

## JOINT COMMITTEE ON VACCINATION AND IMMUNISATION

### Minute of the meeting held on 03 June 2020

#### By teleconference

##### Members

Prof Andrew Pollard (Chair)	Prof Adam Finn
Prof Wei Shen Lim (Chair – COVID-19)	Prof Rob Read
Prof Anthony Harnden (Deputy Chair)	Prof Anthony Scott
Professor Jeremy Brown	Dr Maggie Wearmouth
Alison Lawrence	Dr Martin Williams
Prof Simon Kroll	Dr Kevin Brown
Dr Rebecca Cordery	

##### Co-opted members

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

##### Medical Advisor

Prof Jonathan Van Tam

##### Secretariat

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

##### Invited speakers

Dr Partha Basu	Andrew Earnshaw (PHE)
Dr Jamie Lopez Bernal (PHE)	Chris Lucas (PHE)

##### Invited observers from Devolved Administrations

Dr Syed Ahmed (Scotland)	Dr Stephen Thomas (Wales)
Dr Gillian Armstrong (NI)	

##### Invited experts

Prof Judy Breuer

##### Other invited observers

Dr Sandra Anglin (NHS England)	Gary Holden (MoD)
Matthew Olley (NHS England)	Joanne Yarwood (PHE)
Dr Linda Diggle (Jersey)	Julie Nugent (PHE)
Dr Jacqui Dunn (IoM)	Dr Sarah Tarr (PHE)

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Joana Rocha (Guernsey)	David Green (PHE)
Nicola Brink (Guernsey)	Dr Richard Roberts (PHW)
Alex Hawkins-Drew (Guernsey)	Anna Clarke (Eire)
Dr Dipti Patel (NaTHNaC)	Lucy Jessop (Eire)
Dr Michael Edelstein (PHE)	Caroline Trotter (PHE)
Dr Louise Newport (DHSC)	Vanessa Saliba (PHE)
Dr Michael Edelstein (PHE)	Louise Letley (PHE)
Dr Yoon Choi (PHE)	Dr Helen Campbell (PHE)
Dr Sema Mandal (PHE)	

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## Welcome

1. The Chair welcomed all to the meeting. The Chair reminded members and observers that the papers provided for the meeting included information provided in confidence. Attendees were asked not to circulate the papers more widely or discuss the information provided with others outside of the meeting. Attendees were asked not to discuss any considerations of the Committee with others outside of the meeting. Any requests for information should be directed to the Secretariat.
2. The Chair asked members to provide an update about any declarations of interest.
3. The Chair welcomed Prof Judy Breuer to the meeting as an invited expert
4. The Chair noted apologies from Prof Matt Keeling.

### I. Minute of the last meeting

5. The minutes of the February 2020 meeting were agreed.

### II. HPV vaccination

6. The Committee received an update from the Chair on recent discussions at the Committee regarding the potential for one dose schedules of HPV vaccine. The Committee recalled that at the February 2020 meeting, WHO SAGE advice on alternative strategies had been discussed. The SAGE advice had been developed in response to a global shortage of HPV vaccine.
7. In response to the SAGE advice the Committee had agreed that its primary focus and remit was to advise on what was best for the UK immunisation programme in considering any changes.
8. In February 2020 the Committee had received a presentation from Dr Aimee Kreimer on evidence supporting single dose HPV schedules. The Committee had noted good evidence on the persistence of protection and antibody

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response in the bivalent (Costa Rica) and quadrivalent (India) observational studies.

9. As a result, the Committee had agreed that the HPV subcommittee should review the evidence in detail, and to complement this a call for evidence on one dose schedules was issued in March 2020. The Subcommittee had met on 21 May 2020 and reviewed responses to the call for evidence, and additional evidence on single dose HPV vaccination.
10. The Committee considered it important to distinguish between the evidence available for the bivalent, quadrivalent and nonavalent vaccines.
11. The Committee noted that there was good evidence on persistence of protection and antibody for the bivalent and quadrivalent vaccines. Fewer data were available on the nonavalent vaccine, in part because it had been available for a shorter time. However, there was no evidence to suggest that duration of protection or antibody levels would be different for the nonavalent vaccine.
12. The Chair highlighted that it would also be important to also consider single dose vaccination in the context of recent school closures, and the additional pressures this had placed on the immunisation system. Delivery of the HPV programme had been impacted by school closures, including delivery of the first and second dose in eligible cohorts. It would be important to consider whether the evidence on single dose vaccination could assist in delivery of the HPV programme in September 2020, when it was expected that schools would reopen. For example, prioritisation of the first dose of vaccine over delivery of the second dose.
13. The Committee received a summary from the secretariat on responses to the call for evidence. Responses had been received from a range of stakeholders including academics and scientists, the British Association for Sexual Health and HIV (BASHH), the Royal College of Physicians (RCP); Public Health Scotland (PHS) and the two HPV vaccine manufacturers. The manufacturers had responded to all questions, whilst other respondents had addressed questions associated with their specific subject area of expertise.
14. The Committee noted that:
  - good evidence was available on vaccine effectiveness against infection and disease, and duration and stability of the antibody response following a single dose of bivalent and quadrivalent vaccines;
  - although a single dose of quadrivalent and bivalent vaccine elicited lower antibody responses compared with two doses, this was still considered to be immunogenic;
  - data on vaccine effectiveness against infection and disease of a single dose of nonavalent vaccine was not available, however randomised control trials (RCTs) had been initiated;

