Seventy-fifth SAGE meeting on COVID-19, 07th January 2021
Held via Video Teleconference

Summary

1. The numbers of cases, hospital admissions and deaths have increased to high levels across the country and in most areas are still increasing. This is putting pressure on the NHS in many places. The B.1.1.7 variant is now the dominant strain in London, South East England, and East of England, and is an increasing proportion of cases in all regions of England.
2. Mortality reductions from vaccination will not begin to be seen before the end of January at the very earliest, and more likely it will be later in February. The pressures on the NHS will take longer to reverse. This is because on average, the age of those being hospitalised and entering ICU is lower than the age of those who die, so many of the people going into hospital and ICU are not in the groups which will be vaccinated first, though they are still largely from groups within the JCVI phase 1 priority list.
3. The impact of vaccination on the overall epidemic is critically dependent upon uptake, and upon how effective vaccines are in reducing transmission as well as severe disease. It is important to have good data on who is being vaccinated (including age, location and with which vaccine) and to be able to link to medical records.
4. There are theoretical and experimental data supporting the possibility that SARS-CoV-2 variants may arise which are less susceptible to pre-existing or vaccine-induced immunity. The E484K mutation is of concern as it has been associated with evasion of neutralisation by monoclonal antibodies. This mutation is present in the B.1.351 variant which has been identified in South Africa.
5. The unquantifiable but likely small probability of the delayed second dose generating a vaccine escape mutant must be weighed against the measurable benefits of doubling the speed of vaccine-induced protection to the most vulnerable. These benefits are particularly significant when prevalence is high.

Situation update

6. The numbers of cases, hospital admissions and deaths have increased to high levels across the country and in most areas are still increasing. This is putting pressure on the NHS in many places. The most recent measures in England and Scotland will not yet have had a significant impact or be reflected in the data.
7. SPI-M estimates that there are between 117,000 and 287,000 new infections per day in England. The ONS community infection survey for the most recent week of the study (27th December to 2nd January) estimates that an average of 1,122,000 people had COVID-19 in the community in England (45,900 in Scotland, 44,100 in Wales, 9,100 in Northern Ireland).
8. Whilst there is some positive news with vaccine rollout underway and ramping up, the coming months will be challenging. Vaccines take 2-3 weeks to induce an immune response, and there are further lags between infections, hospitalisations and deaths. Mortality reductions from vaccination will therefore not begin to be seen before the end of January at the very earliest, and more likely it will be later in February.
9. The pressures on the NHS will take longer to reverse. This is because on average, the age of those being hospitalised and entering ICU is lower than the age of those who die, so many of the people going into hospital and ICU are not in the groups which will be

vaccinated first though they are still largely from groups within the JCVI phase 1 priority list.

