Minutes of the NERVTAG COVID-19 Fortieth Meeting: 11 December 2020

Date & Location: 11:00 – 13.00 11 December 2020 - Via telecon only
In attendance: Chair: Peter Horby (PH) NERVTAG Members: Peter Openshaw (PO), Andrew Hayward (AH), Julian Hiscox (J Hi), John Edmunds (JE), Neil Ferguson (NF), Robert Dingwall (RD), Muge Cevik (MC), Wendy Barclay (WB), James Rubin (JR), David Connell (DC), Jim McMenamin (JMM), Wei Shen Lim (WSL), Lisa Ritchie (LR), Ben Killingley (BK), Kevin Rooney (KR) NERVTAG Secretariat: Ruth Parry, Elaine Stanford, Stephen Barnard PHE Observers: Gavin Dabrera (GD), Maria Zambon (MZ), Meera Chand (MCh), Jamie Lopez-Bernal (JLB) until 12.00 DHSC Observers: Sadia Dorsani (SD), Jonathan Van Tam (JVT) Invited experts/ presenters: Nick Gent (NG) SAGE Secretariat: [redacted], [redacted] COVID19 Cabinet C-19 Task force: [redacted] DfID: Cathy Roth (CR) DAs: Wales, Rachel Jones (RJ)
Apologies: Chloe Sellwood (CSe), Cariad Evans (CE), Calum Semple (CSm), Ian Brown (IB), Charlotte Gower (CG)

Contents

Summary of 40th Meeting

- The committee reviewed the paper on immunity certification submitted to SAGE on 10 December and considered the request to provide a combined paper with SPI-B. This will be prepared after feedback from Cabinet Office and DHSC on proposed use cases.
- The committee discussed the possible request from SAGE to provide an update on face coverings. This will be prepared in collaboration with EMG once the request has been confirmed.
- The changes in case fatality rate between the first and second waves of COVID-19 were described. It was noted that the second wave increase in case fatality rates was most marked in those over 70 years of age. The paper will be shared with DHSC and NHS England for action.
- The new SARS-CoV-2 variant emerging in Kent was discussed and the developments were considered a matter for concern. The actions proposed by PHE were endorsed and in addition NERVTAG proposed enhanced sequencing of PCR products from Lighthouse laboratories and urged DHSC to consider whether there is a need to intensify control in affected areas.

List of actions:

	Item		**Actions**
2.	SAGE paper on immunity certification	**40.1**	*PH to seek updated data from David Wiley on the hospital/fire/police cohort for inclusion in the paper on immunity certificates*
		40.2	*SAGE secretariat to confirm with Cabinet Office and DHSC the potential use cases for immunity certificates and inform NERVTAG and SPI-B. NERVTAG and SPI-B to produce a new combined paper incorporating any new data and apply to proposed use cases.*
		40.3	*PK to follow up on the potential request of NERVTAG to review the recent data on facemasks and come back to the committee.*
3.	Case fatality rates	***40.4***	*Pass the paper on the changes in case fatality rate prepared by JE to DHSC and NHS England for action.*
4.	New SARS-CoV-2 variant emerging in Kent	***40.5***	*MCh/PHE to fill in the risk assessment framework for the Kent variant*
		40.6	*NERVTAG to provide readout of discussions and advice on the 'Kent variant' to JVT/DHSC by 16.00 on 11 December.*