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- data on the immunogenicity and kinetics from one dose of the nonavalent vaccine was limited;
  - some data on single dose nonvalent vaccines had been provided in confidence, and concerns had been raised on whether a single dose was sufficiently protective for the additional five HPV vaccine types in the vaccine;
  - HPV type lineage variation might impact on the effectiveness of the nonavalent vaccine globally but less so in the UK;
  - it was hypothesised that the ordered, repetitive and dense display of epitopes by the virus like particles (VLPs) in the vaccines was why the vaccines were so highly immunogenic;
  - it was considered that a single dose schedule might present fewer opportunities for girls to receive the vaccine, and therefore widen inequalities in uptake and disease;
  - however, a single dose schedule might improve uptake, creating more capacity for mop-up vaccination;
  - a single dose schedule would likely be more acceptable to the population;
  - there was good evidence to support a move from a three dose to a two-dose schedule for children and adults over the age of 15 years old; and
  - there was good evidence that the time between prime and boost could be extended beyond two years, with a robust booster response seen six to eight years after the first dose.
15. The Committee agreed that there was good evidence to support single dose vaccination schedules for the bivalent and quadrivalent vaccine. Data were now available up to ten years post vaccination. Looking at the antibody kinetics, there were no reasons to expect any sudden drop in antibody levels and associated protection.
16. It was considered likely that one dose of the nonavalent vaccine would be non-inferior in terms of immunogenicity and duration of protection to one dose of the quadrivalent HPV vaccine for the four quadrivalent vaccine types. There were some data to support this, and it was noted that the nonavalent vaccine had more antigen for HPV types 16, 18 and 6 compared with that in the quadrivalent vaccine.
17. The Committee received a presentation from Dr Partha Basu on the latest results from the WHO International Agency for Research on Cancer (IARC) study, which now had 10 years of data. The Committee noted that due to external factors the study had stopped early, which meant that a large number of girls only received a single dose of HPV vaccine.

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18. The girls were not randomised to receive a single dose, but as they had not self-selected for the schedule received, there was less potential for a bias between the populations that received one, two or three doses of the vaccine.
19. The study had been initiated in 2009 to compare two versus three doses in 10-18 year old unvaccinated unmarried girls, with plans to recruit 10,000 girls for each arm of the study across nine sites. When the RCT was halted, over 4000 girls had received a single dose with roughly similar numbers receiving 2 doses (0, 2 months), 2 doses (0, 6 months) and 3 doses (0, 2 and 6 months)
20. Participants became eligible for cervical sample collection for HPV genotyping (Luminex multiplex HPV assay) after reaching age 18 and being married for 18 months. 95% of those eligible (10,000) had provided at least one sample. The study aimed to collect four samples yearly in this group. At the age of 25 women were screened using the hybrid capture 2 HPV test, with those positive undergoing colposcopies. So far 4500 participants had been screened.
21. Age matched controls of unvaccinated married cohorts were introduced and followed with the first cohort (aged 18-23 years) introduced in 2012 and the second in 2017 (aged 25-28 years).
22. Antibody titres to HPV16/18 for the different doses were measured using the Luminex assay, and evidence indicated an inferior response for single dose compared with two or three doses. However, antibody kinetics were similar, with an early increase in titre, followed by a decline and plateau, with antibody levels remaining stable out to 48 months. The more sensitive neutralisation assay (PBNA) showed a similar picture, and stability at 60 months was higher than the mean antibody titre in unvaccinated women.
23. So far almost 3000 women in the single dose group had provided at least one cervical sample and over 2000 had provided at least two samples. This had allowed incident and persistent HPV infection to be assessed. Analysis of the data showed that HPV16/18 incident infection was three times higher in unvaccinated women compared with vaccinated women, and the incidence was the same in the one, two and three doses arms of the study.
24. For persistent infections of HPV 16/18, a high level of protection was observed after 10 years of follow up, and no difference was observed by dose number. Unvaccinated women had a 24 times higher proportion of persistent infection than vaccinated women (2.4% vs 0.1%).
25. Adjusted vaccine efficacy for one dose against incident and persistent HPV 16/18 infections, after exactly 10 years of follow up, was non-inferior for one dose compared to two or three doses, and very high against persistent infection at 92%. The next data cut would be in December 2020.