10. The impact of vaccination on the overall epidemic is critically dependent upon uptake, and upon how effective vaccines are in reducing transmission as well as severe disease.
11. It is important to have good data on who is being vaccinated which can be linked to medical records (including data on age, location and with which vaccine), as well as on those who refuse and any reasons for refusal. It is also important for modellers to have access to rollout plans.
12. Incidence varies across the country and is particularly high in London, the South-East of England, and Essex. Case rates in older age groups are also high in these regions, which will lead to continued high numbers of hospital admissions. The fastest increases in positive tests are seen in other areas which, although having lower (but still high) levels of prevalence, have limited NHS capacity available and so which would face significant pressures if rates were to continue increasing.
13. Community infection levels and hospital admissions continue to be a key driver of nosocomial transmission. There is significant variation in levels of nosocomial transmission across hospital trusts, and whilst some of this relates to factors which cannot readily be changed (e.g. building design), some trusts have been successful in reducing transmission. Sharing the lessons from successful trusts will be important.
14. There remains no evidence that the relative increase in transmission associated with the new variant is greater in some settings than others; it will spread faster in all settings than the wild-type variant. In the presence of the new variant, it is even more important to have mitigation measures in place in all settings, and particularly in high-risk settings as increased transmissibility increases the likelihood of outbreaks. There is currently no evidence of changes in the routes of transmission though further work on this is ongoing.
15. The latest SPI-M-O estimate of R in the UK is between 1.0 and 1.4, while England is between 1.1 and 1.4. Estimates of R for Scotland, Wales, and Northern Ireland are between 0.9 and 1.3, 0.8 and 1.1, and 1.0 and 1.4 respectively.
16. R estimates rely on lagged data and cannot yet account for the most recent impact of policy changes or any changes in transmission that have not yet been reflected in epidemiological data. These estimates are based on the latest data available up to 4th January. These estimates, therefore, do not account for the latest measures across the four nations including the lockdown in England from 5th January 2021 and may not have fully incorporated any increase in transmission that might have occurred over the festive period and due to the progression of the B.1.1.7 variant outside of southern England. As anticipated, changes and disruption to data streams over the festive period add uncertainty to the current epidemiological picture. These factors lead to greater uncertainty than usual around SPI-M-O's estimates.
17. The 6-week projections produced by SPI-M are a counterfactual scenario where recent measures have no impact and the epidemic continues to follow the trends seen in the data up to 4th January. In practice, the measures taken are expected to reduce R, though it is not known whether they will reduce R to below 1. The 6-week projections therefore reflect a worst-case scenario.
18. The first good evidence of the impact of the lockdown in England will likely be given by the ONS Community Infection Survey and the REACT study, most likely during the week commencing 18th January.
19. SAGE noted emerging data suggesting changing patterns of mortality by ethnicity. It will review these further at its next meeting when more data are available.

ACTION: Cabinet Office to set out what further advice is needed on mitigation measures.

ACTION: Brooke Rogers and **Charlotte Watts** to work with DfE to review the evidence on impacts on children of school closures and effectiveness of mitigation measures.

New Variants of SARS-CoV-2 and immune escape

20. The B.1.1.7 variant is now the dominant strain in London, South East England, and East of England, and is an increasing proportion of cases in all regions of England. In regions where it is not yet dominant, it is highly likely to become so in the coming weeks (high confidence).
21. The age and sex distribution of cases of the new variant is similar to the overall distribution of cases. The B.1.1.7 variant is now dominant in all age groups.
22. Secondary attack rates estimated from contact tracing data are observed to be higher where the index case has the new variant strain, at around 15% of named contacts. Secondary attack rates where the index case has the wild-type variant are around 11% of named contacts, and overall secondary attack rates are around 13% of named contacts. This analysis of the contact tracing data using S-gene target failure as a proxy suggests an increase in secondary attack rate of 30-50%. This is consistent with other analysis indicating an increase in transmissibility.
23. PHE and partner laboratories are carrying out studies on growth kinetics and neutralisation to develop an understanding of vaccine escape, and reactivity of vaccine sera against the new variant.
24. Preliminary investigation indicates that the B.1.1.7 variant grows well in airway cells, which could be associated with higher viral loads and provide an explanation for the increased transmission, but further work is needed to confirm this.
25. Preliminary investigation also indicates that this variant is likely to be susceptible to immunity induced by the currently approved vaccines.
26. There are however theoretical and experimental data supporting the possibility that novel SARS-CoV-2 variants may arise which are less susceptible to monoclonal antibody therapies, convalescent plasma therapy, vaccine-derived immunity, or naturally-acquired immunity. Variants which show reduced neutralisation by convalescent plasma have been generated experimentally and have also been observed in an immunocompromised patient with persistent infection treated with convalescent plasma.
27. The E484K mutation is of particular concern as it has been associated with evasion of neutralisation by monoclonal antibodies. This mutation is present in the B.1.351 variant which has been identified in South Africa. It is also present in some other variants which PHE is investigating.
28. Cases of the B.1.351 variant continue to be found, despite the imposition of travel restrictions between the UK and South Africa two weeks ago. Two potential cases identified do not have travel history and are being investigated further. Other countries have detected this variant as well but are not sequencing as much as the UK. In many countries there is limited sequencing of local populations which makes it difficult to identify where or when variants of concern may emerge.
29. The decision has been taken in the UK to delay the second vaccination dose until 12 weeks after the first. The unquantifiable but likely small probability of the delayed second dose generating a vaccine escape mutant must be weighed against the measurable benefits of doubling the speed of vaccine-induced protection to the most vulnerable. These benefits are particularly significant when prevalence is high.

