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

JOINT COMMITTEE ON VACCINATION AND IMMUNISATION

Minute of the meeting on 01 February 2017

Skipton House, 80 London Rd, London SE1 6LH

Members

Professor Andrew Pollard (Chair)
Dr Andrew Riordan (Deputy Chair)
Prof Anthony Harnden (Deputy Chair)
Dr Peter Baxter
Prof Judith Breuer
Prof Matt Keeling
Prof Adam Finn
Alison Lawrence
Prof Anthony Scott
Prof Robert Read
Dr Maggie Wearmouth
Dr Fiona van der Klis

Co-opted members

Julie Yates (England)
Dr Lucy Jessop (NI)
Anne McGowan (Wales)
Dr Lorna Willocks (Scotland)

Secretariat

Dr Gayatri Amirthalingam
Andrew Earnshaw
Jonathan Crofts
Catherine Mackenzie
Dr Mary Ramsay

Invited Speakers

Prof. Ray Borrow (PHE)
Dr Claire Cameron (HPS)
Dr Shamez Ladhani (PHE)
Prof Martin Maiden (Oxford)
Richard Pebody (PHE)
Prof. John Watson (DH Deputy CMO)
Dr Caroline Trotter (PHE)
Dr Hannah Christensen

Invited observers from Devolved Administrations

Dr Anne Kilgallen (DHSSNI)
Dr Nicola Steedman (Scottish Government)
Dr Richard Roberts (HPW)
Andrew Riley (Welsh Government)

Other invited observers

Dr Sandra Anglin (NHS England)
Dr Phil Bryan (MHRA)
Dr Suzanne Cotter (Eire)
Dr Linda Diggle (Jersey)
Jacqui Dunn (IoM)
Dr Vanessa Field / Dr Dipti Patel (NathNac)
Dr Darina O'Flanagan (Eire)
Dr Dipti Patel
Dr Michael Edelstein
Pauline MacDonald (NHSE)
Dr Vanessa Saliba (PHE)
Ruth Howlett-Shipley (MoD)
Joanne White (PHE)
Joanne Yarwood (PHE)
Dr Sema Mandel (PHE)
Dr Peter Grove (DH)
Dr Ian Feavers (NIBSC)

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. Any requests for information should be directed to the Secretariat.

2. Apologies had been received from Prof Martin Postma and Dr Peter Elton.

3. Registered conflicts of interest were provided to the Committee and members were given the opportunity to provide updates. An update provided by one member ahead of the meeting was recorded.

4. The Chair informed the Committee that the meeting would be the last one for Dr Peter Baxter, whose final term on the Committee would end in March 2017. The Chair thanked Dr Baxter for all his work on the JCVI, and for his Chairing of the Travel sub-committee.

I. Minute of the June 2016 meeting

5. The Committee agreed the minute of the October 2016 meeting was an accurate reflection of the discussion and the minute was approved without change.

II. Matters arising

Actions from the last meeting

6. The Committee noted that:
    - more information on the concomitant use of Vaxelis® and Bexsero® would be provided when it became available;
    - the secretariat were looking to the option of setting up a nosocomial working group or sub-committee later in 2017;
    - a report on the latest evidence on BCG vaccination would be provided at a later meeting of the Committee;
    - the secretariat has held two teleconferences to further discuss options on introducing more formal consideration of research gaps identified by the Committee, and a written process should available for the June 2017 meeting;
    - information on coverage of routine vaccinations in secondary schools had been requested from the relevant contributors, and would be discussed under item 10;

- a presentation on the cost-effectiveness of continuation of the MenACWY adolescent programme, and full results of the baseline meningococcal carriage study (UKMenCar4) would be provided under item 4.
- data on immunogenicity of the proposed HepB schedule for children born to hepatitis B positive mothers, and on the need for a 12 month booster dose would be provided when available
- PHE was working to identify a suitable cohort of healthcare workers in whom pertussis vaccination should be a priority, and was considering the issuance of guidance on the vaccination of healthcare workers;

7. The Chair noted that following an update on the UKMenCar4 study at the October 2017 meeting, he had written to the Department of Health regarding the planned meningococcal carriage study. The letter had been circulated to and approved by members prior to being sent. The letter advised the Department that the meningococcal carriage study should proceed as currently defined. This position had been reached following consideration of additional information from those involved in the UKMenCar4 study, by the Chair and the Chair of the Meningococcal sub-committee. The Committee noted that they would receive the latest analyses from the UKMenCar4 study under item 4.