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26. Cervical screening results to date (using the independent hybrid capture 2 test) indicated a very low incidence of infection, with only one woman in the one dose group positive for HPV16,18 and 45 (0.1%). At this stage in the study the CIN2 and CIN3 detection rate was low in the participants but four cases of CIN 2/3 detected in the unvaccinated group were positive for HPV16/18. No case of HPV 16/18 positive CIN 2/3 was detected in the vaccinated women.
27. On the potential to move from three to two doses in those over 15 years, it was noted that antibody and neutralising antibody titres were noninferior in 15-18 year old girls who received two doses of vaccine compared with girls in the same age range who received three doses. The same strong antibody response was observed for both groups, with non-inferiority for effectiveness in terms of incident infection and persistent infection.
28. The intention was to continue follow-up of participants in the study until at least 2026, to demonstrate durability of protection and antibody persistence over 15 years. By then robust data from 50000 cervical samples would be available.
29. The Committee noted the subcommittee had considered that data on a single dose of quadrivalent and bivalent vaccine strongly indicated persistence of antibody and efficacy over time. For the nonavalent vaccine, there were no data available to show persistence of antibody to the additional 5 HPV types. and it was open to question whether this would be the case.
30. There were no long-term data for the quadrivalent HPV types in the nonavalent vaccine, but there was also no evidence to indicate one dose of the nonavalent vaccine would (or would not) be non-inferior to one dose of the quadrivalent vaccine for the four quadrivalent types.
31. The Committee noted that additional data were expected later in 2020 and in 2021 from ongoing RCTs for single dose schedules, which would provide around two years of immunogenicity data on the nonavalent vaccine. If the trajectory was similar in terms of antibody kinetics, it was considered that there was unlikely to be any biological reason to expect the nonavalent vaccine to have different characteristics of antibody response in the longer term. For the bivalent and quadrivalent vaccines there was already good data up to 10 years post vaccination, which would continue to accumulate.
32. The Committee agreed the evidence strongly indicated that a single dose of quadrivalent vaccine would provide protection over a long period of time, and there was no evidence to indicate this would fade between 10 and 15-years post vaccination.
33. In the context of delivering the HPV programme after the reopening of schools, it was agreed that there should be excellent protection from a single dose, and this should be prioritised on resumption of the programme, where delivery of the programme had been interrupted.

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34. The Committee noted that there was substantial pressure on immunisation services, and prioritisation of the first dose was strongly supported. NHS England agreed this was not a change to the service but noted there were contracting responsibilities to be mindful of. The priority was for those who missed the first dose in the 2019/20 cohort and those in next year's cohort to have at least the first dose.
35. It was suggested, subject to contracting, that providers could plan to deliver the second dose alongside the doses of Men C and Td-IPV which also had to be caught up. These options could be considered by NHSE, PHE and the devolved administrations, to ensure as many as possible were offered at least one dose of the HPV vaccine.
36. The Committee agreed that the data from the main post-hoc trials for the quadrivalent and bivalent vaccines were unlikely to change and that efficacy data from the RCTs would not be available for some time. For the nonavalent vaccine there was the potential to have immunogenicity data later in 2020 or in 2021 to support considerations on this vaccine.
37. The Committee agreed there was enough evidence to support a single dose schedule for the bivalent and quadrivalent vaccines, and it would like to see more data on the nonavalent vaccine, before providing advice on the HPV programme.
38. The Committee agreed that the direction of travel was towards single dose schedules, and the evidence was sufficient to advise prioritisation of the first dose of quadrivalent vaccine in the current context of disruption to the programme due to school closures.
39. The Committee agreed that it should be possible to decide on a single dose nonavalent schedule based on immunogenicity data alone, and there was the potential to conclude their advice on this issue in the next one to two years.

[NB – Following the meeting JCVI developed a statement on delivery of the HPV programme in light of school closures associated with COVID-19 – this is appended at **Annex A**]

### **III. Influenza**

#### Update from last season.

40. The Committee received an update from PHE on the 2019/2020 influenza season.
  - there had been an early start to the season around week 48 of 2019;
  - school acute respiratory outbreaks had occurred at the start of the season and these had been followed by care home outbreaks;
  - RCGP ILI consultation rates in England had reached 'low' levels for eight weeks, a later increase in ILI rates had been linked to COVID-19;