30. Effective monitoring of variants across the UK, including national data infrastructure will be important. It is also useful to have testing which can give an indication of the type of variant (as S-gene target failures have done for B.1.1.7), as well as having sequencing capacity. It may be possible to develop primer sets which can do this.
31. It is a realistic possibility that over time, immune escape variants will emerge, most likely driven by increasing population immunity following natural infection.
32. There may be circumstances in which a strategy of vaccinating under-16s might be considered beneficial to reduce transmission, but this would be dependent on a vaccine with good effects on transmission reduction, an appropriate safety profile and sufficient vaccine supplies. Vaccines studies in children are ongoing and transmission blocking vaccination strategies are under regular review by JCVI.
33. SAGE endorsed the NERVTAG paper on immune escape subject to minor changes.
34. SAGE will consider variants again at its next meeting if more lab data are available as expected.

ACTION: NERVTAG to update immune escape paper to reflect SAGE discussion.

ACTION: Charlotte Watts and **John Edmunds** to work with **DfT, HO** and **PHE** to produce a short paper to review evidence on importations & seeding, and the potential reduction in risk from testing and isolation.

List of Actions

Cabinet Office to set out what further advice is needed on mitigation measures.

Brooke Rogers and **Charlotte Watts** to work with DfE to review the evidence on impacts on children of school closures and effectiveness of mitigation measures.

NERVTAG to update immune escape paper to reflect SAGE discussion.

Charlotte Watts and **John Edmunds** to work with **DfT, HO** and **PHE** to produce a short paper to review evidence on importations & seeding, and the potential reduction in risk from testing and isolation.

Attendees

Scientific Experts (37): *Patrick Vallance (GCSA), Chris Whitty (CMO), Angela McLean (MoD CSA),Cath Noakes (Leeds), Charlotte Watts (FCDO CSA), Calum Semple (Liverpool), Fliss Bennee (Wales), Graham Medley (LSHTM), Ian Boyd (St Andrews), Ian Diamond (ONS), Iain Bell (ONS), Ian Young (NI), Jeremy Farrar (Wellcome), Jim McMenamin (Health Protection Scotland), John Edmunds (LSHTM), Julia Gog (Cambridge), Kamlesh Khunti (Leicester), Maria Zambon (PHE), Mark Walport (UKRI), Mark Wilcox (NHS), Michael Parker (Oxford), Peter Horby (Oxford), Stephen Powis (NHS England), Wendy Barclay (Imperial), Nicola Steedman (Scotland), Harry Rutter (Bath), Rob Orford (Wales, Health CSA), Sheila Rowan (Scotland CSA), Sharon Peacock (PHE), Susan Hopkins (PHE/NHST&T), Jeanelle de Gruchy (ADPH), Andrew Morris (HDR UK), Wei Shen Lim (Nottingham), Yvonne Doyle (PHE),* [redacted]*, Brooke Rogers (KCL), James Rubin (KCL)*

Observers and government officials (21): *Paul Monks (BEIS CSA),* [redacted] *Julian Fletcher (CO),* [redacted] *Jennifer Rubin (HO CSA), Rupert Shute (HO dCSA), Andrew Curran (HSE CSA), Daniel Kleinberg*

(Scotland), Gideon Henderson (DEFRA CSA), Osama Rahman (DfE), Alan Penn (MHCLG CSA), James Benford (HMT) Ben Warner (No.10), [redacted] *Anna Seale (JBC),* [redacted] *Tom Rodden (DCMS CSA), Rob Harrison (CO)*

Secretariat (all GO-Science) (22): *Stuart Wainwright, Simon Whitfield,* [redacted] *Crystal Moore,* [redacted]

Total: 80