JOINT COMMITTEE ON VACCINATION AND IMMUNISATION

# Minute of the JCVI Extraordinary Meeting on COVID-19 Immunisation prioritisation held 6 July 2020 13:00-17:00

**Members**

Prof Wei Shen Lim (Chair)
Prof Anthony Harnden
Professor Jeremy Brown
Prof Simon Kroll
Dr Rebecca Cordery
Prof Matt Keeling
Dr Fiona Van der Klis
Prof Adam Finn
Prof Anthony Scott
Prof Rob Read
Dr Maggie Wearmouth
Dr Kevin Brown
Prof Maarten Postma

**Co-opted members**

Dr Jillian Johnston (NI)
Dr Lorna Willocks (Scotland)
Mrs Anne McGowan (Wales)
Dr Julie Yates (England)

**Medical Advisor**

Prof Jonathan Van Tam

**Secretariat**

Andrew Earnshaw
Ruth Parry
Jonathan Crofts
Chris Lucas
Dr Mary Ramsay
Dr Gayatri Amirthalingam

**Invited experts/presenters**

Dr Jamie Lopez (PHE) – agenda item 2
Dr Gayatri Amirthalingam (PHE) – agenda item 3
Dr Sema Mandal (PHE) – agenda item 6
Edwin Van Leeuwen (PHE) - agenda item 6
Dr Ines Campos-Matos (PHE) – agenda item 6
Professor Julia Hippisley-Cox (University of Oxford) – agenda item 6
Dr Katherine Donegan (MHRA) – agenda item 8

**Invited observers from Devolved Administrations**

Dr Syed Ahmed (Scotland)

**Other invited observers**

Dr Jacqui Dunn (IoM)
Alex Hawkins-Drew (Guernsey)
Professor Maria Zambon (PHE)
Dr Louise Newport (DHSC)
Stacey Jones (PHE)
Ellie Rose (DHSC)
Dr Richard Roberts (PHW)
Lucy Jessop (Eire)
David Green (PHE)
Louise Letley (PHE)
Suzanna Macdonald (PHE)
Dr Claire Cameron (PHS)

Morwenna Carrington (DHSC)
Bethan Loveless (DHSC)
Nita Mesha (DHSC)
Jenny Harries (DHSC)
Louise Letley (PHE)
Frank Sandmaan (PHE)
Laura Craig (PHE)
Arne Blackman (Go-Science)

**Apologies**
Dr Phil Bryan (MHRA)

**Welcome and Introduction**

1. The Chair welcomed everyone to the meeting and thanked them for attending the second extraordinary meeting on vaccines for SARS-CoV-2 (COVID-19).
2. The Chair reminded attendees of the confidential nature of the discussions, presentations and papers for the meeting.
3. The Chair asked Members to indicate any additional conflicts of interest over and above those declared at the last meeting. None were declared.
4. Apologies were noted from Dr Martin Williams.

## I. Minute of the last meeting

5. The Committee ratified the minutes of the last meeting as an accurate record.

## II. Review of epidemiological data

6. The Chair invited PHE to update the Committee on the epidemiology of COVID-19 in England.

Case detections

7. The Committee noted that case detections through Pillar 1 (NHS and PHE laboratories) and Pillar 2 (Lighthouse laboratories) were continuing to decline. Around 5,000 cases per week were currently being seen, with around three quarters of the cases being detected through Pillar 2.
8. It was noted that detections had reduced in all age groups, with more cases being detected in older age groups throughout the epidemic.
9. The cumulative age/sex distribution across both Pillars showed the largest number of cases in working age females, potentially accounted for by the number of female healthcare workers.
10. Maps of cases by Upper Tier Local Authorities (UTLA) indicated that the highest numbers cumulatively had been in the North West of England. In week 26 (week commencing 22 June) the highest number of detections had been in Leicester and parts of Yorkshire.

Exposure survey

11. An exposure survey of individuals tested in both Pillars, carried out between 19 and 21 May, indicated that in Pillar 1 the vast majority of cases were in healthcare workers or care home workers, with the latter having the highest odds of testing positive. Being a contact of a case was strongly associated with testing positive. Having symptoms was associated with a higher odds ratio. Those who reported black or minority ethnic background had almost three times the odds of being positive compared to white respondents.
12. In Pillar 2 healthcare and care home workers had higher odds of being positive, with higher odds of testing positive also seen in public-facing occupations, including those working in the retail and leisure sectors. Those

who reported contact with a case had higher odds of infection, particularly if this was a household contact. Higher odds of infection were also seen in workplace contacts of a case. Black and minority ethnic groups had higher odds of testing positive. People who exercised outdoors had lower odds of infection.