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- influenza levels in 2019/20 were below the levels seen in 2018/19;
- hospitalisations started early, with moderate impact levels, and had peaked at around the same level as in the previous season;
- in 2019/20 most cases of influenza were A/H3N2;
- ICU rates were lower than during the 2018/19 season;
- there was significant excess all-cause mortality in all ages between weeks 51 to 01, an increase in all-cause mortality seen several weeks later had been associated with COVID-19;
- the majority of the influenza A strains that were characterised were A/H3N2, with 79% belonging to the 3C.3a genetic clade, the same clade as the vaccine strain;
- all of the influenza A/H1N1 strains that were genetically characterised belonged to the 6B.1A clade, the same clade as the vaccine strain;
- of the 44 influenza B strains characterised, 43 were in the genetic clade 1A of the B Victoria lineage, the same clade as the vaccine strain;
- vaccine uptake in those aged 65 years and over, and vaccine uptake in healthcare workers was slightly higher than in the last season, but uptake in risk groups and pregnant women was lower;
- there had been a delay in starting the programme, due to the impact of the delay in the WHO decision on vaccines for the 2019/20 season;
- 80% of those 65 years of age and over had received the adjuvanted vaccine, and around 80% of those in risk groups had received QIVe;
- in pre-school children the uptake of LAIV was slightly lower than in the 2018/19 season;
- in school aged children uptake in each year group was the same or higher than in the 2018/19 season;
- children in year 6 (England) were offered immunisation for the first time in the 2019/20 influenza season;
- of the swabs available for the test-negative case control study (TNCC) in primary care, 3510 were controls;
- in the remainder, the viruses identified were: 123 A/H1N1; 744 A/H3N2; 26 A (not known) and 115 were influenza B;
- from October 2019 to April 2020 the overall adjusted vaccine effectiveness (VE) was 42.7% (95% CI - 27.8-54.5) and for the dominant strain, A/H3N2, vaccine effectiveness was 31.2% (95% CI - 10.3-47.2);



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- for the 2-17 years old age group, the vaccine effectiveness breakdown was similar to all other age groups, although vaccine effectiveness was higher for influenza/B;
- in those 18-64 years old age group, the confidence intervals overlapping, although the cell-based vaccines had a higher point estimate for vaccine effectiveness;
- for those 65 years of age and over, the point estimate for QIVc was the highest of the two vaccines used, but the confidence intervals were very wide.

41. The Committee thanked PHE for the update.

#### Flublok® influenza vaccine

42. The Committee noted that Flubok® had been used extensively in the US and was anticipated to receive licensure for use in the UK in late 2020.

43. The Committee noted an update from DHSC on vaccine policy considerations for the 2020/21 season, in light of the COVID-19 pandemic. DHSC officials indicated that consideration was being given to a strengthened influenza vaccination programme, and that they were seeking to procure additional vaccine supply to support this.

44. It was noted that once the availability of additional supply had been confirmed, officials would be informing Ministers and would recommend that a view from JCVI was sought.

45. DHSC officials indicated that in seeking further supplies of influenza vaccine they had considered products that were not currently licenced in the UK, but which may be gaining a licence in time for the 2020/21. The understanding was that the final authorisation for Flublok® was likely to be in November 2020.

46. It was noted that Flublok® was a recombinant vaccine produced in an insect cell line and would potentially avoid issues with vaccines effectiveness associated with 'egg adaptation' with H3 egg-based influenza vaccines.

47. It was noted that for those aged 65 years and over, the priority was currently for adjuvanted vaccine. It was noted that the Committee would usually update its advice on influenza vaccine preference each year. An influenza subcommittee before the October JCVI meeting was suggested.

48. The variability in vaccine effectiveness in successive years was noted, and the Committee cautioned about reacting to low vaccine effectiveness for any one vaccine in any one year.

49. It was noted that a potential Parvovirus B19 vaccine produced in insect cells had been withdrawn because of adverse events.

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50. The Committee noted that it would be possible to consider vaccine advice for 2021/22 by correspondence with sub-committee members. The secretariat would review any new evidence available for this, and form a view with the Chair on taking forward preparation of advice for the 2021/22 season..
51. It was noted that, based on the papers presented to the Committee, the safety of Flublok® in the groups immunised was similar to that of other vaccines.
52. The Committee agreed that Flublok® was suitable for use in the influenza immunisation programme.

#### **IV. Horizon Scanning**

##### Horizon Scanning

53. The Secretariat summarised the horizon scanning exercise and report undertaken for 2020.
54. Between March and May 2020, 128 manufacturers and research institutions were directly approached, and new information was provided on 44 vaccines in clinical development. Although there were more direct contacts, there was a similar response rate compared with 2019, likely due to pressures of the SARS-CoV-2 (COVID-19) pandemic in 2020. It was therefore unlikely that the report covered all vaccines in development which were aiming for licensure in the next five years.
55. The secretariat outlined some key information around clinical trial phases and timelines to licensure for a number of vaccines in development.
56. The Chair noted that due to the SARS-CoV-2 (COVID-19) pandemic it was possible that some clinical trials would be delayed.
57. The Chair also noted a submission from Sanofi Pasteur on their hexavalent vaccine, for which JCVI had previously recommended research into concomitant administration with Bexsero®. This research requirement had been reviewed by the DHSC research funding group, but the research was now underway through funding by Sanofi Pasteur. It was anticipated that results would be delayed due to the SARS-CoV-2 pandemic.
58. The Chair thanked the secretariat.

