

Public Health England

The New and Emerging Respiratory Virus Threats Advisory Group (NERVTAG)

5th Annual Report January 2020 - June 2021

November 2021

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1. Chair's Foreword

The New and Emerging Respiratory Virus Threats Advisory Group (NERVTAG) was established in 2014, replacing the UK Scientific Pandemic Influenza Advisory Committee (SPI) and extending the role of the group to cover not only pandemic influenza but any new, emerging respiratory virus threat to the UK. With this expanded remit, NERVTAG has routinely considered a range of respiratory viral threats, including avian influenza viruses and Middle-East Respiratory Syndrome Coronavirus.

NERVTAG first met to assess the threat posed by the respiratory virus outbreak in China on 13th January 2020. Since then, NERVTAG has met around 75 times, often weekly, to review emerging evidence and provide independent scientific advice to Government. With the standing-up of the Government's Scientific Advisory Group for Emergences (SAGE) later in January 2020, NERVTAG began reporting into SAGE as well as directly supporting the Department of Health and Social Care (DHSC).

This report, which covers 18 months of intense work on COVID-19, provides an insight into the wide range of scientific advice provided by NERVTAG. The ethos of NERVTAG is to provide independent, transparent scientific advice and further details of the work summarised in this report can be found in the minutes and papers produced by NERVTAG, which have been made publicly available since the very beginning of the pandemic.

The scope of work of NERVTAG evolved over the course of the pandemic as new policy questions arose and as new advisory groups were established to take on specific topics that required more dedicated resources. For example, the topic of aerosol generating procedures was taken up by a separate group from July 2020 and the Environmental Management Group was established in July 2020. This evolution is reflected in the content of this report.

NERVTAG membership was expanded in response to the pandemic, increasing the representation of coronavirus experts, virologists, clinicians and seconding additional expertise as needed. All NERVTAG members are volunteers and I am indebted to them for their contribution. They have given generously of their time whilst being incredibly busy responding to the pandemic in their day-jobs: caring for patients, running diagnostic laboratories, or leading research to better understand SARS-CoV-2.

Despite extreme pressures, the members of NERVTAG have at all times maintained the highest level of scientific integrity, reviewing evidence impartially and critically, giving frank advice and respecting and acknowledging differences of opinion and interpretation that are an inevitable part of science.

NERVTAG is supported by a professional scientific secretariat from Public Health England and by civil servants at DHSC and I cannot thank them enough for their superb service, without which we would have floundered. I would also like to thank Dr Catherine Huntley for her invaluable support to NERVTAG.

I hope this report not only acts as a record of the work of NERVTAG during the pandemic but also gives a flavour of the evolution of scientific thinking over the last 18 months and of the important contribution of independent scientific advice to Government.

2. Introduction

It is the aspiration of DHSC to embed scientific advice in the policy-making process. It is clear that scientific advisory committees must be independent of Government and NERVTAG, being comprised of experts in the field or working in organisations (such as the NHS) which would be in the front line of the response to an emerging new respiratory infection or influenza pandemic, are well placed to advise. The group draws on the expertise of scientists and health care professionals, including clinicians, microbiologists and public health practitioners, and colleagues in related disciplines. The group is supported by a scientific secretariat from Public Health England (PHE) and is scientifically independent.

From its establishment in 2014, it has been the role of NERVTAG to act as an independent scientific advisory group to the Chief Medical Officer (CMO) across the range of new and emerging respiratory viruses, and related preparedness functions. The scope of the group includes new and emerging respiratory virus threats to human health including strains of influenza virus (regardless of origin) and other respiratory viruses with potential to cause epidemic or pandemic illness, or severe illness in a smaller number of cases. Outputs from NERVTAG feed into the Department of Health and Social Care (DHSC) pandemic preparedness arrangements, and during pandemics, outputs feed into a Scientific Advisory Group for Emergencies (SAGE), chaired by the CMO and Government Chief Scientific Advise

r (GCSA). The Terms of Reference are at Appendix A. NERVTAG does not advise directly on matters of policy but provides scientific and clinical advice that may underpin the formulation of policy by DHSC. NERVTAG members are independent experts who volunteer to provide their expertise to the DHSC. They are required to declare any actual or perceived conflicts of interest to any matters discussed at NERVTAG and are not remunerated for their contribution.

From 2014 to 2019 there have been 2-3 NERVTAG meetings per year with additional subcommittee meetings as required. The advent of the global SARS-CoV-2 pandemic led to a substantial increase in NERVTAG's activities, as the group met on a regular basis to review emerging evidence and ensure their advice met the ongoing needs of the DHSC and SAGE and remained up to date. This report covers the period of January 2020 to June 2021, during which NERVTAG played a key role in providing advice and expertise to support UK's pandemic response.

Alongside the provision of advice pertaining to the SARS-CoV-2 pandemic, NERVTAG continued to monitor avian and swine influenza viruses and MERS-CoV and held three non-COVID NERVTAG meetings over this period.

3. Activities

3.1 Meetings and subcommittees

On 13 January 2020 an extraordinary meeting of NERVTAG was called to consider the risk posed by the 'Wuhan novel coronavirus'. This first meeting was the start of a series of meetings of the NERVTAG COVID-19 group, of which there were 40 full committee meetings in 2020 and 16 to the end of June 2021. In addition, there were 11 "Birdtable"¹ meetings in 2020, which largely focussed on a review of emerging data and horizon scanning. Extraordinary meetings were held to consider specific topics; novel therapeutics in February and March 2020, non-invasive ventilation (NIV)/high flow nasal oxygen (HFNO) in March 2020, contact tracing in April 2020, and four meetings on new SARS-CoV-2 variants in December 2020 and January 2021.

In total, this amounted to 75 NERVTAG related meetings over a period of 18 months.

NERVTAG subcommittees were established in 2020 and 2021 to consider specific issues of importance. These subcommittees included a Risk Stratification Subgroup, which considered clinical risk stratification; a non-invasive ventilation (NIV) and Infection Prevention and Control Subcommittee, which provided written scientific and management advice relating to the risk of nosocomial transmission of COVID-19 infection with non-invasive respiratory supportive therapies; and a novel therapeutics subcommittee.

Risk Stratification subgroup In response to a commission from DHSC and the CMO's office in May 2020, a subgroup to consider clinical risk stratification was established. The team was led by Professor Julia Hippisley-Cox (University of Oxford) and included NERVTAG members, external experts and representatives from DHSC and DCMO's office. Twelve meetings of the subgroup were held between May and December 2020.