Hospitalisations

13. The Committee noted that more hospitalisations were recorded in the older age-groups, with more hospitalisations in males, which was particularly noticeable in admissions to ICU.

Mortality

14. The Committee noted that excess all-cause mortality broken down by age-group showed the highest rate in the oldest age group. It was noted that in the last two weeks of June no excess all-cause mortality had been observed in any age group.

Outbreaks

15. It was noted that outbreaks of acute respiratory infections in care home had been a feature of the epidemic from the beginning. Genomic evidence indicated multiple introductions into care homes. More recently care homes had accounted for a smaller proportion of incidents reported to Health Protection Teams (HPTs), with increases seen in educational settings, workplaces and other settings.

16. Since schools re-opened in June some clusters and outbreaks had been reported, the majority being in the East Midlands, Yorkshire & Humber and the Northwest. In the outbreaks it had been mainly school staff affected. It was noted that the increase in reports from schools coincided with the increase in testing.

Discussion

17. Members commented that there could be biases associated with the questionnaires. Members noted that the response rate was low and healthcare workers may have been more likely to respond than others.

18. In the primary school outbreaks, the index case was often an adult. In those cases where it was a child, they had often been children of healthcare workers. Teachers had not been identified to be at particularly high risk of infection.

19. The excess all-cause mortality had not been adjusted for influenza outbreaks in the last five years, but it was noted that most of the pandemic had taken place outside of the influenza season, so it may not have had any effect.

## III. COVID-19 sero-epidemiology

20. The Chair invited PHE colleagues to present on serological testing and surveillance.

COVID-19 serology convalescent sera testing

21. The Committee noted that a collection of samples from confirmed SARS-CoV-2 patients had been established. These had been identified through the FF100, Occupational Health Services at PHE or through the RCGP. The cases were predominantly non-hospitalised.

22. Sequential samples had been collected and sent to the Manchester Sero-Epidemiology Unit (SEU) and from there distributed to Colindale and Porton for serological testing. There had been a total of 270 samples from 181 patients, with the majority (57) being in the 50-59 years age group. There were more females than males in the collection.

23. 104 individuals provided a single sample, 69 provided two samples, and seven provided three or more samples.

24. The structure of the virus was described, and it was noted that the most abundant protein, the nucleoprotein (N), had homology with seasonal coronaviruses. It was noted that the Spike protein (S) was required for viral entry and that the Receptor Binding Domain (RBD) of the S protein was predicted to be the main site for binding of neutralising antibodies.

25. The three different assays used for antibody testing were noted; they were Euroimmun IgG, a commercial ELISA which targeted IgG antibody to the S1 protein, Abbott, a commercial CMIA-based assay which targeted antibody to the N protein and included blockers for seasonal coronavirus cross-reactivity, and the RBD assay, a PHE developed in-house ELISA targeting IgG antibody to the RBD of S1. Given the different cut-offs and ranges of the assays, direct comparison was difficult.

26. It was noted that specificities for all assays were determined by testing baseline pre-2020 samples and a panel of confounder samples; all assays had good specificity.

27. Out of the PCR-confirmed positive samples:

    - some samples were positive in the first 14 days post symptom onset, but a significant number were negative in all assays in this time period;
    - in the 14-28 day post symptom onset window the Abbott assay was positive for all samples, this was not the case for the S based assays; and
    - 28 days or more post symptom onset there was an increasing trend for samples to be negative in all three assays,

28. There was a good correlation between results from the two S-based assays.

29. Results from the Abbott and Euroimmun IgG assays indicated that antibody to N appeared first, followed by the anti-S antibody.

30. It was noted that 4 of 181 PCR-positive individuals did not develop an antibody response as measured by any of the assays.

31. It was noted that of 42 paired samples for which the first sample was at 28 days post symptom onset or later, all assays indicated a reduction in antibody over time. It was not yet known whether antibody waning would plateau or continue to drop over time. It was also not known whether there would be a similar drop in neutralising antibody over time.

Discussion

32. Members asked for detail on the severity of illness in those providing samples. It was noted that the patient samples were typically from individuals who had mild illness, although data were not available for a small number of individuals. Ethnicity and hospitalisation data were not currently available. Most individuals did not have any underlying illness.