Minutes of the meeting

1 Review of actions from the last meeting

1.1 Actions from the 39th NERVTAG COVID-19 meeting were reviewed

Actions from 39th NERVTAG COVID-19 meeting held on 4 December 2020				
	Item		**Actions**	**Status**
2.	Risk assessment framework for SARS-CoV-2 variants	***39.1***	*PH to revise the risk assessment framework for SARS-CoV-2 variants and forward to PHE for piloting with the 'mink variant', to be brought back to NERVTAG when completed.*	*COMPLETE*
3.	SAGE paper on immunity certificates	***39.2***	*MZ and team to investigate the denominator in Care Home L and bring back to NERVTAG as soon as possible.*	*COMPLETE*
		39.3	*AH to put all data on protection from infection together into Forest Plots including other studies in the literature; one on protection against disease and another on protection from infection. NF to check against the published papers.*	*COMPLETE*
		39.4	*PH to ask Susan Hopkins about rates in susceptible and non-susceptible and Ct values in the SIREN study.*	*COMPLETE*
		39.5	*JE to request data from Adam Kucharski on swabbing in California and Texas*	*COMPLETE*
		39.6	*MZ to provide AH with updated Care Home data by close on 7 December.*	*COMPLETE*
6.	Surveillance reports	***39.7***	*JE and CSm, with contribution from NF, to bring a paper on the changes in case fatality rate over time, to NERVTAG on 11 December*	*COMPLETE – on the agenda for 11 December*

2 SAGE paper on immunity certification

2.1 The paper had been presented to SAGE on 10 December; it had been reasonably well received. A correction to a reference will be made by PH. MZ noted that David Wyllie may be able to provide updated data on Kaplan-Meier against symptomatic disease and infection in those that are seropositive versus those that are seronegative for

cohort number 6 (hospital/fire/police), mentioned in table 1 of the paper.

Action 40.1 – *PH to seek updated data from David Wyllie on the hospital/fire/police cohort for inclusion in the paper on immunity certificates.*

2.2 SAGE had requested that the paper was updated by providing an integrated paper with the SPI-B. A paper had been presented on the same day, which had considered use cases etc. PK will discuss with Cabinet Office and DHSC to confirm the use cases and come back to NERVTAG to determine if any additional work is needed.

Action 40.2 – *SAGE secretariat to confirm with Cabinet Office and DHSC the potential use cases for immunity certificates and inform NERVTAG and SPI-B. NERVTAG and SPI-B to produce a new combined paper incorporating any new data and apply to proposed use cases.*

2.3 PH noted a discussion at SAGE indicating that there may be a request for a joint NERVTAG/EMG review of face coverings. PK will follow up on the request and come back to NERVTAG.

Action 40.3 – *PK to follow up on the potential request of NERVTAG to review the recent data on face coverings and come back to NERVTAG.*

2.4 The likely new data on face coverings was discussed and it was suggested that much of it would be observational data, which would be difficult to interpret. There are a number of papers on the blocking of droplets, which should be reviewed by EMG, but NERVTAG should also be involved in any SAGE paper. SD noted that a DHSC commissioned PHE peer review of face coverings will be shared with NERVTAG once completed.

2.5 KR referred to a request from the clinical community for guidance from NERVTAG on intubation and bag valve mask ventilation. PH noted that there is a separate AGPs Panel which will follow up on such requests. LR indicated there is ongoing work for the Panel to review the extant list with NHIR. KR can send the request to LR to be forwarded to the Chair of the independent AGP Panel.

3 Case fatality rates (CFR)

3.1 NF noted that when comparing the 28-day deaths in hospitals with the NHS SitRep COVID-19 admissions 4 days earlier the trend is the same. The data early on is very weak, but for the bulk of the first wave the average CFR was about 27%. The CFR had dropped since the first wave but there has been an upturn since early September.

3.2 JE had analysed CO-CIN data and considered changes in hospital fatality rate excluding any deaths after 31 days. In the over 70s the hospital fatality rate was very high at the beginning of the epidemic in the UK, dropped to a nadir in July and then has increased again from July onwards. Deaths in the under 70s dropped during the latter part of the first wave and has not increased again.

3.3 In patients who had been admitted to ICU a decline in CFR was observed from March to July, followed by an increase to the present time. For non-ICU patients there was a decline to 15% around July, which stayed at the same level until a small increase in October. The change in patterns of admissions to ICU were noted, with a decline in the last few weeks. There has also been a change in case mix admitted to ICU as well as a change in the age range admitted to hospital as well as changes in treatment patterns.