The Chair of JCVI Prof Andrew Pollard left the meeting at this point

##### COVID-19 Horizon scanning

59. The Committee noted that Prof Wei Shen Lim would Chair this section of the meeting.

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60. The Committee noted that the secretariat had approached developers of SARS-CoV-2 vaccine for information, but had received limited responses. This was likely due to the number of approaches each developer was receiving, as well as alternative approaches by the UK Government. There was a UK Vaccine Taskforce in place with oversight of manufacturing, funding for clinical trials, and fill and finish capabilities.
61. The secretariat then presented on the current SARs-CoV-2 vaccines in development.
62. The Committee noted that SARS-CoV-2 was a Beta coronavirus of lineage B. It encoded a spike protein which would bind to the host cell receptor (ACE-2). The spike protein was a key target for vaccine developers. Other viral proteins were also potential targets, and RNA-based (or nucleic acid-based) vaccines were also in development.
63. Information about the immune response to SARS-CoV-2 was limited, with questions around timing, immunity, longevity of immunity and protective levels of antibody. However, assays available which tested for antibody to the spike or nuclear protein were being used, and suggested a detectable antibody response appearing between 10 and 14 days following symptom onset. Work was ongoing around assessment of functional antibodies and evidence of correlation between spike protein and neutralisation assays.
64. Current data showed detection of IgG or IgM at least 2 months following infection. Most of those with PCR confirmed infection would develop an antibody response.
65. There were around 13 vaccines currently in clinical development globally at phase I, phase II or entering phase III. A substantially larger number of vaccines were in pre-clinical development.
66. Vaccines were being developed on a range of platforms, including non-replicating viral vectors e.g. chimp adenovirus, mRNA, saRNA, inactivated virus, protein subunits, DNA and recombinant proteins. The target antigen was primarily the spike protein, although some groups were developing inactivated virus vaccines or minigene vaccines. Several of these platforms had been used in other developmental products, although none were in widespread use.
67. The different manufacturers were at different stages of development, although the University of Oxford/Astra Zeneca (AZ) collaboration were one of the furthest ahead and currently entering phase III. AZ had announced capacity to deliver doses by September 2020. Other manufacturers expected vaccine to be available late 2020 or through 2021.
68. The UK Government were supporting vaccine manufacturing and development, and PHE had begun planning the delivery of a vaccination programme.

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69. Oxford had recently published pre-clinical results showing partial or complete protection in Rhesus Macaques. Phase I results for the Oxford/AZ vaccine were anticipated in the next few weeks. Moderna had announced limited results in May 2020, noting neutralising antibody production following vaccination. Cansino had also published phase I results showing increased neutralising antibodies following vaccination.
70. There were several outstanding questions including on the safety, immunogenicity and efficacy of any vaccine, especially in older adults, in those with underlying conditions and in children.
71. The Committee noted that there was a risk that efficacy studies would be impacted by reducing levels of SARS-CoV-2 in the general population.
72. The Committee noted that data from pre-clinical studies of the Oxford vaccine did not provide any evidence that the vaccine would prevent infection, although results did indicate it could have an impact on disease severity. The Committee considered that it would be important to have data in older adults. If a vaccine were to additionally prevent infection and onward transmission, then safety data in younger age groups would be important. Modelling and information on the vaccine characteristics would allow the committee to identify groups to vaccinate to maximise health benefits. The Committee agreed that this information should be fed back to developers to ensure optimal trial designs.
73. Issues around vaccine acceptability were raised and it was agreed that continual review of data on vaccine safety would be crucial, and good communications with the public would be important in any programme.
74. The Committee agreed that more detail on groups most at risk would be important to inform development of their advice. PHE outlined that it was important not to overcomplicate the risk groups to ensure programme delivery was efficient and effective and NERVTAG were working on clinical risk factors that could feed into the Committee's discussions.

#### Data on co-administration with influenza vaccine.

75. DHSC noted that they would welcome any views from the Committee on the safety of co-administration of influenza vaccines with SARS-CoV-2 vaccines, and whether a gap between vaccinations would be required.
76. This was considered important if the timelines for influenza and SARS-CoV-2 vaccination programmes overlapped.
77. JCVI agreed that data on the safety and immunogenicity seen with co-administration of SARS-CoV-2 vaccines with influenza and pneumococcal vaccines would be helpful in determining whether the vaccines could be given concomitantly. Such studies would be dependent on timely supply of both vaccines.

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78. The Committee indicated that it would be helpful to be able to review studies involving co-administration with influenza vaccines.

79. It was noted that safety of any new vaccination programme would be under constant review. The MHRA noted that a programme of active surveillance of the safety of SARS-CoV-2 vaccines was planned.