33. It was noted that there was a trend for higher antibody levels from 30 to 50 years of age followed by a drop in older ages, but this was not significant.

34. It was suggested that if the assays were set to have equivalent specificity they would all be equally sensitive. PHE agreed to review this.

Serological surveillance for COVID-19 in England

35. Three primary sources of sera were:

    - residual sera collected opportunistically as part of the collection at the SEU in Manchester, established in the 1980s, to which participating microbiology labs across England submit samples on a regular basis;
    - samples from the community submitted through the RCGP programme including 100 practices across the country; and
    - What's the STORY – an NIHR funded study of children and adults under 25 years across England.

36. As well as attempting to enhance and expand the existing collections, additional collections were established with the aim of obtaining 1000 samples per week. A collaboration with NHSBT provided 2000 samples per week, sampling two different regions each week. Engagement with Great Ormond Street Hospital initially supplied 100 samples per week but was supplemented by residual sera from a number of paediatric centres across the country.

37. Longitudinal studies in adults (ESCAPE and London-COVID) and children of healthcare workers (RAPID-19) had been set up. Outbreak investigations had also provided the opportunity to carry out serological testing.

Adults

38. It was noted that adult blood donor data (NHSBT) were able to provide regional and national prevalence estimates, which were shared with SAGE on

a weekly basis. The national adjusted prevalence was estimated to be 8.6% from 30 April to 22 May and 7.8% from 28 May to 22 June.

39. A clear age trend in prevalence was noted in both time periods, with the highest prevalence in those aged 17-29 years, declining with age.

40. In the first time-period there appeared to be a higher prevalence in males, but that could not be seen in the second time-period, with prevalence by gender looking similar.

41. It was noted that London had the highest prevalence over time, having increased rapidly and reaching a point-prevalence close to 16% in week 21. The lowest sero-prevalence was seen in the South West. In the most recent sampling most areas had plateaued or were lower than preceding weeks. It was noted that changes to the geographical spread of donors may have contributed to the variations in prevalence observed.

42. It was noted that ONS has tested 3,298 individuals aged 16+ and found overall 6.3% positive for antibodies, with 9.1% in London and 2.7% in the South West between 26 April and 27 June.

43. React-2 interim results (86,294 samples) gave an adjusted prevalence overall of 5.1% in those aged 18+, 7.4% in 18-24 years and 2.9% in 65 to 74 years old from 20- 30 June.

Children

44. Paediatric sero-prevalence performed on the Abbott assay showed an increase in adjusted prevalence from 0.2% from 1 February to 1 March, to 5.5 - 6% up to the start of June. The samples from What's the Story had adjusted prevalence of around 3%.

RCGP over 65s

45. It was noted that sero-prevalence in those over 65 years of age was overall relatively low compared with other age groups.

ESCAPE

46. A longitudinal study of PHE and NHS employees was being undertaken, with testing on the Abbott and Eurommun IgG assays. Sampling was being undertaken at three different sites. The overall positivity was 18% in Wythenshawe (largely frontline NHS workers), 10-11% in London PHE (laboratory and office-based workers) and 6% in Manchester (PHE/MRI office and lab-based staff). A small number of individuals had gone from antibody positive to antibody negative.

Discussion

47. It was noted that the inclusion of blood donors with COVID-19 symptoms changed in early June from post 14 days to post 28 days, although this was unlikely to have had a significant change in practice by the time of the meeting. It was queried whether those with COVID-like symptoms would

attend for blood donation, but thought that individuals who were asymptomatic or with milder illness would still attend. There was also a convalescent plasma programme and it was noted that NHSBT were transferring the exposed blood donors to this programme which now had over 1000 units banked for use.

48. It was suggested that the serological data could be used to determine which groups were spreading the virus and noted that modellers were already using the data.

49. The Committee queried whether the lower incidence in those 65 years of age and over was due to lower exposure or due to poor immune responses in older adults. It was noted that the RCGP data (healthy older individuals attending for routine blood testing) showed much lower prevalence compared to care homes where outbreaks had been more common. It was noted that the low prevalence in the over 65s amongst the RCGP collection was unlikely to reflect an inability to respond to SARS-CoV-2, given the very high sero-positivity seen in some care home outbreak investigations.

50. The Committee asked about rates of seroconversion and whether PHE was able to track changes over time. It was noted that PHE had multiple collections, and it was considered that this would allow interpretation of changes in rates of seroconversion. The NHSBT data could show changes over time by geographic region. Additionally, longitudinal studies such as ESCAPE, would give changes within specific age groups, although it would not necessarily be comparable across different studies.