The subgroup's objective was to produce a risk prediction algorithm to estimate COVID-19hospital admission and mortality outcomes in the UK adult population. The prediction tool should have versatility to be applied in a variety of health and care settings, including for GPs and specialists to use in patient consultations.

The <u>protocol</u> for the risk prediction model developed by the subgroup was published in June 2020, with a <u>press release</u> by the University of Oxford. The subgroup sought co-ordination across the four UK nations on this project, which would allow the model to be validated and used in the UK to inform mathematical modelling of the potential impact of national public health policies on shielding and preventing infection and in helping to prioritise vaccination. The details of the risk prediction model (<u>QCovid</u>) were released in the BMJ in October 2020. Work continued on the validation of the model into 2021.

In May 2021, a <u>publication</u> in the Lancet Digital Health showed that the QCovid populationbased risk algorithm performed well in validation, showing high levels of discrimination for COVID-19 deaths in men and women for selected time periods. There is the potential for QCovid to be recalibrated for different datasets and dynamically updated as more data becomes available, which enables it to be used effectively in guiding national policy.

3.2 Papers, statements, and education

¹ "Birdtable" meetings were introduced as regular informal horizon-scanning meetings at which NERVTAG members could raise and rapidly review and digest emerging data or propose new areas for consideration.

Another core element of NERVTAG's work was the preparation of papers and statements to summarise available evidence and make recommendations on particular issues of concern. In some cases, these papers are written in response to specific commissions from the DHSC or SAGE, while in others, they are initiated by NERVTAG members. In the 18-month period covered by this report, NERVTAG prepared and published 37 papers on topics ranging from SARS-CoV-2 transmission dynamics, to changes in the viral phenotype. A full list of papers published during this period, with links to where they have been published online, can be found in Appendix B

In addition to the above, NERVTAG issued three COVID-19 public statements, two of which summarised the evidence on increased transmissibility of the B.1.1.7 (alpha) variant, and one which summarised NERVTAG's position on cardiopulmonary resuscitation (CPR) as an AGP.

NERVTAG was also instrumental in sharing knowledge of SARS-CoV-2 as it became available. The Chair hosted two teaching sessions on SARS-CoV-2 immunity and variants for employees of the Cabinet Office and DHSC.

3.3 Membership, appointments and re-appointments

Members

In addition to the core members in place at the beginning of 2020, a number of others were temporarily co-opted to bring their additional expertise to the COVID-19 response. Details are found at Appendix C. Some NERVTAG members were also SAGE members and/or members of other SAGE subgroups.

In October 2020 the appointments of the following core NERVTAG members were extended by one year: Dr Ben Killingley, Dr James Rubin, Prof Peter Openshaw, Prof Andrew Hayward, Prof Calum Semple, Prof John Edmunds, Prof Neil Ferguson, Prof Robert Dingwall and Professor Wei Shen Lim.

In April 2021 a restructure and re-weighting of the committee was undertaken to better suit the needs of NERVTAG and the scientific advice that will be required in the upcoming months and years. As a result of that the following core members were reappointed for one year, effective from 20 July 2021: Professor Peter Horby, Professor Peter Openshaw, Dr Ben Killingley, Dr Cariad Evans, Dr James Rubin, Dr Jim McMenamin, Professor Andrew Hayward, Professor Calum Semple, Professor John Edmunds, Professor Neil Ferguson, Professor Wei Shen Lim, Professor Wendy Barclay.

Observers

Regular PHE observers/contributors included Prof Maria Zambon, Dr Jamie Lopez-Bernal, Dr Gavin Dabrera, Dr Jake Dunning, Dr Colin Brown and Dr Meera Chand.

An observer/observers from the Chief Medical Officer's office regularly attended meetings.

Observers from Northern Ireland, Wales and Scotland regularly attended meetings.

Observers from other advisory committees included SPI-M secretariat and SAGE secretariat.

Intermittent observers from other organisations/Government departments included the Government Chief Scientific Adviser (GCSA) office, FCDO, DHSC, Vaccine Taskforce, Cabinet Office COVID-19 Taskforce.

Support

In addition to data and evidence shared by NERVTAG members themselves, the committee considered data/information from a wide range of contributors in order to develop their advice for Government/DHSC; in total, more than 50 individuals attended and provided information; ranging from modellers and statisticians to investigators in studies of different groups of COVID-19 patients, studies in healthcare workers and in 2021, studies in COVID-19 vaccine recipients. A similar wide range of experts contributed to NERVTAG papers submitted to SAGE.

Secretariat support was provided by PHE staff. Camille Tsang provided secretariat support from the beginning of 2020 until April, with Emma Petty supporting minute-taking from March. Emma continued providing secretariat support, particularly for the Risk Stratification tool subgroup until October 2020. Fran Parry-Ford provided secretariat for the group from April to July 2020 and Ruth Parry took on the role from the end of July 2020 to the present date. Admin support was provided by Elaine Stanford, Stephen Barnard and Helena Bird.

From January to June 2021 Dr Catherine Huntley, a public health registrar in CMO's office, provided support for committee members by coordinating and writing papers commissioned by, or offered to SAGE.

3.4 Internal review

In January 2021, the Chair initiated an internal review of NERVTAG's organisation, the conduct of meetings and behaviour of members. The purpose was to identify what had worked well and what areas could be improved. To ensure feedback was frank, a process was established for confidential feedback via a third party. Overall, the feedback from members was positive with no major issue reported. Some areas for improvement in NERVTAG processes were identified and acted upon. There was overwhelming recognition of the importance of the NERVTAG role and achievements to date under Peter Horby's chairmanship.

Sir Patrick Vallance, the GCSA, joined a NERVTAG meeting in the latter half of 2020 to thank the members for their work supporting the Government throughout the pandemic.

4. Areas of review and advice

In 2020 and 2021 the NERVTAG COVID-19 group provided independent advice and expertise to the Department of Health and SAGE on a wide range of topics. A brief summary of some of the main themes considered in 2020 and 2021 is provided below. Much greater detail is available in the minutes of NERVTAG meetings, which can be found <u>here</u>.

Discussions at all meetings were informed by a variety of sources, including: early prepublication findings from research studies, commissioned pieces, PHE surveillance reports, CO-CIN reports, from mid-August, weekly PHE and JBC badged situational awareness summaries and from December 2020 Technical Briefings prepared by the PHE coordinated Variant Technical Group.