National Vaccine Evaluation Consortium

8. The Chair asked the Department of Health to provide the Committee with an update on plans regarding the future of the National Vaccine Evaluation Consortium (NVEC), which would be replaced by a newly formed group in 2018. The Department advised that they wished for representation from JCVI and PHE in an oversight group which would be setting the overall direction of NVEC, and its successor group. It was currently planned that NVEC would continue until August 2018, following an extension from the originally planned end-date of August 2017. There would be an overlap between the successor group and NVEC, as it was anticipated this new group would be formed later in 2017.

CEMIPP

9. The Chair asked the Department of Health for an update on progress in consideration of the report from the Cost Effectiveness Methodology for Immunisation Programmes and Procurements (CEMIPP) group. The Department of Health advised that the report was under consideration by the Department of Health Appraisal Alignment Working Group (AAWG), and that the report would not be published until it had been fully considered by the AAWG and Ministers. No decision had yet been made on whether a consultation would be undertaken following publication.

10. The Committee noted the update and commented that it was important to ensure that groups involved in the work of CEMIPP, including charities, were kept aware of developments. Members commented that uncertainty about future methodology led to a wider range of scenarios being modelled than would otherwise be required, and this was time consuming for those involved.

Horizon Scanning

11. The Committee noted that the annual horizon scanning exercise was to begin shortly, with a report to be provided at the June 2017 meeting. Members were asked to provide thoughts on particular areas of interest, beyond those vaccines already known to be in late stage development. The Committee advised that information on the following issues would be of particular interest:

    - alternative methods of vaccine delivery;
    - malaria vaccines;
    - vaccines targeted at adults and older age groups;
    - vaccines targeted at nosocomial infections;
    - influenza vaccines manufactured without the use of eggs;
    - respiratory syncytial virus vaccines (RSV);
    - new pneumococcal vaccines (particularly higher valency conjugate or protein vaccines);
    - group B streptococcus (GBS) vaccines; and
    - hepatitis C vaccines.

III. Pneumococcal epidemiology

The Committee received a presentation from PHE on the epidemiology of invasive pneumococcal disease (IPD) in England and Wales. The Committee noted that:

- PPV23 had been introduced in 1983 for all individuals at increased risk of IPD ≥ 2 years of age;
- PCV7 for children < 2 years of age at increased risk of IPD was introduced in 2002;
- PPV23 for those ≥ 80 years of age had been introduced in England and Wales in 2003, for those ≥ 75 years of age in 2004, and for those ≥ 65 years of age in 2005;
- PCV7 was added to the routine childhood immunisation programme in 2006 as a 2+1 schedule for all children < 2 years with catch-up to 2 years of age;
- PCV13 replaced PCV7 in 2010, with no catch-up
- the PCV programme continued to have a large impact on overall IPD, especially in children;

- IPD due to PCV13 serotypes had possibly plateaued over the last two years, at a low incidence, but above zero;
- since 2013/14 serotype replacement disease had increased, particularly for serotypes 8 and 12F, with replacement disease mainly being seen in adults;
- serotype 8 was currently responsible for >20% of all IPD, especially in older adults;
- the case fatality rate had declined since the introduction of PCV13, potentially indicating that the replacement serotypes were causing less serious disease, although more analysis was required on this.

12. The Committee expressed concerns about the recent increases in replacement serotype IPD. The Committee considered that there was a significant need for new pneumococcal vaccines, including vaccines targeted at the elderly which protected against serotypes not included in PCV13. The Committee further commented that a move to PCV10 vaccine would potentially lead to a rise in disease associated with serotypes 19A and 3, as disease associated with these serotypes was still being seen in unvaccinated groups and in other countries. It was also noted that the serotypes covered by PCV13 which were not covered by PCV10, typically had a higher case fatality rate that those included only in PCV10.

13. The Committee noted that additional data would be ready by the Autumn, and asked for an update on pneumococcal epidemiology at the October 2017 meeting.

IV. Adolescent MenACWY impact and cost-effectiveness modelling and carriage study update

14. In October 2014, the Committee had agreed that replacement of MenC monovalent vaccine with quadrivalent MenACWY vaccine in the adolescent and fresher programmes was likely to be beneficial in controlling IMD, especially MenW disease. In the absence of cost-effectiveness analysis, the Committee had advised the use of the quadrivalent vaccine if this could be procured at a comparable price to the monovalent vaccine.