51. The Committee queried whether seroprevalence data supported vaccination of younger groups to prevent transmission to other at-risk groups. PHE outlined that modellers were using the data to assess transmission risk, however there was an issue around the complexity of antibody response in different groups and how to apply this in models. Current modelling suggested that the best target for vaccination would be the at-risk groups, due to the lower mortality and morbidity in the younger ages groups. Vaccination may also limit transmission, but this would require vaccination of a large number of the younger population to outweigh a programme targeting just those at risk.

52. The Committee noted that prevalence was estimated around 5-8%, but queried whether this was an accurate representation of exposure, or whether confounders, such as asymptomatic individuals, meant the incidence was likely to be higher. It was noted that those with more severe infection were likely to have higher antibody levels, but the immune response to SARS-CoV-2 was still being investigated and it was not possible to answer this question yet.

## IV. Delivery of candidate COVID-19 vaccines

Delivery considerations

53. Members were asked by NHSE&I regarding on-the-day contraindications to COVID-19 vaccination. It was agreed that general principles in the Green

Book: Immunisation against infectious disease, would apply, and if an individual was acutely unwell (for example with a fever above 38.5 C), immunisation may be postponed until they have fully recovered. This was to avoid wrongly attributing any new symptom or the progression of symptoms to the vaccine. It was also noted that those with symptoms consistent with COVID-19 should not attend for vaccination to reduce the risk of onward transmission.

54. Members considered that it would be important to have trial data on vaccination in SARS-CoV-2 sero-positive individuals to fully understand the safety of vaccination following infection. Data would be required for each developmental vaccine. It was noted that some care home residents could have very high levels of sero-positivity following outbreaks, and that frontline health and social care workers could have a reasonably high probability of infection, vaccination and later re-exposure. It was noted that vaccination after recovery could lead to a longer lasting protection against future disease. It was noted that the EMA was requesting data on the safety of vaccination in sero-positive individuals.

55. Members considered that vaccination during the influenza season could lead to situations where individuals had recently (last 28 days) received an influenza vaccine or could be scheduled to receive an influenza vaccine within 28 days of a COVID-19 vaccine. Concomitant administration could also be logistically desirable. Members considered that data should be developed on the safety and immunogenicity of concomitant administration of influenza and candidate COVID-19 vaccines.

56. Members noted that there were limited data available to determine intervals between vaccines at this time. Generally, advice in the Green Book: Immunisation Against Infectious Disease should be followed regarding intervals between vaccines unless data from vaccine trials indicated otherwise. The Committee agreed that without data to indicate otherwise there should be a 28 days interval between COVID-19 and influenza vaccines. It was noted that many of the candidate vaccines could be two-dose schedules. It was considered possible that the Committee could advise, dependent on data to support it, prioritising administration of the first dose in as many eligible individuals as possible, before considering an offer of the second dose. Sequencing of vaccines would, in part, be dependent on whether influenza vaccine was a priority at that time of year. Data on responses to a single dose of COVID-19 vaccines would be required for further consideration.

57. It was considered that there should be a gap of around six weeks between treatment for COVID-19, including convalescent plasma therapy and dexamethasone, and COVID-19 vaccination.

58. Members were asked by NHSE&I whether they would consider off-label use for under 18s or pregnant women (assuming no trial data were available for

this group). It was noted that the question was difficult to answer in the absence of safety data on the candidate vaccines, but it was agreed that the committee would consider off-label use, as had been done with other vaccines.

59. Exceptions might be a live attenuated vaccine which had teratogenic potential in pregnant women or nucleic acid vaccines. Pre-conception administration of vaccines may also be a consideration. It was noted that the UKOSS data suggested that there was no increased risk from COVID-19 in otherwise healthy pregnant women, but the situation could be different for under 18s or pregnant women who had some other risk factor.

60. In line with all vaccines, a risk/benefit assessment would be required, and as the risk from COVID-19 in pregnant women was not considered high, a precautionary approach in relation to vaccination should be considered in the absence of safety or trial data.

61. It was noted that there would be data on immunisation of under 18s coming out of some of the trials, but not on pregnant women.

62. Members were asked by NHSE&I to advise on how much time could elapse between defrosting and administration of vaccines, and how long vaccines could be held at room temperature. The Committee agreed that it was not possible to answer these questions as they did not have the relevant information available on storage conditions for the vaccine candidates.