4.1 Clinical management of COVID-19

The clinical management of COVID-19 cases formed a regular component of NERVTAG discussions throughout the year, with a particular focus on novel therapeutics, such as antivirals, biologics, and host-directed therapies. NERVTAG made several recommendations and suggestions for further research in this area, including the prioritisation of research into experimental therapeutics. Advice was given on principles for trialling COVID-19 treatments in the UK. The role of convalescent plasma in managing cases of COVID-19 was also discussed.

Early in 2020, NERVTAG also discussed how SARS-CoV-2 might affect vulnerable populations such as children and older adults and adapted their advice as evidence emerged. The duration of hospitalisation episodes and ICU admission rates were regularly reviewed to gain understanding of the impacts of COVID-19. The influence of co-morbidities on disease severity and outcomes was discussed, including obesity as an independent predictor of in-hospital mortality. Evidence for other risk factors for severe disease and poor outcomes were also reviewed, including occupation.

NERVTAG also considered evidence on the severity of COVID-19 in children. Paediatric Inflammatory Multisystem Syndrome (PIMS) was discussed and recommendations made for appropriate research in this area.

Throughout the year, NERVTAG considered the risk of co-infection with SARS-CoV-2 and other pathogens, including influenza, other respiratory viruses, or bacteria. The impact of these coinfections on winter planning was also considered.

In September 2020 DHSC requested NERVTAG to consider the topic of 'long-COVID'. A consortium to study the longer-term health effects of COVID-19, the Post-HOSPitalisation COVID-19 (PHOSP-COVID) study coordinated by Professor Chris Brightling, had been funded. NERVTAG considered the scope of work of the consortium and fed back to Professor Brightling and to DHSC on additional work or considerations needed. NERVTAG indicated that the proposed workplan appeared comprehensive, covering most aspects apart from transcriptomics and linking with virology to address potential viral factors.

4.2 Contact tracing and contact management

At the end of April 2020, prior to the easing of the first lockdown and in advance of the launch of the NHSX App and the widening of what was then the PHE-led contact-tracing service, NERVTAG was asked to provide advice on various aspects of contact tracing. This advice was provided, considering input from SPI-M and SPI-B.

In May NERVTAG advised SAGE on a case definition for the contact tracing App and NHS111. In June, NERVTAG advised on the optimum window for contact tracing of asymptomatic people who test positive. In November SAGE commissioned NERVTAG to provide advice on management of contacts e.g. to quarantine for a set period or to introduce 'test and quarantine' or a 'test and release' policy. This was discussed at some length and a number of NERVTAG members contributed to a paper on the topic.

4.3 COVID-19 symptoms and case definitions

In early 2020, NERVTAG worked with PHE to establish an initial case definition and the clinical criteria that should be used to define COVID-19 cases, which were updated throughout the year as new data emerged. The symptoms and symptom clusters associated with SARS-CoV-2 were reviewed on a regular basis, including the presence of anosmia and ageusia, and the use of these symptoms as diagnostic features. The presence and importance of abdominal symptoms in COVID-19 was also reviewed. The likely proportion of cases that were asymptomatic, as well as the relationship between symptoms and infectiousness, were discussed on several occasions. NERVTAG also discussed the presentation of COVID-19 in the elderly, as well as the importance of delirium as a symptom.

4.4 Decontamination and environmental survival

At the beginning of February 2020, PHE Virology Cell presented a paper on virus viability and environmental decontamination; NERVTAG was content with the general approach and principles but asked for more data on certain aspects. At the end of March PHE shared with NERVTAG some data on environmental sampling in healthcare settings.

A SAGE subgroup; the Environmental Modelling Group (EMG) was set up and thereafter took the lead on aspects of environmental survival and transmission that had previously been considered by NERVTAG. The possibility that SARS-CoV-2 could be airborne was recognised and noted in NERVTAG Minutes of 13 January 2020. The EMG had presented a paper on this topic on 14 April 2020. NERVTAG members continued to contribute via joint EMG and NERVTAG papers on hand hygiene (July 2020), an updated paper on the role of airborne transmission (August 2020) and seasonality and its impact on COVID-19 (October 2020).

Differences in survival of the virus in the environment were considered again by NERVTAG in 2021 in the context of the emergence of variants. In a NERVTAG paper on the growth rate of SARS-CoV-2 B.1.1.7 submitted to SAGE in April 2021, the authors concluded that "data suggest that the environmental survival of B.1.1.7 is not meaningfully different from other variants (moderate confidence)".

4.5 Epidemiology of SARS-CoV-2

Reviewing the national and international epidemiology of SARS-CoV-2 formed a key component of NERVTAG's work, allowing the group to give informed advice on the current and predicted nature of the pandemic. NERVTAG regularly reviewed various epidemiological models and predictions of the trajectory of case numbers and fatalities due to SARS-CoV-2 in the UK. Phylogenetic trees and other genomic data were considered to show the growth and evolution of the virus. In addition, reports of outbreaks in various settings such as geographic regions, schools, prisons, and workplaces, were reviewed in order to understand contact patterns and epidemiological dynamics of SARS-CoV-2.

4.6 Establishment of the G2P consortium

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As variants emerged, it became clear that there was a gap in understanding of how the genomic changes/mutations affected the phenotype of the virus and the implications for transmissibility, severity of illness and potential to evade immunity. In May 2020, recognising the potential for variants to emerge, NERVTAG recommended to SAGE and DHSC that funding was made available for "co-ordinated research into functional implications of virus variants on diagnostics, vaccines, drug resistance, etc". In November 2020, when the Cluster 5 mink variants emerged, NERVTAG recommended that risk characterisation work was carried out including analysis of the fitness of variants in human respiratory epithelial cells and evaluating both vaccine and naturally acquired immunity in animals. The Chair again recommended to Go-Science that investment was put into a virus phenotyping platform. Subsequently, in January 2021, a new national research project to study the effects of emerging mutations in SARS-CoV-2 was launched with funding from UK Research and Innovation. It is known as the genotype to phenotype (G2P-UK) national virology consortium.

4.7 Immunity to SARS-CoV-2

A key consideration for NERVTAG during the early stages of the pandemic was the potential for re-infection with SARS-CoV-2, which was discussed on a number of occasions. A case definition for true reinfections was suggested, and methods for identifying reinfections were discussed.