3.4 Possible reasons for the upturn in CFR were discussed. It was noted that the proportion of hospitalisations coming from nursing homes is now recorded in the SitRep but has not been recorded throughout the pandemic. Other factors might be hospital capacity and busyness. It was noted that this had been considered in the first wave and no clear pattern had been observed.

3.5 It was noted that CO-CIN is not complete, and this has changed over time. In the first wave it covered over 70% of hospital admissions. This dropped to 40-50% over the summer. JVT shared an age specific comparison of hospital CFR between the first and second waves, provided by CO-CIN and SPI-M combined. The CFR in males below 59 years has more than halved between the first and second waves. Over the age of 60, the reduction in CFR since the first wave is less marked.

3.6 NG noted that PHE modellers had analysed SARI data which also is showing similar patterns, including an increase in the elderly non-ITU population.

3.7 WSL noted that JE's data showing decreased admission to ICU, fits with the way that respiratory communities are now working. In this wave ICU beds are being used for care of elective patients, so only the sickest go into ICU.

3.8 Planned next steps were discussed. It was noted that others are looking into this issue and that it was briefly discussed at SPI-M earlier in the week. It will not be possible to do any more work on the current paper; it was agreed to pass the paper to NHS R-England and DHSC before Christmas for their action.

Action 40.4 – *Pass the paper on the changes in case fatality rate prepared by JE to DHSC and NHS England for action.*

4 New SARS-CoV-2 variant emerging in Kent

4.1 It was noted that this was a recent issue which had only emerged in the last few days; identified following a rapid increase in case numbers in Kent over the past few weeks. PHE are carrying out enhanced investigations. The coverage of the routine COG dataset is not large but genomics has indicated that 50% of the cases are in a single phylogenetic cluster; this is not what would be expected. The phylogeny of the Kent cluster indicates that it is part of a larger cluster consisting of around 1,000 genomes; phylogenetically distinct from the rest of the UK dataset. Cases are concentrated in Kent and NE London.

4.2 The routine COG dataset has a 2-3 weeks lag behind test dates and is not random, so may be biased by investigations of outbreaks etc. Nothing in the basic epidemiology or the demographics sheds light on what is going on. There is a concern that, using N501Y as a marker for the strain, the frequency with which the variant is detected has been growing rapidly since mid-October. The relative weekly growth of the N501Y variant is 60% greater than other variants in that region.

4.3 Pillar 2 laboratories have in recent weeks reported a drop-out in results in the S gene target; at the Alderley Park laboratory, over 10% of the positives have this S gene target drop-out and are this cluster. Milton Keynes have also reported a similar pattern There will be a Pillar 2 meeting to discuss, in the afternoon of 11 December.

4.4 WB noted that 501 sits in the interface between the RBD and the ACE2 protein and it is therefore expected to affect the interaction with ACE and could be a place where the virus might mutate and escape antibody binding to the RBD. N501Y is a mutation that adapts the virus to mice. A number of studies have attempted to 'force' escape and 501 is not as important as, for example, 453. There is some level of concern that this virus may be different antigenically. There is a suggestion that the 69/70 deletion is facilitating the spread of changes in other parts of the spike affecting ACE2 interaction. 501Y is a mutation that has been found in immunocompromised patients excreting virus for a long time.

4.5 MCh noted that 4 cases in the cluster appear to have had an infection in the first wave and now are reinfected in this cluster (based on SGSS data).

4.6 MZ noted that the data of some of the national core studies could be helpful; the ATACCC study has two individuals with this variant so there is the possibility of

obtaining a large amount of data including clinical and serological information. There is no information at the moment of the clinical consequence of infection with the variant.