15. In February 2015 JCVI concluded that a continuing rise in cases of MenW across the population was a cause for significant concern. The Committee had considered that levels of disease were consistent with an outbreak situation, with cases and deaths occurring in all age ranges, and constituted a public health emergency. JCVI advised at that time a programme to replace the MenC for adolescents, and undertake a catch-up to those aged 14-18 years, with MenACWY conjugate vaccine should be undertaken as soon as practicable, in order to generate herd protection against MenW for the rest of the population, including infants.

16. PHE provided an update on the latest meningococcal epidemiology in England.

The Committee noted that:

- a new strain of MenW (Clonal complex 11) emerged in the UK in 2009, having originated in South America;
- the number of cases of invasive meningococcal disease caused by the strain increased rapidly from 2009/10 to 2014/15;
- a new "sub-lineage" (2013 strain), which evolved from the original with variations in ~20 genes, was now driving a rapid expansion in case numbers from 2012/13 to 2015/16;
- unlike the earlier strain, the 2013 strain had spread quickly across Europe and Australia resulting in up to 5 fold increases in case numbers;
- the sub-lineage appeared to be associated with an atypical gastro-intestinal presentation, and had a relatively high case-fatality rate;
- in the 2015/16 school year; routine adolescent MenC was replaced with quadrivalent ACWY;
- this was accompanied by a catch up for all children aged 14-18 years of age and university entrants;
- as of 2016, uptake was above 70% in the routine school-delivered cohort and around 35% for the GP-delivered catch up cohorts (school leavers);
- it was noted that coverage in school leavers varied depending on university attendance – with higher coverage being seen in those going on to university;
- following introduction of the programme, overall MenW cases were continuing to increase although they are no longer doubling annually;
- in the past year, 15-19 year olds (i.e. the age group targeted by vaccination) were the only age group in whom there had been a decline in case numbers. 6 cases of MenW were identified in 17-18 year olds in 2016, all of whom were unvaccinated individuals and 5 of whom were not attending university;
- this represented a 68% reduction when compared to projected cases, despite low vaccine uptake;
- MenW cases in infants had also stopped increasing, and it was considered possible that cross-protection from MenB vaccination may be a contributory factor.

17. The Committee thanked PHE for the presentation. The Committee noted similar epidemiological patterns of MenW in other parts of Europe. In Scotland MenW in the 15-24 year age group had decreased markedly in 2016, following completion of a catch-up campaign with high uptake. This was despite continued increases

in <5 and >25 year age groups, leading to an overall increase in MenW disease (14%). In the Netherlands, which did not have a MenW vaccination programme, incidence had reached 0.4 cases per 100,000. The 15-24 and 65+ age groups had been particularly affected, with cases increasing by around 20% and 40% respectively on last year.

18. The Committee concluded that the evidence indicated the adolescent MenACWY vaccination programme was having an impact on MenW cases in young adults. However, the MenW outbreak was ongoing and large case numbers and geographical spread alongside atypical presentation and a high case-fatality ratio remained concerning.

Meningococcal ACWY cost-effectiveness

19. Modelling had been undertaken to assess the impact and cost-effectiveness of continuing the routine MenACWY vaccination.

20. Dr Hannah Christensen, an infectious disease modeller from the University of Bristol, gave a presentation on the impact and cost-effectiveness of continued MenACWY vaccination in England. The Committee noted that:

- the modelling approach considered routine teenage ACWY vaccination as an 'insurance policy' against all future outbreaks;
- it adapted a previous model of MenB to consider a single dose of MenACWY vaccination at 14 years of age, incrementally on a MenC-only programme;
- the model assumed that no increase would be seen in MenC, due to the presence of either MenC or MenACWY vaccination;
- a stop-and-start programme was not considered due to the major operational challenges associated with this;
- the model started from a point of low incidence and assumed that all future MenA, W or Y outbreaks would be averted;
- cases between outbreaks were assumed to be about around 84 per year (based on AWY average lab cases from 2005 – 2012), with a case-fatality of 11.6% (based on MenW case-fatality in England and Wales 2010/11 – 202/13) and a utility loss of 0.282 (based on MenC modelling, with no adjustment factor);
- the frequency of outbreaks was taken as starting every 10 years (5-15 range), with a peak size of 1000 cases annually (500 – 1500 range) and a duration of 20 years (5-30 range). Due to the unpredictability of meningococcal disease, this was based on expert consensus from the PHE Vaccine Preventable Invasive Bacterial Disease Forum (February 2016);

