Ninety-fourth SAGE meeting on COVID-19, 22 July 2021

Held via Video Teleconference

Summary

1. Current levels of hospitalisations are consistent with the medium-term projections reviewed at the previous SAGE meeting and are broadly in line with the roadmap modelling. In the event that increasing hospitalisations were likely to put unsustainable pressure on the NHS, this would need to be identified rapidly and contingency plans enacted within days, given the lag between infections and hospitalisations. Whilst there are signs that the increase in cases may be slowing in parts of the north of England, elsewhere in England cases continue to rise quickly. There is a more varied pattern in other nations of the UK.
2. Risks associated with high prevalence include hospitalisations and deaths; long COVID; workforce absences (including in the NHS); and the increased risk of new variants emerging, as well as the increased pressure put on testing capacity. It is expected that there will be differences in levels and impact of infections between areas and different groups of people. It will be important to continue to monitor the situation carefully. Early autumn may be a particularly risky time, if a return to pre-pandemic behaviours coincides with schools and universities reopening.
3. The prevalence of long COVID symptoms at 12 weeks post SARS-CoV-2 infection is uncertain and estimates vary by study design, ranging from 2.3% to 37% in those infected. 'Long COVID' is likely to be several syndromes. Symptoms may be substantially less for individuals who are vaccinated (low confidence). There are limited data available for children, but the data which are available suggest that long illness duration after SARS-CoV-2 infection in school-aged children is uncommon (low confidence).
4. Data suggest that those who have been vaccinated who become infected with the delta variant may still have a high viral load (medium confidence).
5. It is not yet known how long vaccine-induced protection against SARS-CoV-2 infection will last but it is highly likely that it will wane over time (high confidence). It is also likely that protection against severe disease will wane, but to a lesser extent (medium confidence).
6. The biggest longer-term threat to the UK's health security and response to the SARS-CoV-2 pandemic is the emergence (and establishment within the UK) of variants that either have increased transmissibility, increased severity, escape prior immunity or a combination of these characteristics (high confidence). At this point in the epidemic, with a high degree of population immunity, an immune escape variant would be of particular concern (high confidence). Increased international vaccination has the potential to reduce the risk to the UK (medium confidence).

Situation update

7. Current levels of hospitalisations are consistent with the medium-term projections reviewed at the previous SAGE meeting and with the roadmap modelling. Estimates of R and growth rate are now provided through UKHSA and not through SAGE. Whilst there are signs that the increase in cases may be slowing in parts of the north of England, elsewhere in England cases continue to rise quickly. There is a more varied pattern in other nations of the UK. The medium-term projections show a plateauing of cases under assumptions of no significant behaviour change apart from as a result of school holidays.
8. It continues to be the case that those being hospitalised are increasingly from younger adult age groups where vaccination levels are lower and infection rates are higher. As infections concentrate in younger age groups, changes which

disproportionately affect the contact patters of these age groups (e.g., schools closing or nightclubs opening) will have a significant effect on the trajectory of the epidemic.

9. Delta remains the dominant variant in the UK and there are currently no signs of growth of other variants. ONS data show an increase in the proportion of those infected self-reporting symptoms since mid-May when the delta variant became dominant. The symptoms reported are consistent with those which were reported when alpha was dominant. There are some differences in symptoms reported between adults and children.
10. Other respiratory viruses will also have increased in prevalence as mixing has increased, some of which may lead to symptoms similar to COVID-19. This increase in prevalence is likely to continue, and evaluation of multiplex testing is underway at PHE/UKHSA. Multiplex testing has several benefits including enabling better surveillance, faster treatment decisions, and more targeted isolation.
11. People who have been vaccinated in regulated clinical trials should now be able to obtain equivalent certification in the UK to those who have been vaccinated with approved vaccines. Work is continuing to enable those people to have equivalent recognition of their vaccination status in other countries. Volunteers' participation in vaccine trials is an essential part of the development and approval of vaccines and it is important not to disincentivise participation.
12. SAGE welcomed the publication of a report by the Academy of Medical Sciences on preparing for winter 2021-22, and a report from the Royal Academy of Engineering on infection resilient environments. Both of these reports have recommendations that should be considered by a number of government departments.