At several points throughout the past 18 months NERVTAG considered data on the nature, strength, and duration of the immune response to SARS-CoV-2. NERVTAG considered the proportion of people infected that will mount an immune response, the types of immune response mounted, and how long these might last. Evidence for protective immunity against infection, symptomatic disease, and severe disease was reviewed. NERVTAG also considered the strength of the science behind immunity certification and made recommendations for further research.

4.8 PPE and IPC guidance

In January 2020, NERVTAG discussed the use of Personal Protective Equipment (PPE) in different settings, and the suitability of the pandemic PPE stockpile for use on medical or respiratory wards should sustained community transmission occur. In February, NERVTAG made recommendations to SAGE on infection prevention and control (IPC) measures to stop transmission amongst the public, including advice around face coverings and other preventive measures for different groups. PPE for first responders and IPC guidance in secondary care were also discussed.

Consideration of PPE and IPC was passed to Public Health England and NHS England later in the year, who produced and maintained up-to-date infection prevention control guidance.

4.9 Aerosol Generating Procedures (AGPs)

At the end of March NERVTAG reviewed a modified AGP section of the IPC document and over the next few months discussed the potential for various procedures, such as cardiopulmonary resuscitation (CPR) to be AGPs. A NERVTAG consensus document on CPR as an AGP was published in April 2020. Subsequently the Independent Panel on High Risk Aerosol Generating Procedures (AGP) was established to provide practical and scientific advice to the Chief Medical Officers(CMOs) for England, Scotland, Wales and Northern Ireland on specific high risk AGPs in the context of the COVID-19 pandemic; their first meeting being held in July 2020. One NERVTAG member was part of the Panel and reported back to NERVTAG on occasion.

4.10 SARS-CoV-2 and travel screening

On 13 January 2020 an extraordinary meeting of NERVTAG was called to consider the risk posed by the 'Wuhan novel coronavirus', at which time 41 cases and one death had been reported in Wuhan and SAGE had not yet been stood up. Although at the time there had been no reports on human-to-human transmission, NERVTAG stated that DHSC "should be cautious at this point in making conclusions about the absence of human to human transmission." NERVTAG was asked if it supported the position that port of entry screening is not advised at that time. NERVTAG supported this position based on previous analyses indicating that port of entry screening, whilst not having zero effect, had very low efficacy.

4.11 SARS-CoV-2 in care homes

The committee was presented with a PHE weekly COVID-19 surveillance report from the end of March. Amongst the community surveillance data, it was clear that a significant proportion of the reported outbreaks were in Care Homes. At the end of April, the committee was made aware of a PHE study of outbreaks over the Easter weekend in six London Care Homes.

Concerns were expressed over the situation in Care Homes and the Chair wrote to the CMO on 11 May. In May NERVTAG was asked to consider the potential for asymptomatic transmission from test-positive individuals, with specific consideration for closed environments, such as care homes; their comments on the potential for PCR positive asymptomatic individuals to be infectious were fed back to PHE/DHSC to operationalise.

The committee considered updates in July, October and November 2020 and February 2021 on follow-up of the London Care Home outbreaks, expanded to thirteen Homes, as well as the VIVALDI study which focused on Care Homes in England. Data from these studies was helpful in forming opinion on duration of immunity and likelihood of re-infections in the elderly.

4.12 SARS-CoV-2 reinfection

In early 2020, NERVTAG considered the potential for re-infection with SARS-CoV-2 and the possible impact of reinfection on the COVID-19 pandemic. The Scientific Pandemic Influenza Group on Modelling (SPI-M) requested a view from NERVTAG on this matter in order to inform their epidemiological modelling, including the suitability of the use of SIR (susceptible, infected, recovered) models for making predictions about SARS-CoV-2.

To answer this question, NERVTAG considered evidence around the development of sterilising immunity following infection with a coronavirus. Extrapolation from other respiratory viruses provided a base assumption that infection may not result in lifelong immunity, but evidence on the duration of sterilising immunity to SARS-CoV-2 was lacking owing to its status as a novel pathogen. At the time of discussion, only a single case report of SARS-CoV-2 reinfection had been published.

Taking into account data from other coronaviruses and the expertise of NERVTAG members, a conclusion was reached that although it was not possible to confirm or exclude the possibility of reinfection based on the limited data available, data were sufficient for the committee to recommend modelling the scenario of reinfection. At this time, NERVTAG noted the importance of ensuring that appropriate studies were in place to obtain the data necessary to determine the duration of sterilising immunity.

In October 2020, the issue of reinfection arose again as NERVTAG noted that case reports of reinfection with SARS-CoV-2 were accumulating. The group set out to understand the likelihood

of SARS-CoV-2 reinfection, in whom it might occur, and when it might be seen in England. To answer this question, NERVTAG drew heavily on studies designed according to the recommendations made earlier in the year.

Using data accumulated from longitudinal cohort studies of SARS-CoV-2 and evidence collected on other similar respiratory viruses, NERVTAG was able to conclude that reinfection with SARS-CoV-2 should be expected. The group noted that re-infection would occur due both to waning immunity and to the accumulation of genetic changes that will inevitably occur in SARS-CoV-2.

4.13 SARS-CoV-2 variants

In the first half of 2020, NERVTAG advised on the likelihood of viral variants arising and the potential mechanisms for this. Based on the existing NERVTAG Risk Assessment tool, a framework was proposed for the risk assessment of new SARS-CoV-2 variants, which included data on virus transmissibility, infection severity, response to naturally or vaccine-acquired immunity, and susceptibility to therapeutics.

The variant risk assessment tool was first used to assess the risk of the so called 'Cluster 5 mink variants', in November 2020. Triggers for the use of the framework were 1) evidence of a lineage becoming predominant in the UK; 2) In-vitro evidence of concerning virus characteristics regardless of geographic location; 3) clinical concern raised regardless of geographic location. At that time, it was agreed that the outputs must be informative with respect to both research and policy needs.

The framework was modified over the following weeks and used for assessment of the risk posed by another variant which had emerged in the UK in December 2020, now known as B.1.1.7 (or the Alpha variant). In addition to the tabulated indicators, the modified Risk Assessment included an overall assessment of the level and nature of the risk and the level of confidence in the evidence. There was also a list of recommendations from PHE and NERVTAG which were communicated with DHSC.