- the model considered vaccination over a hypothetical 100 years with 3.5% discounting and a £20k per QALY threshold, or 1.5% discounting and a £15k/QALY threshold as a sensitivity analysis;
- if vaccination with an uptake of 70% could prevent all outbreaks it could be cost-effective at prices higher than the list prices for MenACWY vaccine, marginal on the price of the pre-existing MenC programme and assuming a £20,000 per QALY threshold and 3.5% discounting;
- if higher uptake was needed to avert all the outbreaks the cost would need to be lower;
- changing the QALY threshold and discounting rate did not have a large effect on vaccine price;
- including network QALYs (QALY losses by friends and family) would improve the cost-effectiveness;
- sensitivity analyses were conducted around different outbreak scenarios, including, the most conservative scenario (outbreaks every 15 years, 5 years duration, peak of 500 cases) and the most vaccine-favourable scenario (outbreaks every 5 years, 30 years duration, peak of 1500 cases);
- the sensitivity analyses gave a range of positive prices both above and below the list price for MenACWY vaccines, although it was noted that the price of MenC vaccine would need to be deducted from the list price to obtain the incremental price of MenAWY vaccination;
- delaying the start of the first outbreak by 25 years reduced the marginal vaccine price in the base case to one close to the list price of MenACWY vaccines, once the cost of MenC vaccine was taken into account;

21. The Committee noted that the model assumed a low starting incidence (i.e. that the initial MenACWY programme had already controlled the current outbreak), but this would not be the current situation, as numbers of MenW were still increasing each year. To assess the potential impact of an initial four year programme in 14 year olds (with catch up to 17), the original MenB transmission dynamic model was also adapted to consider MenW disease only. This model assumed a steady state incidence, based on data from 2014/15, vaccine effectiveness of 95% against disease, 60% vaccine effectiveness against carriage and duration of immunity of ten years. The results suggested that if the programme was stopped at the end of the catch-up, then disease rates would return to outbreak levels, but the exact timing of this was dependent on the exact rate of carriage.

22. Overall, the modelling indicated that continued MenACWY vaccination was highly likely to be cost-effective, although the vaccine price was sensitive to the assumed pattern of future outbreaks. In addition, withdrawing MenACWY prematurely, whilst incidence was still increasing, may lead to resurgence of the

current outbreak.

23. The Committee thanked Dr Christensen for her work, and further discussed its assumptions.

24. It was noted that the model assumed that vaccination would prevent all outbreaks, which meant that no duration of protection was needed. The duration of protection was likely to be at least 10 years, which was thought by the Committee to be sufficient to prevent all outbreaks.

25. It was noted that the utility loss was assumed to be 0.282, based on previous work on MenC disease. The Committee heard that this was based on a study using EQ-5D questionnaires in teenagers suffering from ST11 strains of MenC. As EQ-5D was not thought to underestimate QALY loss in teenagers, and this was the age group which bore the largest burden of disease, the Committee concluded that the current assumptions were reasonable and that no adjustment factor was needed.

26. Network QALYs were welcomed as a sensitivity analysis but it was agreed that they should not be included in the base case.

27. The Committee discussed the most likely epidemiological scenarios in the absence of vaccination. It was noted that meningococcal disease was difficult to predict. Strain-typed data were available for the past 20 years, however these data were not ideal as public health interventions would have modified the scale of outbreaks. Based on their experience, and accounting for the effects of public health interventions, the Committee felt that the base case of outbreaks every 10 years, 20 years duration, peak of 1000 cases was reasonable. However, the committee agreed that most conservative scenario (Outbreaks every 15 years, 5 years duration, peak of 500 cases) was too conservative. It was noted that it could be helpful to present information as the number of discounted cases prevented.

28. The Committee noted that every scenario explored for a permanent MenACWY programme had a positive vaccine price, and that the prices seemed in most cases to be realistic for use in procurement, given the list prices of the vaccines. It was noted that any advice would need to be reviewed if further evidence became available, including information about cross-protection from MenB vaccination.

Conclusion

29. The Committee considered evidence on the epidemiology of invasive meningococcal disease in England, and modelling on the impact and cost-effectiveness of continuing the MenACWY programme. MenW rates had continued to increase in the UK in 2016, and the strain was associated with an atypical gastrointestinal presentation that was difficult to diagnose and had a relatively high case-fatality rate.

30. A reduction in disease in 17 and 18 years olds following introduction of the MenACWY programme indicated direct protection, however the continuing rise in cases outside of the vaccinated cohorts indicated that population level protection had yet to be achieved. Continuing increases in MenW rates highlighted the need for continuation of the MenACWY programme as part of outbreak control measures.