Issues to monitor over the coming months

13. SAGE has previously advised on the risks associated with high prevalence (e.g. SAGE 93). The risks highlighted remain relevant including hospitalisations and deaths; long COVID; workforce absences (including in the NHS); and the increased risk of new variants emerging, as well as the increased pressure put on testing capacity.
14. In the event that increasing hospitalisations were likely to put unsustainable pressure on the NHS, this would need to be identified rapidly and contingency plans enacted within days, given the delays between infection and hospitalisation (i.e., because hospitalisations will continue rising for a time even once infections start to fall). Having clear trigger mechanisms for this in place is strongly advised.
15. It will be more difficult to identify these issues rapidly if testing capacity is overwhelmed or if testing behaviours change. Sequencing capacity is also important to identify the emergence of any new variants.
16. It is expected that there will be differences in levels and impact of infections between areas and different groups of people. Taking into account this heterogeneity, it will be important to continue to monitor the situation carefully. As identified in the Academy of Medical Sciences report, early autumn may be a particularly risky time if a return to pre-pandemic behaviours coincides with schools and universities reopening.
17. There are unknown effects on vaccine effectiveness in a high prevalence environment where transmission pressure is high. As infections increase so will the number and strength of challenges from SARS-CoV-2 that vaccinated individuals will face; to date, vaccine effectiveness has been estimated in the context of comparatively low prevalence. PCR cycle threshold (Ct) values have decreased as the delta variant has become dominant, which indicates that infected people have higher viral loads which may further increase force of infection.

ACTION: SPI-M to set out its data requirements for PHE and NHSE, including the requirement for linked data on vaccination status and hospitalisations.

ACTION: NHSE and **JBC** to provide analysis of local and national NHS impacts at different levels of hospital or ICU admissions or occupancy.

ACTION: SAGE Secretariat to share AcMedSci and RAEng reports across government.

Human challenge studies

18. A human challenge study inoculated 27 healthy, seronegative volunteers aged 18–30 with a variant of SARS-CoV-2 isolated in summer 2020. A low dose of the virus (10 infectious units) was administered to each volunteer, resulting in 16 of the 27 becoming infected. All infected individuals had only mild symptoms.
19. Virus shedding was detected 2 days after inoculation and for some individuals was detectable in the throat before it was detectable in the nose. Virus shedding then continued for around 10 days. This is consistent with previous understanding of the duration of infectiousness and NERVTAG did not identify a need to change any recommendations around isolation based on this new information.
20. There was a rapid early increase in viral replication (peaking in the nose or throat at around 3 days after inoculation), which highlights the importance of early isolation and testing in preventing transmission.
21. Nose shedding correlated better than throat shedding with detection of infectious virus on face masks, on surfaces and in the air. This suggests that nose shedding may be more important for transmission than throat shedding. This reinforces the importance of face coverings covering both the mouth and the nose.
22. Lateral flow assays (LFAs) correlated quite well with virus culture, which supports the utility of LFAs in detecting infectious people, including detecting early infection although there were a few instances where the very first swab was infectious but missed by LFA.

ACTION: NERVTAG to update note to acknowledge the high ventilation rate in the rooms used in the study.

ACTION: HOCI group consider whether it needs to review advice on the use of PPE in healthcare settings.

Long COVID

23. The prevalence of prolonged symptoms at 12 weeks post SARS-CoV-2 infection (long COVID) is uncertain and estimates vary by study design, ranging from 2.3% to 37% of those infected. Those reporting symptoms that limit their daily living range from 1.2% in young adults to 4.8% in middle age. Fatigue is the most commonly reported persistent symptom.
24. No clear individual syndromes have yet been identified, but it appears that there are likely to be at least four distinct syndromes. There are similarities in the symptoms for those who have been hospitalised and those who have not, and it is not yet clear how syndromes or symptom clusters link to severity of initial disease.
25. Rates of medium-long term multi-organ sequelae (respiratory disease, major adverse cardiovascular event, diabetes, renal failure, and liver disease) are elevated in patients hospitalised with COVID-19 compared with matched general population and are similar to those hospitalised with pneumonia; however, estimates of the incidence of post-infection adverse events in non-hospitalised COVID-19 cases are lacking.

26. Consistent risk factors across studies include increasing age, female sex, being overweight/obesity, pre-existing asthma, pre-pandemic poor physical and mental health, and severity of the initial illness.
27. There are limited data available for children, but the data which are available suggest that long illness duration after SARS-CoV-2 infection in school-aged children is uncommon, with around 2% experiencing symptoms at 8 weeks post infection (low confidence). For those children who do suffer long illness duration, there may be a need for guidance to parents, carers and schools on how to support them.
28. The limited data available on the impact of vaccination suggest that prevalence of symptoms may be substantially reduced in individuals who become infected after double vaccination compared to those who are not vaccinated (low confidence).
29. Data from studies which are underway should help answer some of the outstanding questions. Research into treatments will be important and these studies may also have relevance to other similar syndromes. Studies have given insight into some of the biological changes that occur with long term symptoms.
30. Data from the UK on long COVID are broadly consistent with international comparators.