Observation period

63. The Committee discussed the principles regarding post-vaccination observation periods to aid with planning for the possibility of mass vaccinations using a drive-through model for delivery, and whether a post-vaccination observation period would be required.

64. A number of papers were noted; two from Australia in particular, in which 15 minutes of observation in the drive-through and 5 minutes in GP practices was advised.

65. It was noted that evidence indicated that syncope was unlikely to occur beyond 15 minutes and that anaphylaxis was rare (about one in one million) and could occur 24 hours or more post vaccination.

66. It was suggested that this was a generic issue, as some vaccinations were already taking place in cars in the UK and other countries. This was being considered for COVID-19 immunisations, because of the need to immunise a large number of people in a short period of time.

67. It was noted that the Green Book did not advise a specific time period for observation.

68. It was proposed that the advice for vaccinations would be that the person who was receiving the vaccine does not drive, or they should wait 15 minutes if they are driving. If the model was similar to the drive-through swabbing

venues, there would be separate areas for parking after the immunisation had been carried out. No observation period would be required where the individual was not driving.

## V. Influenza programme – considering COVID-19

69. It was noted that a discussion by correspondence had taken place regarding advice on the use of additional influenza vaccine in the 2020/21 season. It was confirmed that this has been received by DHSC.

70. It was noted that co-infection with SARS-CoV-2 and influenza had been described, but data on whether the illness was more severe was lacking at present. This was considered an area to keep under review.

## VI. Risk factors for serious disease and mortality

71. It was noted that at the last SARS-CoV-2 vaccine meeting, the Committee had discussed prioritisation in the event of there being limited supplies of vaccine and that an interim statement had described principles for any programme, but had not provided an in depth position on risk-groups, and that this further discussion would provide information on risk groups for serious disease and mortality for COVID-19.

Disparities in the risk and outcomes of COVID-19

72. PHE introduced a presentation on 'disparities in the risk and outcomes of COVID-19' based on a review published on 2 June 2020. This was a descriptive review of the surveillance data available at the time and described the factors that might influence the risk in being diagnosed and dying from SARS-CoV-2.

73. It was noted that COVID-19 replicated and in some cases, increased, existing inequalities.

Age and sex

74. It was noted that diagnosis rates in Pillar 1 increased with age. Diagnosis rates were higher in females under the age of 60, and higher in males aged 60 or older. Hospitalisations were higher in older age groups, with highest rates in lower levels of care in the over 80s, but with small numbers of over 80s in critical care. Mortality rates were higher in males and in people in older age groups.

Deprivation

75. It was noted that people who lived in the most deprived areas of the country were more likely to be diagnosed with COVID-19 than those in the least deprived. A similar observation was made for deaths.

Ethnicity

76. It was noted that the relationship between ethnicity and health was complex and likely to be the result of a combination of factors. The focus of the review was on the factors that led to increased risk of acquiring the infection and the factors that led to increased risk of poorer outcomes.

77. A new analysis, not in the published report, on testing and ethnicity up to 11 May 2020 was presented. It was noted that the majority of ethnic groups had higher odds of being tested than the white British population, apart from Bangladeshi, Chinese, white and Asian mixed, white Irish and black and white Caribbean. The odds of positivity remained similar, apart from white Irish and white and black Caribbean mixed. The 'any other Asian' group had the highest odds of positivity.

78. The multivariable analysis of odds of being tested and positivity reinforced the observations about age and sex, with those over 80 having higher odds of being tested and being positive, and with males having lower odds of being tested, but higher odds of being positive.

79. It was noted that one of the limitations of this analysis was that co-morbidities and occupation were not accounted for.

80. It was noted that the highest age standardised diagnosis rates were in those in the 'other and black ethnic' groups, with the lowest in the white ethnic groups, but the rates in the 'other' group was thought to be artificial as a result of the way in which the ethnicity information was derived by linking to HES.

81. Almost 90% of people admitted to lower levels of care were white, with 60% admitted to critical care being white. All other ethnic groups were more likely to be in critical care.

82. The risk of death amongst those who were positive for SARS-CoV-2 was two times higher for the Bangladeshi group when compared to the white British, followed by Pakistani, Chinese and Indian groups.

83. All-cause mortality was increased for all ethnicities; the baseline was normally highest for whites, compared to Asian, black and mixed ethnic groups. However, in 2020 it was reversed; much of this being driven by COVID-19 deaths.