4.7 It might be postulated that this variant is more transmissible but there is no evidence apart from the rapid spread. There is speculation that it might have originated in an immunodeficient person, although it is possible it might have originated in another animal species.

4.8 It was noted that mutations in spike occur in other coronaviruses, so changes in the spike of SARS-CoV-2 are not unexpected. It is important that the vaccine platforms are agile and the number of people infected with SARS-CoV-2 are reduced to minimise the number of variants that emerge. It is important that COG UK can detect variants such as these and the matter has already been raised with them.

4.9 PHE Porton are ready to examine viruses that are submitted to ensure that they are detected by current testing platforms and can carry out neutralisation studies against convalescent plasma and plasma from trial vaccine recipients.

4.10 It was noted that less than 6% of labs use S gene targets for their diagnostics and that most of the protocols in use for sequencing across the country have long-standing problems in S gene drop-out anyway.

4.11 JVT will pick up communications with the public on this matter with policy colleagues.

4.12 There are a number of concerns – if it has a higher R number controlling the epidemic is much harder; it may be underdiagnosed if the diagnostic tests do not detect it; the possibility of reinfection; the possibility of vaccine escape; the possibility of therapeutics escape.

4.13 Currently live virus is not available, but a meeting is planned, including WB and NG to discuss the investigations which need to be coordinated over the next week. Samples from Kent are at Colindale and are going to WB and Porton, but it will take about 4 days to culture virus and then another 3 or 4 to confirm its identity.

4.14 NERVTAG endorsed the proposed actions listed in the PHE paper. They are - enhanced surveillance in Kent and London, sampling to obtain a viral culture, assess fitness in primary human airway cultures, carry out neutralisation studies on convalescent plasma and post vaccination sera/plasma, look for international datasets. In addition, NERVTAG suggested enhanced sequencing from other Lighthouse labs.

4.15 PH requested that MCh or someone in the team complete the risk assessment tool.

Action 40.5 - *MCh/PHE to fill in the risk assessment framework for the Kent variant*

4.16 JVT requested short interim readout with advice from NERVTAG by 16.00 today

Action 40.6 – *NERVTAG to provide readout and advice on the 'Kent variant' to JVT/DHSC by 16.00 on 11 December.*

4.17 JHi agreed to put together a paragraph to share with others on the committee for forwarding to DHSC, indicating that NERVTAG are concerned and that all the actions in the PHE proposal are appropriate and urgent and there are a few additional things recommended, one of which is, as the data emerges, to urge DHSC to consider whether there is a need to intensify control in affected areas. The paper, as presented to NERVTAG should be appended.

5 Surveillance Reports

a. PHE

5.1 In the surveillance report an increase in sample positivity <10s and in London/East of England was noted. New Fig 11 gives positivity by reported symptom status (increase in positivity in symptomatic). Also new slide 8 in the graphs slideset gives positivity by

reason for test.

b. CO-CIN

5.2 Not discussed due to insufficient time

6 Thematic Updates

a. Antibody response and immunity

6.1 PO noted a science media centre Press briefing on the Nature paper published by Kenny Baillie on the genetic mechanisms of critical illness in COVID-19.

b. Virology

6.2 Not discussed

c. Clinical

6.3 WSL had nothing to raise

d. therapeutics

6.4 PH noted that studies are getting closer to an answer on convalescent plasma, with 6000 patients randomised.

6.5 **e. IPC measures**

6.6 Not discussed

7 Any Other Business

7.1 PH noted that the interview of a Public Health registrar to be seconded to NERVTAG had taken place, but it was not known if she had yet accepted the offer.

7.2 GD noted that there had been further H5 detections in birds with no evidence of infections in humans. Previously NERVTAG have given advice on the criteria for stepping down and may be required to do so again for one of the subtypes.

7.3 WB – updated that there is a consortium of academic virologists who hope to put together a holistic consortium to consider things such as virus variants. They are seeking funding from UKRI.

7.4 The meeting finished at 12.43