Vaccine efficacy

31. Vaccines currently in use in the UK for COVID-19 are highly effective in protecting against severe disease and death. However, vaccines do not produce sterilising immunity (where infection is completely prevented).
32. A range of studies are regularly reviewed to estimate the effectiveness of vaccines against infection, symptomatic disease, severe disease and transmission. For the vaccines considered so far (primarily Pfizer-BioNTech and AstraZeneca), the effectiveness against severe outcomes appears similar for the alpha and delta variants (although effectiveness against delta is probably reduced to some extent). Other vaccines and variants will be reviewed as more data accumulate.
33. For these two vaccines, protection against infection with alpha is around 80-85% from 2 doses (low confidence). Recent ONS data suggest that protection against infection with delta may be lower (low confidence).
34. Protection after two doses against symptomatic disease for delta is around 70% for AstraZeneca (medium confidence) and around 85% for Pfizer-BioNTech (high confidence).
35. Protection against hospitalisation, for both vaccines, is c.80% after one dose and c.95% after the second dose (there is currently a higher degree of confidence for the Pfizer estimates than the AZ estimates).
36. Understanding of the effectiveness of the vaccines not widely administered in the UK, and of VE against other VOCs not currently circulating widely here will be important if there is to be a more open international travel policy.
37. ONS data suggest that for those who have been vaccinated who do get infected with the delta variant, PCR cycle threshold (Ct) values are generally lower than for those infected with alpha, suggesting that vaccinated people may still have a high viral load with delta infection (medium confidence). This may mean that there is limited vaccine effect against on onward transmission for the delta variant.

Waning of vaccine-derived immunity

38. It is not yet known how long vaccine-induced protection against SARS-CoV-2 infection will last, but it is highly likely that it will wane over time (high confidence). It is also likely that protection against severe disease will wane, but to a lesser extent (medium confidence).
39. The level of serum antibodies can act as a proxy for measuring immunity. Monitoring this at population level could help guide decisions on vaccine booster doses.

Antibodies are not the only part of the immune response, and even as antibody levels decrease there is likely to remain some protection against severe disease, and any repeat infection is likely to bolster that immunity.

40. There are different rates of antibody waning in different populations and for different vaccines and dosing intervals. Older people are likely to show lower antibody rates initially after vaccination and have faster waning of antibody levels. Data from REACT-2 and the ONS have shown that after two doses of vaccine, antibody levels remain high over at least several months though ONS data show that for Pfizer there are differences in the antibody response by age.
41. Older and more clinically vulnerable vaccinated people will be particularly important to monitor. Since they may experience waning of immunity earlier than others, monitoring antibodies in a cohort of these individuals may produce an early warning signal of when waning immunity is likely to become an issue for the wider population. Identifying any increase in cases or hospitalisations in this group will also be important and is another reason why linking vaccination status and hospital data is necessary.

ACTION: UKRI and **NIHR** to consider need for longitudinal studies on vaccine-derived immunity.

ACTION: Wendy Barclay and **Sarah Walker** to share papers with DCMO and JCVI.

Long-term viral evolution

42. It is almost certain that the emergence of new variants of SARS-CoV-2 is related to the amount of circulating virus, with higher rates of circulation and transmission creating more opportunities for new variants to emerge (high confidence).
43. There are a number of possible scenarios which could lead to the emergence of a variant which is more transmissible, causes more severe disease, or has a degree of immune escape.
44. A variant which causes more severe disease could emerge through recombination, where it is produced in an individual infected with two separate variants or acquire other genetic material from other viruses or the host (realistic possibility). Current vaccines are highly likely to continue to provide protection against serious disease for such new variants. However, since no vaccine is completely effective, there would likely still be an increase in morbidity and mortality from such a variant.
45. An immune escape variant could emerge in several ways. This includes through antigenic shift, where natural recombination events change the spike glycoprotein of the virus (realistic possibility). It could also emerge through animals becoming infected, the virus mutating within that population and then later this new variant infecting humans (realistic possibility). A new variant could also emerge through antigenic drift, where antigenic variation eventually leads to current vaccine failure (almost certain). These could occur over different timeframes. It is unknown how levels of immunity change the risk of the establishment of such a variant.
46. Reducing transmission, increasing vaccination levels, monitoring new variants and preparing to update vaccinations would mitigate the risks of such new variants.
47. A new variant could emerge that evades current antiviral strategies. Reducing the likelihood of such a variant emerging requires careful use of antivirals. This includes taking particular care in the treatment of immunocompromised people, or others infected for a long period, in whom viral evolution is more likely to happen. In particular, those working with infected immunocompromised individuals should take extra precautions to prevent onwards transmission.

48. Although unlikely in the short term, in the long term it is a realistic possibility that variants will arise that are more transmissible but with reduced virulence. This reduced virulence, along with high population immunity, could eventually lead to the virus causing a much less severe disease.
49. As antiviral drugs become available it will be very important to use them in a way that does not induce viral escape from their effects, for example using them in combinations.