84. ONS analyses indicated that the highest rates of death from COVID-19 were amongst men working as security guards, taxi drivers, bus and coach drivers, chefs, sales and retail assistants and lower skilled workers in construction and processing plants as well as men and women working in social care.

85. PHE had carried out a slightly different analysis and found that deaths in the 20-64 years age group were 1.5 times higher than average and that three occupation groups were higher than this; caring personal services, elementary security occupations and road transport drivers.

86. The increase in all-cause mortality was highest amongst people who were born outside UK and Northern Ireland.

Comorbidities

87. A similar percentage of deaths with cardiovascular disease were recorded with and without COVID-19 (44%). However, for other comorbidities, such as diabetes, hypertensive disease, chronic kidney disease, COPD and dementia, the percentage was higher.

88. In all deaths there was a higher proportion of deaths among black ethnic groups that mentioned diabetes, and this was particularly high amongst those that had mentioned COVID-19 on the death certificate.

Discussion

89. It was noted that the distribution of intensive care admissions in the lower age groups probably reflected the selection criteria for intensive care, rather than severity of disease.

PHE vaccination modelling considerations

90. It was noted that modellers were focussing on the impact of vaccination strategies on mortality, QALYs lost, the need for non-pharmaceutical interventions and the net benefit.

91. Lessons could be learned from influenza vaccination modelling, but that there were important differences between the two infections.

92. Modellers had commenced scenario modelling using a compartmental model, with a base scenario of prevalence remaining stable due to non-pharmaceutical interventions. The important unknowns were outlined, including the vaccine efficacy and the duration of immunity.

Discussion

93. It was noted that cost-effectiveness considerations were not required at this time.

94. It was suggested that QALYs saved could help to decide on which groups to immunise if there was insufficient vaccine initially.

95. It was noted that a US calculation model estimated that a vaccine of 70% efficacy would require 70% coverage in order to negate the need for social distancing measures. PHE confirmed that their model could be used to develop predictions such as this.

Oxford Risk Prediction Tool

96. The Chair welcomed Professor Julia Hippisley-Cox, University of Oxford, who had been working with the CMO's office and around ten different academic teams from across the UK to develop a prediction model which would predict the risk of COVID-19-related mortality and hospital admissions.

97. It was noted that the QResearch database was used, which had a representative sample of 10.4 million patients from across England including

detailed GP records with self-assigned ethnicity in around 80% of the cohort, as well as information about age, sex, and risk factors.

98. This has been linked to individual cause of death from hospital mortality records from ONS, the hospital episodes statistics (HES) and the COVID test results from Public Health England. More recently it has been linked to systemic anti-cancer treatment agents.

99. The use of the model was demonstrated, using the example of calculating the adjusted hazard ratio of COVID-19 related death in men; adjusted for variables of deprivation, age and BMI. A significant independently associated risk with ethnicity was noted.

100. There were specific risks associated with learning disabilities, which was separate and smaller than the large increase in relative risk associated with Down's syndrome.

101. Kidney failure was graded into five different categories and then stage 5 subdivided according to whether a transplant had taken place or whether the individual was on dialysis.

102. It was noted that it factored in different potential risk factors, building on the original 'shielded patients' list as a starting point, noting that factors indicating that individuals should be on the original 'shielding list' had been retained as people may have modified their behaviour and isolated for the ninety-day period over which the data were collected, thus attenuating their actual risk.

103. Use of the QCovid™ risk calculator was demonstrated, combining the hazard ratios with underlying risk functions to derive an absolute risk calculation, similar to existing risk tools

104. It was suggested that the model underlying the calculator could be applied to a patient database (eg a GP record system) and could be used to calculate a score for everyone and rank them according to where they fell in the distribution.

105. It was suggested that the ranking could be used to prioritise people for vaccination if there was a limited supply of vaccine.

106. It was noted that the ranking had been applied to the population and it had been found that about 4% of the highest-risk stratified population (a population size equivalent to the shielded population) would account for 75% of all the deaths that had occurred until the end of March. The shielded list accounted for 20% of the deaths, however it was noted that (in the model) those shielding could have been at a lower risk of infection due to social distancing.

107. It was noted that the sensitivity at the top 10% of risk would account for 88% of all deaths, at the top 20% of risk, that increases to 95%. In the top 50% of risks, 99% of deaths were accounted for.