### Conclusions

80. The Committee concluded that it would be important to collect and review all data available on vaccine safety. Concomitant administration with other vaccines, particularly influenza vaccines, should form part of vaccine trial designs.

81. It was noted that some of the SARS-CoV-2 vaccines platforms had been used in the development of vaccines against other diseases. The Committee agreed that they would want to review any available safety data for these vaccines at a future meeting.

82. It was agreed that JCVI would not revise their statement until further evidence was available.

DRAFT

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<b>Prof Andrew Pollard (Chair)</b>
<p>Professor Pollard receives no personal payments from the manufacturers of vaccines</p> <p>He is Director of the Oxford Vaccine Group in the Department of Paediatrics, University of Oxford and has current research funding from the Bill and Melinda Gates Foundation, the National Institute for Health Research, the European Commission, Medical Research Council, Wellcome Trust, Innovate UK, Meningitis Research Foundation, and the Global Alliance for Vaccines and Immunisation. He chairs the scientific advisory group on vaccines for the European Medicines Agency and is a member of WHO's SAGE.</p> <p>Other investigators in the Department conduct research funded by vaccine manufacturers and the Department has received unrestricted educational grant funding for a three-day course on paediatric infectious disease from Gilead, and GSK in June 2019.</p> <p>Professor Pollard is a lead investigator on studies involving the ChAdOx1 SARS-CoV-2 (COVID-19) vaccine. Professor Pollard does not attend any discussions at the Committee regarding SARS-CoV-2 vaccination.</p>
<b>Prof Anthony Harnden (Deputy Chair)</b>
<p>Professor Harnden has no registered conflicts of interest.</p>
<b>Prof Adam Finn</b>
<p>Professor Adam Finn receives no personal payments from the manufacturers of vaccines.</p> <p>Professor Finn undertakes unpaid advisory work for Astellas on a klebsiella-pseudomonas vaccine.</p> <p>Professor Finn's Department receives funding for consultancy work from VBI vaccines on a developmental Hep B vaccine, and Bionet on a developmental pertussis toxin vaccine.</p> <p>The University of Bristol conducts research funded by GSK on meningococcal carriage, by Pfizer on pneumococcal carriage and transmission.</p> <p>Professor Finn is the local Principle Investigator at Bristol for trials of the University of Oxford ChAdOx vaccine.</p>
<b>Prof Matt Keeling</b>
<p>Professor Matt Keeling has no registered conflicts of interest.</p> <p>Professor Matt Keeling is a member of SPI-M and occasionally sits on SAGE</p>
<b>Prof Wei Shen Lim</b>

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<p>Professor Wei Shen Lim's Department has funding from Pfizer for work indirectly related to pneumococcal vaccines.</p> <p>Professor Wei Shen Lim is a member of the New and Emerging Respiratory and Viral Threats Advisory Group (NERVTAG)</p> <p>Prof Wei Shen Lim is a co-investigator of the NIHR-funded (COVID19) RECOVERY Trial.</p>
<b>Prof Jeremy Brown</b>
<p>Professor Brown has received payment for consultancy work from ImmunoBio on a novel pneumococcal vaccine.</p> <p>Professor Brown's Department has undertaken work for Novartis on the effects of monoclonal antibodies on vaccine responses.</p>
<b>Dr Martin Williams</b>
<p>Professor Martin Williams has no registered conflicts of interest.</p> <p>Professor Williams holds a contract for work with Public Health England.</p>
<b>Dr Fiona Van der Klis</b>
<p>Dr Fiona van der Klis has no registered conflicts of interest</p>
<b>Ms Alison Lawrence</b>
<p>Ms Alison Lawrence has no registered conflicts of interest</p>
<b>Prof Maarten Postma</b>
<p>Professor Postma has received honoraria from SPMSD (health economics) MSD (health economics) and is an advisor to companies on Rotateq and Rotarix vaccines.</p> <p>Professor Postma works for the University of Groningen which receives grants from SPMSD and GSK for work related to influenza vaccines.</p> <p>Professor Postma attends advisory boards unrelated to vaccines or vaccine industry</p> <p>Professor Postma organized a conference which was financially supported by Pfizer relating to Health Economics.</p> <p>Professor Postma works for the University of Groningen which has an external PhD student who is employee at Sanofi Pasteur working on a thesis on high dose influenza vaccine.</p>
<b>Prof Robert Read</b>