Impact of international vaccination

50. The biggest threat to the UK's health security and response to the SARS-CoV-2 pandemic is the emergence (and establishment within the UK) of variants that either have increased transmissibility, increased severity, escape prior immunity or a combination of these characteristics (high confidence). At this point in the epidemic, with a high degree of population immunity, an immune escape variant would be of particular concern (high confidence).
51. Substantial global circulation of SARS-CoV-2 will lead to the evolution of new variants and continued risk of importation to the UK (medium confidence). Reducing prevalence globally will therefore reduce the risk to the UK. Multilateral coordination will be important in achieving this.
52. Increased international vaccination (e.g., by sharing of doses or supporting increased manufacture) has the potential to reduce the appearance and establishment of variants internationally, as well as the risk of their importation to the UK (medium confidence). There are also strong ethical reasons for supporting international vaccination efforts. Targeting international vaccination efforts (e.g., to countries where there are higher numbers of immunocompromised people, for example due to HIV infection) may be particularly beneficial.
53. The choice of vaccine is likely to be important and may change over time. Although using single doses would allow more people to be reached with limited supply, it may also result in more people having partial immunity which may increase the risk of an immune escape variant developing or spreading.
54. Border measures may also reduce the risk to the UK, though these will delay rather than prevent the importation of variants. Reducing global prevalence may lessen the need for border measures. Strengthening global surveillance of variants (as well as continued surveillance in the UK) will be important in understanding the risk. SAGE strongly supports the need for effective surveillance systems in the UK (UKHSA) and the presence of a global surveillance system as envisioned in the G7 communique. In addition to sequencing, studies on biology including transmission fitness and antigenicity will be required to understand which variants may become dominant.

ACTION: FCDO and **CO** to consider the evidence on the benefits to the UK of international vaccination.

List of actions

SPI-M to set out its data requirements for PHE and NHSE, including the requirement for linked data on vaccination status and hospitalisations.

NHSE and **JBC** to provide analysis of local and national NHS impacts at different levels of hospital or ICU admissions or occupancy.

SAGE Secretariat to share AcMedSci and RAEng reports across government.

NERVTAG to update note to acknowledge the high ventilation rate in the rooms used in the study.

HOCI group consider whether it needs to review advice on the use of PPE in healthcare settings.

UKRI and **NIHR** to consider need for longitudinal studies on vaccine-derived immunity.

Wendy Barclay and **Sarah Walker** to share papers with DCMO and JCVI.

FCDO and **CO** to consider the evidence on the benefits to the UK of international vaccination.

Attendees

Scientific experts (35): *Patrick Vallance (GCSA), Chris Whitty (CMO), Ann John (Swansea), Brooke Rogers (KCL), Calum Semple (Liverpool), Catherine Noakes (Leeds), Charlotte Deane (UKRI), Charlotte Watts (FCDO, CSA), Chris Brightling (Leicester), Fliss Bennee (Welsh Government), Graham Medley (LSHTM), Harry Rutter (Bath), Ian Boyd (St Andrews), Ian Diamond (ONS), Ian Young (Northern Ireland Executive, Health CSA), Jeanelle De Gruchy (ADPH), Jenny Harries (UKHSA), John Edmunds (LSHTM), Julie Fitzpatrick (Scottish Government, CSA), Julia Gog (Cambridge), Julian Hiscox (Liverpool), Linda Partridge (Royal Society), Mark Walport , Mark Wilcox (Leeds), Meera Chand (PHE), Melissa Heightman (UCLH), Michael Parker (Oxford), Nicola Steedman (Scottish Government, dCMO), Nishi Chaturvedi (UCL), Roz Eggo (LSHTM), Sarah Walker (Oxford), Stephen Powis (NHS England), Susan Hopkins (PHE/NHST&T), Wendy Barclay (Imperial), and Yvonne Doyle (PHE).*

Observers and government officials (27): *Alan Penn (MHCLG, CSA), Andrew Curran (HSE, CSA),* [redacted] *Anna Seale (JBC), Charlette Holt-Taylor (DHSC), Christopher Williams (PHW),* [redacted] *Fergus Cumming (JBC) Gideon Henderson (Defra, CSA), Giri Shankar (PHW), Henry Cook (No.10), Jennifer Rubin (HO, CSA), Laura Bellingham (CO),* [redacted] *Louise Tinsley (HMT),* [redacted] *Paul Monks (BEIS),* [redacted] *Rob Harrison (CO),* [redacted] *Thomas Waite (DHSC) and Tom Rodden (DCMS).*

Secretariat (all GO-Science) (16): [redacted] *Simon Whitfield, and Stuart Wainwright.*

Total: 78

POST MEETING ADDENDUM

Prior to 04 February 2022, references to the Human Challenge Study in these minutes were redacted because the study's investigators were preparing to publish an academic paper on their findings. This paper has now been submitted for publication and the pre-print can be found at: https://www.researchsquare.com/article/rs-1121993/v1. Therefore, this redaction i s now rescinded as of 04 February 2022.