108. A paper was in preparation by the Oxford team and would soon be publicly available.

Discussion

109. It was noted that the absolute risk depended on the incidence, the size of the peak and number of infections, so if there was another peak, it was likely that the rank order of people would remain the same, but the absolute risk would change according to number of people who were infected and the level of pre-existing immunity.

110. It was noted that it was difficult to disentangle higher risk patients for whom there was an intervention at the time when the data were collected (ie shielding) from the model. A separate analysis of the shielded group may be warranted.

111. Some factors had not been taken into account in the analysis, such as occupation and household size and that the former would be investigated further when the model was reviewed.

112. Oxford group had received a grant which would enable them to carry out work to look further into the ethnicity-related risks.

113. The Committee agreed that they had reviewed extensive data on risk groups for disease and death, and that the work of the Oxford group was very helpful in understanding the risk groups, but the missing data were the immunogenicity and effectiveness of the candidate vaccines in those groups, so at this point it was not possible to issue further advice.

114. It was noted that a position on occupational risk was needed. DHSC officials indicated that a combination of the individual risk and the risk associated with the individual's occupational setting could be taken into account when considering an individual's prioritisation. It was considered that the risk of serious disease and death, the benefits from vaccination, and occupation could all be taken into account in their advice.

115. The Committee agreed that the work of the University of Oxford on clinical risk stratification was very helpful and could assist in determining the priority groups for vaccination based on clinical endpoints.

116. The Committee agreed that three specific groups should be considered for vaccination:

    - those that were at risk of becoming seriously ill and dying;
    - those who were at particular risk of becoming infected because of their occupation; and
    - those who provided key public services.

117. The two groups referred to in the JCVI interim statement were still considered to be the highest priority and the Committee agreed that they would wait until

there was more information on vaccines before reconsidering that prioritisation.

118. It was noted that the Secretariat would work with Professor Hippisley-Cox to understand whether the risk prediction tool could be applied to prioritisation for vaccination.

119. A separate session in which the committee could consider models or an explanation of how the two ways of identifying risk groups might be used was proposed. It was agreed that PHE would discuss with Professor Hippisley-Cox and modellers.

120. It was agreed that the published statement would not be updated at this time.

## VII. Vaccine platforms

121. The secretariat introduced a paper on the various vaccine platforms being utilised for potential SARS-CoV-2 vaccines.

122. It was noted that a number of them had been utilised for potential MERS-CoV and Ebola vaccine and that there had been some safety signals reported with an inactivated MERS-CoV vaccine candidate inducing antibody enhanced disease when challenged, and a Parvovirus B19 baculovirus expressed Virus Like Particle (VLP) vaccine had been withdrawn from trials because of adverse events.

## VIII. Vaccine development update

123. The secretariat noted a table in the meeting pack detailing nineteen candidate vaccines that were in clinical evaluation, or otherwise of interest to the UK.

124. The candidate furthest on in development was the Oxford/AstraZeneca vaccine which was in Phase 3 trials, with results from Phase1/2 expected shortly, and Phase 3 results expected later in 2020.

125. Others in Phase 1/2 or 2 were noted, including the CanSino, Moderna, Sinovac, Novavax, and Pfizer vaccines. Very little information was available on timelines for vaccine availability or trial readouts.

126. It was noted that the Imperial group were including children in their immunogenicity bridging trial. Very few trials included children, infants or older age groups.

MHRA Safety Surveillance planning

127. It was noted that the Commission on Human Medicines had convened an expert working group to advise the MHRA on their safety surveillance strategy. One of the key issues that has been identified was the need for individual patient level data on vaccine exposure, particularly if any vaccine was to be administered in more novel settings. This would require links to primary care electronic healthcare records. The MHRA was now engaged with NHS England, PHE, NHS Digital and NHSX and DHSC to ensure that a

system was put in place to call patients for vaccination and ensure that administration was adequately captured.

128. The group had agreed the outcomes that were needed for proactive monitoring and that this would be kept under review.

129. More detailed protocols would be available in July and August, alongside a timeline of when data would become available. These documents would be shared with the committee.

130. It was noted that MHRA had also started to develop a proposal for an app or online platform for active surveillance of specific pre-defined cohorts of patients immunised with any COVID-19 vaccine, capturing data directly from the patients themselves. The intention of this approach was to provide rapid real-world safety monitoring of any vaccine. The limitations of the approach were recognised.