31. Cost-effectiveness modelling indicated that continuing the MenACWY programme in the long term was likely to be highly cost-effective. The base case scenario was considered by the Committee to be well parameterised, and produced an incremental price above the list price for MenACWY vaccines. All other scenarios, forming a series of sensitivity analyses, indicated positive vaccine prices under the usual Departmental rules for setting the cost effective vaccine price.

32. In response to a request from officials, the Committee agreed that the most conservative uncertainty scenario was a particularly pessimistic view of the impact of the vaccine, and other less conservative sensitivity analyses were more appropriate for use as a sensitivity test on the base case scenario in the Department's determination of a cost effective price.

33. The Committee agreed that, given the evidence provided, ending the programme was highly likely to result in resurgence of MenW disease, and it would not be appropriate to move to a monovalent MenC vaccine at any point in the future. The Committee therefore advised that MenACWY vaccination should no longer be considered a temporary programme and should become part of the routine adolescent vaccination programme.

Characterisation of meningococcal carriage isolates from the UKMenCar4 Study

34. The Committee received a presentation from Professor Martin Maiden on the UKMenCar4 study. The Committee noted that:

- the data were considered preliminary and detailed information was not to be disseminated further until after publication;
- the fourth UK meningococcal carriage survey was conducted by the meningococcal carriage group from September 2014 to March 2015;
- the UKMenCar4 survey was undertaken to investigate the population of carried meningococci at a time of relatively low incidence of invasive meningococcal disease, compared to the rates of disease that occurred from the early 1980s to the early 2000s;
- the UKMenCar4 survey was undertaken at a time of increasing serogroup W meningococcal disease;
- the work aimed to establish the rates of carriage of meningococci; the prevalence and expression of different serogroups; the prevalence of

variants of the Bexsero® antigens and likely immunological cross-reactivity; and the meningococcal genotypes present and their prevalence;
- data collection and analyses were complete for over 1000 isolates from around 20,000 individuals;
- carriage rates were substantially lower in the UKMenCar4 study, compared to earlier UKMenCar surveys, which was consistent with changes in disease epidemiology since the introduction of MenC vaccines in 1999;
- serogroup B carriage was considerably lower than previously , and the carriage of serogroup W has substantially increased.

35. The Committee thanked Prof Maiden for the presentation. The Committee agreed that the information provided gave them greater confidence in the sample size for the planned meningococcal carriage study to assess the impact of Bexsero® vaccination on meningococcal carriage.

V. Vaccine-associated suspected adverse reactions reported via the yellow card scheme during 2016

36. The Committee noted a written report from the MHRA and a verbal update from an MHRA representative. The Committee noted the update on UK suspected adverse reactions (ADRs) associated with routine and/or commonly used vaccines reported to the MHRA via the Yellow Card Scheme during the time period of 1 January 2016 to 31 October 2016. The MHRA reminded the Committee that a report of a suspected ADR to the MHRA does not necessarily mean that it has been caused by the vaccine, as many factors have to be taken into account in assessing the relationship between a vaccine and suspected reaction such as the possible role of underlying or undiagnosed illness. The Committee noted that overall the MHRA had not identified any significant new safety issues in the period under consideration.

37. The Committee noted an additional report summarising the UK safety experience following introduction of Bexsero® into the UK vaccination programme. The report was based on evaluation of Yellow Card reports received up to November 2016 and an ad hoc analysis of data from the Clinical Practice Research Datalink (CPRD) undertaken by MHRA.

38. The Committee noted that, as with any major new vaccine programme, the MHRA had in place a proactive pharmacovigilance strategy to monitor the safety of Bexsero in near real-time. The strategy focused on continuous evaluation of several pre-specified ‘outcomes of interest’, as well as routine detection of any new and unexpected safety concerns.

39. The overall reporting rate of suspected ADRs to Bexsero was around half of what would typically be expected based on experience with other major new vaccines during the first year of introduction in the UK. Available safety data following

immunisation of around a million children aged five years and under across the UK indicated that the safety profile of Bexsero was broadly as expected, and no serious new safety signals had been identified to date.

40. The Committee noted a report from Health Protection Scotland (HPS) on hospital admissions for fever in infants aged less than one year potentially associated with Bexsero®. The Committee noted that there was an increased risk of fever when Bexsero® was given concomitantly with other childhood vaccines in infancy, and that they had advised the use of prophylactic paracetamol in such instances.

