly and was maintained throughout.

Copies of Written Advice

114. Due to the efforts of colleagues at TAG, the modelling sub-group and Welsh Government, a lot of documents were produced in real time to summarise the advice. I have attached copies of the documents that include or refer to our analyses. They include 51 modelling or subject-specific reports, and 99 evidence summary publications. The schedule of documentation is attached as an appendix here.

Statement of Truth

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: 28th October 2023

Appendix 1

Unique ID	Exhibit reference	File name description
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