## IX. Immune responses to infection

131. It was noted that a wide range of publications on antibody testing were available, which described different targets and assay formats. It was difficult to compare between assays as, although NIBSC have prepared a standard, it was not widely available or used.

132. Many of the studies had relatively short follow-up periods, rarely beyond six weeks.

133. Specificity was derived in varying ways, for example one assay only basing their specificity on eight negative samples.

134. It was noted that a key aim was to detect neutralising antibody and the assumption was that this was associated with antibody to the receptor binding domain. However, a correlate of protection had not been identified, meaning at present, the presence of neutralising antibody alone was insufficient to infer protection.

135. It was noted that a number of studies had investigated T cell responses, and that these were seen, particularly to non-structural proteins, in people in whom antibody had not been detected, or who had not been exposed to SARS-CoV-2. The significance of this was not known.

136. One of the papers described ‘reinfection’. PHE had been investigating the time elapsed between positive results and have found 1000 individuals who were positive 25 days apart, 100 that were positive more than 50 days and 10 more than 70 days apart. This was considered unlikely to be infectious virus, but the significance of these findings was not fully known.

137. There were concerns about how long protection following infection would last, and it was noted that with seasonal coronaviruses, reinfection occurred about once every three years, with immunity lasting six to twelve months.

## **Declarations** – (Conflicts of interest specific to COVID-19 vaccines)

| **Prof Wei Shen Lim (CHAIR)** |
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| Professor Wei Shen has no registered conflicts of interest<br><br>Other information<br>Member of the New and Emerging Respiratory and Viral Threats Advisory Group (NERVTAG)<br><br>Co-investigator of the NIHR-funded (COVID19) RECOVERY Trial. |
| **Prof Anthony Harnden (Deputy Chair)** |
| Professor Harnden has no registered conflicts of interest. |
| **Prof Adam Finn** |
| Professor Adam Finn receives no personal payments from the manufacturers of vaccines.<br><br>Non personal interest: The local Principle Investigator at Bristol for trials of the University of Oxford tChAdOx vaccine. |
| **Prof Matt Keeling** |
| Professor Matt Keeling has no registered conflicts of interest.<br><br>Other information<br>Member of SPI-M and occasionally sits on SAGE |
| **Prof Jeremy Brown** |
| Professor Brown has no registered conflicts of interest |
| **Dr Martin Williams** |
| Professor Martin Williams has no registered conflicts of interest.<br><br>Other information<br>Professor Williams holds a contract for work with Public Health England. |
| **Dr Fiona Van der Klis** |
| Dr Fiona van der Klis has no registered conflicts of interest |
| **Ms Alison Lawrence** |
| Ms Alison Lawrence has no registered conflicts of interest |

| **Prof Maarten Postma** |
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| Professor Postma has no registered conflicts of interest |
| **Prof Robert Read** |
| Professor Read receives no payments from the manufacturers of vaccines.<br><br>Professor Read has no registered conflicts of interest |
| **Prof Anthony Scott** |
| Professor Scott receives no payments from the manufacturers of vaccines.<br>Professor Scott has no registered conflicts of interest<br><br>Other information<br>Professor Scott is Director of the Health Protection Research Unit at the London School of Hygiene and Tropical Medicine. He receives research funding from the National Institute for Health Research, the Medical Research Council, the Wellcome Trust and Gavi, The Vaccine Alliance, and the Bill & Melinda Gates Foundation. |
| **Dr Maggie Wearmouth** |
| Dr Wearmouth has no registered conflicts of interest |
| **Professor Simon Kroll** |
| Professor Kroll r has no registered conflicts of interest<br><br>Other information<br>He is the Honorary Medical Director of Meningitis Now |
| **Dr Rebecca Cordery** |
| Dr Cordery has no registered conflicts of interest<br><br>Other information<br>Dr Cordery works for Public Health England |
| **Dr Kevin Brown** |
| Dr Brown has no registered conflicts of interest<br><br>Other information<br>Dr Brown works for Public Health England |
| **Dr Jillian Johnston (co-opted member)** |

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| Dr Jillian Johnston has no registered conflicts of interest |
| **Mrs Anne McGowan (co-opted member)** |
| Mrs McGowan receives no payments from the manufacturers of vaccines<br>Mrs McGowan has no registered conflicts of interest |
| **Dr Lorna Willocks (co-opted member)** |
| Dr Lorna Willocks has no registered conflicts of interest |
| **Ms Julie Yates (co-opted member)** |
| Ms Julie Yates has no registered conflicts of interest |