The tool was used in January 2021 for assessment of the risk posed by B.1.351 (Beta variant), first identified in South Africa and P.1 (Gamma variant), first identified in Brazil. In May 2021 another variant was identified, and the risk assessed using the tool; this was B.1.617.2 (Delta variant), first identified in India.

In 2021, the responsibility for producing and updating these risk assessments was shifted to the Variant Technical Group, coordinated by PHE, and including some NERVTAG members. NERVTAG continues to review and endorse the variant risk assessments produced by this group.

4.13.1 Emergence of the B.1.1.7 (alpha) variant

In early December 2020, NERVTAG noted data from PHE showing a rapid increase in SARS-CoV-2 case numbers in Kent, England. Data showed that 50% of the cases sequenced belonged to a single phylogenetic cluster that was distinct from the rest of the UK dataset. The group expressed concern that this variant, which carried the N501Y mutation, had a weekly growth rate that was 60% greater than other variants in the region. At this stage, there was no basic epidemiologic or demographic explanation for this finding, though the virologists in the group noted that 501 was located in the spike protein in the region of the interface between the spike receptor binding domain (RBD) and the ACE2 receptor on susceptible cells, and therefore could be a site where mutations would affect antibody binding to the RBD.

The rapid spread of the virus lead members to postulate that the newly identified variant was more transmissible; however, evidence was lacking at this time. NERVTAG endorsed PHE's recommendations for action, including enhanced surveillance in Kent and in London, sampling and lab studies of the new variant, and neutralisation studies.

NERVTAG met again the following week (18 December) to discuss new evidence on the variant which had now been labelled B.1.1.7 and classified by PHE as a 'variant under investigation' (VUI). A risk assessment was carried out, during which it was agreed that the genomic growth rate, epidemiological modelling studies, and described Ct values all suggested that B.1.1.7 was more transmissible. At this time, confidence in this finding was moderate, but the group felt the increase in transmissibility was sufficiently substantial to classify the variant as a 'Variant of Concern' (VOC). An extraordinary meeting between SPI-M and NERVTAG was called to consider the evidence for increased transmissibility of this variant and possible public health interventions.

On the 21st of December, representatives of NERVTAG and SPI-M met to consider evidence on the transmissibility and severity of the B.1.1.7 variant. This meeting was observed by DCMOs Professor Jonathan Van Tam and Dr Jenny Harries, and the government's Chief Scientific Adviser, Sir Patrick Vallance. The totality of data considered by NERVTAG thus far, along with new evidence, was reviewed in detail. At this time, it was agreed that there was insufficient evidence to make conclusive statements on the clinical presentation of B.1.1.7, but that both NERVTAG and SPI-M members had high confidence in a substantial increase in transmission advantage for this variant.

Following this meeting, NERVTAG released a public statement on 21 December 2020, detailing its findings on the transmissibility of the B.1.1.7 variant. B.1.1.7 was one of the first variants of concern to emerge, and NERVTAG's rapid research and expert response made it the first groups to highlight the finding of increased transmissibility associated with the new variant. This finding influenced the public health response to SARS-CoV-2 across the globe and highlighted the need for greater genomic surveillance of the virus.

4.13.2 Severity of the B.1.1.7 (alpha) variant

In early 2021, a signal emerged in the UK indicating that there was a realistic possibility that infection with VOC B.1.1.7 was associated with an increased risk of death, compared to infection with non-VOC viruses.

NERVTAG prepared a paper for SAGE on the 21st of January, summarising the available evidence that had accrued on this topic, including a summary of the results of several independent analyses demonstrating an association between B.1.1.7 and increased disease severity. In this paper, NERVTAG recommended further research to increase the confidence of their findings. By February, further evidence had accumulated, and NERVTAG prepared a second paper for SAGE on the 11th of February 2021, outlining this evidence. In this paper, NERVTAG concluded that it was likely that infection with VOC B.1.1.7 was associated with an increased risk of hospitalisation and death compared to infection with non-VOC viruses.

NERVTAG played a key role in characterising the phenotype of the emerging B.1.1.7 variant, enabling the most appropriate response. The group worked rapidly to respond to a newly emerging situation and used its expertise to issue recommendations to the UK government via SAGE and the DHSC.

4.14 Transmission of SARS-CoV-2

The transmission patterns and transmissibility of SARS-CoV-2 have formed an essential part of NERVTAG's discussions throughout the last 18 months. In January 2020, NERVTAG discussed evidence for human to human transmission of the newly emerging respiratory virus.

NERVTAG also reviewed evidence on mechanisms of transmission, including the role of faecal/oral spread (including viral survival in stool), the role of airborne transmission, the importance of superspreading events and clusters, the significance of household transmission, and the risks of transmission associated with singing and choirs. Over time, the content of NERVTAG meetings shifted away from these discussions as new groups were convened that focussed on this area, including SAGE's Environmental Modelling Group (EMG).

The relationship between symptoms and infectiousness was considered on several occasions, including the relative infectiousness of asymptomatic cases, and whether infectiousness was likely to reduce when symptoms resolved. NERVTAG reviewed evidence to determine the link between PCR cycle threshold (Ct) values and infectiousness, and the duration of both viral shedding and infectiousness. The duration of the pre-symptomatic infectious period and its impact on contact tracing was also discussed.

4.15 Virology of SARS-CoV-2

The virology of SARS-CoV-2 was discussed extensively throughout the 18-month period. NERVTAG was involved in early characterisation of the virus soon after its emergence, and regularly updated its assessments throughout the year. NERVTAG also regularly reviewed data on the genetic evolution of the virus. Evidence for changes in the behaviour (the phenotype) of the SARS-CoV-2 virus, in particular changes in its transmissibility and severity, were also discussed.

4.16 Non-COVID-19 topics and non-COVID-19 NERVTAG meetings

PHE and NERVTAG maintained awareness of avian and swine influenza reports, particularly those that had zoonotic potential or were detected in mammalian species, including humans. These were mostly considered in the first half of 2021 and included avian influenza detections in England over winter 2020-21; an update from China of two human cases of avian influenza A(H5N6) and a human case of Eurasian avian-like swine influenza A(H1N1)v in China, considered in January 2021; detection of Avian influenza A (H5N8) in a fox and seals in February 2021; a human case of influenza A (H10N3) of avian origin in China, considered in June 2021 NERVTAG considered a proposal from PHE for public health surveillance of emerging influenza viruses with zoonotic potential; this was endorsed, with a few comments, by the committee.