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<p>Professor Read receives no payments from the manufacturers of vaccines.</p> <p>The University of Southampton receives CASE studentship awards from Novartis and GSK.</p>
<p><b>Prof Anthony Scott</b></p> <p>Professor Scott receives no payments from the manufacturers of vaccines.</p> <p>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 &amp; Melinda Gates Foundation.</p>
<p><b>Dr Maggie Wearmouth</b></p> <p>Dr Wearmouth has no registered conflicts of interest</p>
<p><b>Professor Simon Kroll</b></p> <p>Professor Kroll received research funding from Meningitis Now, to investigate carriage of meningococci and non-pathogenic Neisseria in infants. The funding period ended in 2018.</p> <p>He is the Honorary Medical Director of Meningitis Now</p>
<p><b>Dr Rebecca Cordery</b></p> <p>Dr Cordery has no registered conflicts of interest</p> <p>Dr Cordery works for Public Health England</p>
<p><b>Dr Kevin Brown</b></p> <p>Dr Brown has no registered conflicts of interest</p> <p>Dr Brown works for Public Health England</p>
<p><b>Dr Jillian Johnston (co-opted member)</b></p> <p>Dr Jillian Johnston has no registered conflicts of interest</p>
<p><b>Mrs Anne McGowan (co-opted member)</b></p>



This minute will remain draft until ratified by JCVI at its next meeting  
*The advice of JCVI is made with reference to the UK immunisation programme and may not necessarily transfer to other epidemiological circumstances*

Mrs McGowan receives no payments from the manufacturers of vaccines

Mrs McGowan's employer Public Health Wales develop educational materials with funding from Pfizer, Sanofi Pasteur MSD, Novartis, Astra Zeneca and Wyeth.

**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

DRAFT

## JCVI statement on delivery of the HPV programme in light of school closures associated with COVID-19

### Delivering HPV vaccination during COVID-19

As part of its considerations on the effectiveness of a single dose of HPV vaccine, to advise a potential future move to one dose schedules, the committee discussed the impact of the COVID-19 pandemic on the delivery of the routine HPV vaccination programme to adolescents. The Committee noted that full delivery of the school-based routine programme for 2019/20, was interrupted by the forced closure of schools as part of the lock down measures to control the impact of the COVID-19 pandemic.

JCVI issued a statement on 16 April 2020<sup>1</sup> on the importance of maintaining immunisation services to reduce the risk of vaccine-preventable disease. During this time immunisation services are under pressure to maintain vaccinations and the Committee recognises that resources are stretched. There is the potential for further interruption/delays in delivering the HPV and other immunisation programmes during the COVID-19 pandemic. Delivering the flu programme this Autumn will be a priority.

Taking into account the evidence considered on the immunogenicity and durability of one dose of HPV vaccine, and the impact of the COVID-19 pandemic on immunisation services, the Committee is issuing advice to support planning for the delivery of the routine HPV programme during these challenging times.

The Committee advises that the priority for the delivery of the routine HPV immunisation programme is for all eligible children to receive at least the first dose of the HPV vaccine<sup>†</sup>. This includes prioritising the catch up of those who failed to get the first dose due to school closures. Evidence strongly indicates that one dose of HPV vaccine will provide protection in the short to medium term.

The Committee considers the interval between the first and second dose can be extended by a number of years without compromising protection or the boosting effect of the second dose. Delivery or catch up of the second dose should be considered at the appropriate time, for example alongside the teenage boosters, when circumstances support this according to local planning of immunisation services.

The full outcome of the HPV subcommittee meeting and the June JCVI meeting will be reported in the minutes which will be published on July 15.

### Background

In February JCVI noted evidence on the immunogenicity and efficacy of bivalent and quadrivalent vaccines when offered as a single dose.<sup>2</sup>

The Committee agreed that the data presented, provided compelling evidence that a single dose of vaccine could be sufficient to provide good and long-lasting protection when offered in early adolescence. The Committee agreed that a call for evidence should be issued to ensure all available information was considered by the Committee, before advising on any change to the national immunisation programme. A call for evidence was issued on 18 March 2020<sup>3</sup>, and the JCVI HPV Subcommittee was convened on 21 May to consider the evidence submitted and advise the

<sup>†</sup>The quadrivalent vaccine Gardasil® is currently the only HPV vaccine supplied for the national HPV programme

Committee on whether the evidence was sufficient to advise a move towards a single dose vaccination programme.

The outcome of the HPV Subcommittee's considerations and advice were reported to the main committee on 3 June 2020.

The evidence considered included published and unpublished data on the immunogenicity and efficacy of a single dose of bivalent, quadrivalent<sup>†</sup> and nonavalent HPV vaccine, and the duration of antibody response following vaccination.<sup>4-13</sup> The evidence strongly indicates that one dose of the bivalent or quadrivalent vaccine will provide protection against infection and clinical endpoints for at least 10 years. Evidence regarding the durability of the antibody response to nonavalent vaccine is more limited given that this is a more recent vaccine.<sup>14</sup> The Committee will continue to review the evidence on single dose vaccination, and any advice from the Committee on this will be published separately from this statement.