Routine NERVTAG meetings were held in July and August 2020 and March 2021.

4.16.1 July 2020

NERVTAG discussed the novel swine influenza variant virus known as Genotype 4 Eurasian 'Avian-like' H1N1 (G4 EA H1N1) and reviewed the PHE risk assessment. The group noted the need for a review of the NERVTAG risk assessment tool to clarify the purpose, use and interpretation of the outputs. Members reviewed the routine epidemiological updates on other zoonotic influenza viruses and requested that PHE review the age profile of avian influenza A(H9N2) against other avian influenzas and the sero-epidemiology of H9N2

4.16.2 August 2020

NERVTAG again discussed the novel swine influenza variant virus known as Genotype 4 Eurasian 'Avian-like' H1N1 (G4 EA H1N1), reviewed the age profile of avian influenza A(H9N2) against other avian influenzas, and reviewed a preliminary literature review of the seroepidemiology of H9N2.

4.16.3 March 2021

NERVTAG was updated on detection of swine influenza in humans in Europe, China and North America. It was noted that the pattern and number of cases reported was not unusual. Members noted that analysis of swine influenza viruses indicates increasing diversity in pigs and there was concern that these viruses were not being monitored adequately. A paper on influenza A/H9N2 was presented, concluding that the majority of cases were in children and that seropositivity was highest in older age groups. The implications for population immunity were discussed. Finally, the committee was updated on human cases of avian influenzas A/H9N2, A/H5N6, A/H5N1 and A/H7N9, as well as MERS-CoV. There were either no, or very few cases of any and the risk assessments were not changed.

5. Conclusions

2020 and 2021 were years of remarkable events, with the emergence of a novel respiratory virus and the ensuing global pandemic. Throughout this extraordinary time, NERVTAG has provided high quality advice to the UK Government, and been a trusted source of expertise.

NERVTAG's position at the heart of the pandemic response has necessitated a significant time commitment from its members, with the frequency of meetings increasing from two per annum in a standard year to over 40 in 2020. In addition, NERVTAG members have prepared and published over 30 papers answering scientific questions and summarising available evidence, as well as contributing to many more. NERVTAG members have also conducted education sessions within government, participated in sub-committees, and contributed to papers led by other governmental advisory groups.

Throughout the past 18 months, NERVTAG's membership has grown to include six new coopted members, to support the COVID-19 response. NERVTAG's combination of clinical, virology, epidemiology, and public health expertise has provided the group with unique crossdisciplinary insight into emerging respiratory viruses.

As we move into the latter half of 2021, over 18 months since the first extraordinary meeting of NERVTAG was called to consider the risk associated with the newly identified 'Wuhan novel coronavirus', NERVTAG continues to meet regularly to consider emerging evidence associated with what we now know as 'SARS-CoV-2'. As our knowledge of COVID-19 continues to grow, NERVTAG will continue to provide timely, independent, high quality scientific and clinical advice to the UK Government, on both SARS-CoV-2 and other new and emerging respiratory viruses.

Appendix A - NERVTAG Terms of Reference and membership

Role and establishment

The role of NERVTAG is to act as an Advisory Group to provide the Chief Medical Officer (CMO) and, through the CMO, ministers, the Department of Health (DH) and other Government departments, with scientific risk assessment and mitigation advice on the threat posed by new and emerging respiratory virus threats and on options for their management.

The group will draw on the expertise of scientists and health care professionals, including clinicians, microbiologists and public health practitioners, and colleagues in related disciplines. The group is supported by a scientific secretariat from Public Health England (PHE) and is scientifically independent. Members of the Group are expected to adhere to the Code of Practice adopted by the Advisory Committee on Dangerous Pathogens (ACDP).

The scope of the group would include new and emerging respiratory virus threats to human health including strains of influenza virus (regardless of origin), and other respiratory viruses with potential to cause epidemic or pandemic illness, or severe illness in a smaller number of cases.

Core membership

Chair: external independent health scientist, formally appointed through an independent process

Public Health

Surveillance and epidemiology (national)

Public health microbiology (national)

- · Academic infectious disease epidemiology
- Academic microbiology
- Virology
- · Clinical respiratory medicine
- Emergency preparedness/response
- Modelling
- Behavioural Sciences
- Social Science

Co-opted membership

Nominee on NHS England emergency preparedness

Nominee on NHS England Pandemic influenza resilience

Nominee from APHA on Animal Health

Observers

Nominees from DH, other UK health departments

Nominees from other Government departments

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Additional members as required (depending on nature of threat) Public health local (PHEC and/or DPH) PHE field epidemiology PHE public health microbiology local Public health ethics PHE travel and migrant health

Secretariat

The secretariat function is provided by Public Health England.

Appendix B – List of NERVTAG Publications

NERVTAG: Distance, time, handshakes, 12 March 2020. https://www.gov.uk/government/publications/nervtag-distance-time-handshakes-12-march-2020

NERVTAG: At what point might meaningful results from clinical trials be available? 30 March 2020. https://www.gov.uk/government/publications/nervtag-at-what-point-might-meaningful-results-from-clinical-trials-be-available-30-march-2020

NERVTAG: Duration of infectiousness following symptoms onset in COVID-19, 13 April 2020. https://www.gov.uk/government/publications/nervtag-duration-of-infectiousness-following-symptoms-onset-in-covid-19-13-april-2020

NERVTAG: Face mask use in the community, 13 April 2020. https://www.gov.uk/government/publications/nervtag-face-mask-use-in-the-community-13-april-2020

NERVTAG: Wearing facemasks in a community setting - options and evidence, 16 April 2020. https://www.gov.uk/government/publications/nervtag-wearing-facemasks-in-a-community-setting-options-and-evidence-16-april-2020

NERVTAG: View on SARS-CoV-2 protective immunity, 27 April 2020. https://www.gov.uk/government/publications/nervtag-view-on-sars-cov-2-protective-immunity-27-april-2020

NERVTAG: Assessment of pre-symptomatic transmission of COVID-19, 30 April 2020. https://www.gov.uk/government/publications/nervtag-assessment-of-pre-symptomatic-transmission-of-covid-19-30-april-2020

NERVTAG: Quantifying SARS-CoV-2 transmission suggests epidemic control with digital contact tracing, 30 April 2020. https://www.gov.uk/government/publications/nervtag-quantifying-sars-cov-2-transmission-suggests-epidemic-control-with-digital-contact-tracing-30-april-2020