The Committee also considered evidence on whether the time between prime and boost could be extended beyond two years for a two-dose schedule without compromising individual protection against HPV vaccine type infection and disease. The Committee noted evidence indicating a robust booster effect, up to eight years after the initial dose.<sup>15,16</sup> In November 2019 WHO SAGE issued advice that an alternative schedule with an extended interval of 3-5 years between the first and second dose can be adopted in the context of the global shortage of HPV vaccine.<sup>17</sup>

## References

1. Statement from JCVI on immunisation prioritisation published 16 April 2020 available at: <https://www.gov.uk/government/groups/joint-committee-on-vaccination-and-immunisation>
2. Joint Committee on Vaccination and Immunisation Minutes of the February 2020 meeting. Available at: <https://www.gov.uk/government/groups/joint-committee-on-vaccination-and-immunisation>
3. Single dose of HPV vaccine: call for evidence from the JCVI. Available at: <https://www.gov.uk/government/consultations/single-dose-of-hpv-vaccine-call-for-evidence-from-the-jcvi>
4. Sonawane K, Nyitray AG, Nemutlu GS, et al. Prevalence of Human Papillomavirus Infection by Number of Vaccine Doses Among US Women. *JAMA network open*. 2019;2(12):e1918571.
5. Markowitz LE, Naleway AL, Klein NP, et al. Human Papillomavirus Vaccine Effectiveness Against HPV Infection: Evaluation of One, Two, and Three Doses. *The Journal of infectious diseases*. 2020;221(6):910-918.
6. Brotherton JM, Budd A, Rompotis C, et al. Is one dose of human papillomavirus vaccine as effective as three?: A national cohort analysis. *Papillomavirus research (Amsterdam, Netherlands)*. 2019;8:100177.
7. Rodriguez A M, Zeybek B, Vaughn M et al. Comparison of the Long-Term Impact and Clinical Outcomes of Fewer Doses and Standard Doses of Human Papillomavirus Vaccine in the United States: A Database Study. *Cancer* 2020;126(8):1656-1667. doi: 10.1002/cncr.32700. Epub 2020 Feb 10.
8. Stanley M. HPV vaccines: alternative dosage schedules. *Expert Review of Vaccines*. 2019; 18:12, 1309-1316, DOI: 10.1080/14760584.2019.1704261.

<sup>†</sup>The quadrivalent vaccine Gardasil® is currently the only HPV vaccine supplied for the national HPV programme

9. Markowitz LE, Drolet M, Perez N, et al. Human papillomavirus vaccine effectiveness by number of doses: systematic review of data from national immunization programs. *Vaccine*. 2018;36(s32Pt A):4806–4815.
10. Verdoodt F, Dehlendorff C, Kjaer SK. Dose-related Effectiveness of Quadrivalent Human Papillomavirus Vaccine Against Cervical Intraepithelial Neoplasia: A Danish Nationwide Cohort Study. *Clin Infect Dis*. 2020;70(4):608–14.
11. Whitworth H S, Gallagher K E, Howard N et al. Efficacy and immunogenicity of a single dose of human papillomavirus vaccine compared to no vaccination or standard three and two-dose vaccination regimens: A systematic review of evidence from clinical trials. *Vaccine*. 2020; (38)1302–1314.
12. Kreimer AR, Sampson JN, Porras C, et al. Evaluation of durability of a single-dose of the bivalent HPV vaccine: the CVT Trial. *J Natl Cancer Inst*. 2020 Feb 24. pii: djaa011.doi: 10.1093/jnci/djaa011.
13. Sankaranarayanan R, Joshi S, Muwonge R, et al. Can a single dose of human papillomavirus (HPV) vaccine prevent cervical cancer? Early findings from an Indian study. *Vaccine*. 2018;36(32 Pt A):4783–4791.
14. Sauvageau C, Panicker G, Ungerc E R et al. Priming effect of bivalent and quadrivalent vaccine for HPV 31/33/45/52: an exploratory analysis from two clinical trials. *Human Vaccines & Immunotherapeutics*, 2020;16:3, 590-594, DOI: 10.1080/21645515.2019.1669413.
15. Toh ZQ, Russell FM, Reyburn R, et al. Sustained antibody responses 6 years following 1, 2, or 3 doses of quadrivalent human papillomavirus (HPV) vaccine in adolescent Fijian girls, and subsequent responses to a single dose of bivalent HPV vaccine: a prospective cohort study. *Clin Infect Dis*. 2017;64(7):852–859.
16. Gilca V, Sauvageau C, Panicker G, et al. Antibody persistence after a single dose of quadrivalent HPV vaccine and the effect of a dose of nonavalent vaccine given 3–8 years later - an exploratory study. *Hum Vaccin Immunother*. 2018;1–5.
17. Meeting of the Strategic Advisory Group of Experts on Immunization, October 2019: conclusions and recommendations. *WER* 2019, 94, 541–560.

<sup>†</sup>The quadrivalent vaccine Gardasil® is currently the only HPV vaccine supplied for the national HPV programme