NERVTAG: Case definitions for contact tracing, 7 May 2020. https://www.gov.uk/government/publications/nervtag-case-definitions-for-contact-tracing-7-may-2020

NERVTAG: NT-SARS-CoV-2 variants, 13 May 2020. https://www.gov.uk/government/publications/nervtag-nt-sars-cov-2-variants-13-may-2020

NERVTAG: Asymptomatic SARS-CoV-2 infection, 13 May 2020. https://www.gov.uk/government/publications/nervtag-asymptomatic-sars-cov-2-infection-13may-2020

NERVTAG: Viral dynamics of infectiousness, 3 June 2020.

https://www.gov.uk/government/publications/nervtag-viral-dynamics-of-infectiousness-3-june-2020

NERVTAG: Viral dynamics of infectiousness, 8 June 2020. https://www.gov.uk/government/publications/nervtag-viral-dynamics-of-infectiousness-8-june-2020

NERVTAG/EMG: Hand hygiene to limit SARS-CoV-2 transmission, 2 July 2020. https://www.gov.uk/government/publications/nervtagemg-hand-hygiene-to-limit-sars-cov-2-transmission-2-july-2020 NERVTAG: Assessment of transmission of COVID-19 through musical events, 16 July 2020. https://www.gov.uk/government/publications/nervtag-assessment-of-transmission-of-covid-19through-musical-events-16-july-2020

NERVTAG: Respiratory viral infections, their interactions with SARS-CoV-2 and implications for a winter resurgence of COVID-19, 16 July 2020.

https://www.gov.uk/government/publications/nervtag-respiratory-viral-infections-theirinteractions-with-sars-cov-2-and-implications-for-a-winter-resurgence-of-covid-19-16-july-2020

NERVTAG/EMG: Role of aerosol transmission in COVID-19, 22 July 2020. https://www.gov.uk/government/publications/nervtagemg-role-of-aerosol-transmission-in-covid-19-22-july-2020

Update on immunity to SARS-CoV-2, 2 September 2020. https://www.gov.uk/government/publications/update-on-immunity-to-sars-cov-2-2-september-2020

NERVTAG: Rapid review of the asymptomatic proportion of PCR-confirmed SARS-CoV-2 infections in community settings, 9 September 2020.

https://www.gov.uk/government/publications/nervtag-rapid-review-of-the-asymptomaticproportion-of-pcr-confirmed-sars-cov-2-infections-in-community-settings-9-september-2020

NERVTAG/EMG: Duration of wearing of face coverings, 15 September 2020. https://www.gov.uk/government/publications/nervtagemg-duration-of-wearing-of-face-coverings-15-september-2020

NERVTAG: Community case definitions for COVID-19, 2 September 2020. https://www.gov.uk/government/publications/nervtag-community-case-definitions-for-covid-19-2-september-2020

NERVTAG: Is there evidence for genetic change in SARS-CoV-2 and if so, do mutations affect virus phenotype? - 30 September 2020. https://www.gov.uk/government/publications/nervtag-is-there-evidence-for-genetic-change-in-sars-cov-2-and-if-so-do-mutations-affect-virus-phenotype-30-september-2020

NERVTAG: NERVTAG: Seasonality and its impact on COVID-19, 22 October 2020. https://www.gov.uk/government/publications/nervtag-seasonality-and-its-impact-on-covid-19-22october-2020

NERVTAG: Risk assessment of SARS-CoV-2 variants that have been selected in mink, 12 November 2020. https://www.gov.uk/government/publications/nervtag-risk-assessment-of-sarscov-2-variants-that-have-been-selected-in-mink-12-november-2020

NERVTAG: Certifying COVID-19 immunity, 19 November 2020. https://www.gov.uk/government/publications/nervtag-certifying-covid-19-immunity-19-november-2020

NERVTAG: Immunity certification, 9 December 2020., published July 2021

S0960 NERVTAG Immunity Certification.pdf (publishing.service.gov.uk)

NERVTAG: Brief note on SARS-CoV-2 variants, 13 January 2021. https://www.gov.uk/government/publications/nervtag-brief-note-on-sars-cov-2-variants-13-january-2021

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NERVTAG paper on COVID-19 variant of concern B.1.1.7.

https://www.gov.uk/government/publications/nervtag-paper-on-covid-19-variant-of-concernb117

NERVTAG: Update note on variants of concern, 21 January 2021. https://www.gov.uk/government/publications/nervtag-update-note-on-variants-of-concern-21-january-2021

NERVTAG: Note on B.1.1.7 severity, 20 January 2021. https://www.gov.uk/government/publications/nervtag-note-on-b117-severity-20-january-2021

NERVTAG: Note on variant P.1, 27 January 2021. https://www.gov.uk/government/publications/nervtag-note-on-variant-p1-27-january-2021

NERVTAG: Update note on variant B.1.1.7, 27 January 2021. https://www.gov.uk/government/publications/nervtag-update-note-on-variant-b117-27-january-2021

NERVTAG: Brief note on SARS-CoV-2 B.1.351, 27 January 2021. https://www.gov.uk/government/publications/nervtag-brief-note-on-sars-cov-2-b1351-27-january-2021

NERVTAG: Immunity certification update, 4 February 2021, published July 2021

S1076 NERVTAG Immune Certification Update.pdf (publishing.service.gov.uk)

NERVTAG: Update note on B.1.1.7 severity, 11 February 2021. https://www.gov.uk/government/publications/nervtag-update-note-on-b117-severity-11-february-2021

NERVTAG: note on growth rate of SARS-CoV-2 B.1.1.7, 22 April 2021. <u>https://www.gov.uk/government/publications/nervtag-note-on-growth-rate-of-sars-cov-2-b117-22-april-2021</u>

NERVTAG: Update note on immunity to SARS-CoV-2 after natural infection, 27 May 2021. https://www.gov.uk/government/publications/nervtag-update-note-on-immunity-to-sars-cov-2-after-natural-infection-27-may-2021

Appendix C – List of members and co-opted members

NERVTAG core members

Professor Peter Horby **Chair**: Public health physician and clinical academic; Director of the Epidemic Diseases Research Group at the University of Oxford

Professor Peter Openshaw, **Deputy Chair**: Professor of Experimental Medicine at the National Heart and Lung Institute, Imperial College London and President of the British Society for Immunology

Professor Wendy Barclay: Chair in Influenza Virology, Department of Virology, Imperial College London

Professor John Edmunds: Dean of the Faculty of Epidemiology and Population Health at the London School of Hygiene and Tropical Medicine

Professor Neil Ferguson: Director, Medical Research Council Centre for Outbreak Analysis and Modelling, Imperial College London

Professor Andrew Hayward: Head, Department of Infectious Disease Informatics, Farr Institute at University College London

Dr Ben Killingley: Consultant in Infectious diseases and acute medicine at Whittington Health NHS Trust, with a research interest in the transmission of infection

Professor Wei Shen Lim: Consultant respiratory physician in a large teaching hospital (Nottingham University Hospitals NHS Trust) and Honorary Professor of Medicine (University of Nottingham) with a special interest in respiratory infections

Dr Jim McMenamin: Strategic lead for the respiratory viral team within Health Protection Scotland, responsible for seasonal and pandemic influenza

Professor Malcolm Semple: Senior lecturer in Child Health, University of Liverpool and Consultant in Paediatric Respiratory Medicine, Alder Hey Children's Hospital Liverpool – with research interest in severe acute respiratory infections

Dr James Rubin: Reader in the Psychology of Emerging Health Risks, Kings College London

Professor Robert Dingwall: Consulting sociologist with Dingwall Enterprises Ltd and part-time professor at Nottingham Trent University

Dr Cariad Evans: Consultant Virologist, Sheffield Teaching Hospitals NHS Foundation Trust

NERVTAG co-opted members

Dr Chloe Sellwood: National Lead, Pandemic Influenza, NHS England, within the Emergency Preparedness, Resilience and Response (EPRR) team

Professor Ian Brown: Head of Virology at the Animal and Plant Health Agency - Weybridge and Director of EU/OIE/FAO International Reference Laboratories for Avian Influenza, Newcastle Disease and Swine Influenza

Temporarily co-opted members for COVID-19

Dr Lisa Ritchie: Head of Infection Prevention and Control, NHS England and NHS Improvement; from February 2020 to the present

Dr David Connell: Consultant Physician in Respiratory Medicine, Clinical Lead for winter planning, NHS Tayside; from February 2020 to April 2021

Dr Kevin Rooney: Clinical Director for Critical Care, Clyde sector, Consultant in Anaesthesia and Intensive Care Medicine, Royal Alexandra Hospital, Paisley; from February 2020 to April 2021

Professor Julian Hiscox: Chair in Infection and Global Health, Institute of Infection, Veterinary and Ecological Sciences, University of Liverpool; from April 2020 to the present

Dr Muge Cevik: Clinical Lecturer Infectious Diseases and Medical Virology, University of St Andrews, from October 2020 to the present

Professor Ravindra Gupta: Professor of Clinical Microbiology, Cambridge Institute of Therapeutic Immunology and Infectious Diseases, University of Cambridge, from December 2020 to the present

Attendees at subcommittee meetings

Clinical Risk Stratification Subgroup

Prof Julia Hippisley-Cox (subgroup Chair), University of Oxford

Prof Peter Horby (NERVTAG Chair), University of Oxford

Prof Calum Semple (NERVTAG member), University of Liverpool

Prof Andre Hayward (NERVTAG member), University college, London

Ashley Clift, Clinical Research Fellow, University of Oxford

Aziz Sheikh, Professor of Primary Care Research and Development, University of Edinburgh

Carol Coupland, Division of Primary Care, School of Medicine, University of Nottingham

Chris Robertson, Professor of Public Health Epidemiology, University of Strathclyde

Elizabeth Williamson, Associate Professor of Medical Statistics, London School of Hygiene and Tropical Medicine

Frank Kee, Director, Centre for Public Health, Queen's University, Belfast

Fred Kemp, Deputy Head of Licensing and Ventures, Life Sciences, Oxford University Innovation

John Robson, Clinical Reader in Primary Care Research & Development, Queen Mary University of London

Jonathan Valabhji, National Clinical Director for Obesity and Diabetes, NHS England

Kamlesh Khunti, Professor of Primary Care Diabetes & Vascular Medicine, University of Leicester. Chair, Ethnicity Subgroup of SAGE.

Karla Diaz-Ordaz, Associate Professor of Biostatistics, London School of Hygiene and Tropical Medicine

Nisha Mehta, Clinical Adviser to the Chief Medical Officer, DHSC

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Ronan Lyons, Clinical Professor of Public Health, Medicine, Swansea University

Ruth Keogh, Professor of Biostatistics& Epidemiology, London School of Hygiene and Tropical Medicine

Tony Williams, Consultant Occupational Physician, Working Fit Ltd.

Bethan Loveless, DHSC observer

Jenny Harries, Deputy Chief Medical Officer, DHSC

Ruth Parry, Observer for JCVI secretariat, PHE

David Spiegelhalter, Statistical Laboratory, University of Cambridge

Jonathan Benger, Professor of Emergency Care, University of the West of England, Bristol

Ewen Harrison, Director, Centre for Medical Informatics, University of Edinburgh

Harry Hemingway, Professor of Clinical Epidemiology, UCL Institute of Health Informatics, London

Julian Thomas, NHS

Susan Jebb, Professor of Diet and Population Health, University of Oxford

David Coggon, Professor of Occupational and Environmental Medicine, University of Southampton

NIV and Nosocomial Transmission Subcommittee

Prof Wei Shen Lim (subcommittee Chair), NERVTAG member

Dr Ben Killingley, NERVTAG member

Dr Lisa Ritchie, NERVTAG member

Co-opted:

Anita Simonds

Allan Bennett

Chris Meadows

Daniel Martin

Ronan Driscoll

Novel Therapeutics subcommittee

Peter Horby (Chair of subcommittee and Chair of NERVTAG) Edward Mullins (secretariat) Luke Collet-Fenson (secretariat) Wei Shen Lim (NERVTAG member) Jake Dunning (PHE) Mike Jacobs (UCL)

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Andrew Menzies-Gow (NHSE) Malcolm Qualie (NHSE) Nick Cammack (Wellcome Trust) Nicole Assmann (MHRA) Ursula Wells (DHSC) Kenneth Baillie (University of Edinburgh) Anita Simonds (NHLI)) Kathryn Maitland (Imperial College) Kathy Rowan (ICNARC) Alan Montgomery (Nottingham CTU) Malcolm Jacobs (Royal Free Hospital) Jake Dunning (PHE)