41. The report indicated a lack of evidence regarding adherence to the recommendation for use of prophylactic paracetamol, and suggested that given the very young age of the infants at the time of the first vaccination, there may be some reluctance to give paracetamol before a fever is actually evident, which would reduce the effectiveness of this intervention. The Committee agreed with the findings of the report that further understanding on the current use of prophylactic paracetamol is needed and that communication to parents and health professionals may need re-examined to reinforce guidance.

42. The Committee thanked the MHRA and HPS for their reports, and continued to be reassured regarding the safety of vaccines used in the UK.

VI. Influenza –interim data from the 2016/17 season

43. The committee received an overview of the current influenza season so far and noted that:

- the 2016/17 influenza season, which started before Christmas, had been dominated by influenza A(H3N2) with the highest number of cases and rates in the elderly population with numerous outbreaks reported in care homes and hospital settings;
- genetic characterisation of the circulating A(H3N2) virus so far showed a good match with the vaccine strain though fewer isolates had been antigenically typed;
- in England, children aged 2 to 4 years old and school years 1, 2 and 3 had been included in the childhood flu campaign in 2016/17 as well as some regional pilots which vaccinated children in school years 4-6;
- vaccine uptake had been good overall compared with last year with a higher uptake seen in healthcare workers and children and similar uptake in the elderly;
- preliminary mid-season vaccine effectiveness (VE) results indicated good protection in children aged 2-17 years old (who mostly receive the live attenuated influenza vaccine (LAIV)) with a high VE point estimate, but a

much lower VE point estimate for the elderly (who receive inactivated influenza vaccine);

- Finland, which also used LAIV for children in some areas (together with IIV), was publishing regular mid-season VE estimates, with the latest showing higher influenza VE in children 44.9% (32.0% -55.3%) compared with the elderly 22.4% (18.6% -26.0%);
- the Advisory Committee on Immunization Practices (ACIP) had decided not to recommend the use of LAIV in the US this season owing to low VE results in children there last year and in some previous seasons;
- the manufacturer of LAIV were to present their latest findings to the Advisory Committee on Immunization Practices (ACIP) at the end of the month, and that based on the evidence so far, the most plausible hypothesis for low VE seen in the US in 2015/16 (and in several other settings compared to IIV) was that the A(H1N1) Bolivia attenuated strain in LAIV had reduced replicative fitness;
- the UK, which is continuing to use LAIV in its childhood programme would also be presenting the interim 2016/17 VE estimates at the ACIP meeting;
- in the absence of any use of LAIV in the US programme, ACIP were now looking to those countries using LAIV to help inform their assessments and advice concerning the future use of this vaccine;
- CIP would like evidence of an improved VE against A(H1N1pdm09 and it looked likely that WHO would recommend the A(H1N1)pdm09 vaccine strain changes for the Northern Hemisphere flu vaccine composition next season;
- this would entail the manufacturer using a new H1N1 strain in LAIV, and they had been looking at potential candidates that show improved replicative fitness compared to the A/Bolivia (H1N1)pdm09 strain;
- in the UK various studies were planned or ongoing to look at LAIV effectiveness and performance in light of the low effectiveness observed in the US;
- these included the test negative case control influenza VE surveillance work; electronic primary care cohorts in England and Scotland to look at prior vaccination history; protection against severe disease endpoints and clinical studies in collaboration with Imperial college to look at LAIV shedding and immunogenicity;
- PHE also recently published a paper showing evidence of LAIV effectiveness against hospitalized lab confirmed infection during 2015/16 in England;

- using electronic record linkage Health Protection Scotland has also shown LAIV was significantly more effective in protecting against lab confirmed hospitalization than IIV over the last two influenza seasons.

44. The Committee noted that overall ILI rates according to MEM thresholds so far appeared to be lower again in Scotland and Northern Ireland (who have higher coverage and a full roll out of the childhood programme in primary school) compared with England and Wales (where the programme has not yet been fully rolled out in primary school age). Moreover, so far the whole of the UK appeared to have experienced a milder flu season than that seen on continental Europe. The Committee speculated that these ecological observations might be due to the overall effect of the childhood programme reducing transmission in the UK.

Conclusion

45. The Committee agreed that the mid-season estimates from the childhood programme were very encouraging and that there was currently no cause for concern on the effectiveness or safety of the LAIV.

46. The Committee was pleased to continue to support the programme and suggested no changes to the programme for the coming season other than that it would like to see higher coverage achieved in children in England.

47. The Committee would continue to monitor the programme closely and would be looking to see the outcome of the manufacturers work to improve the H1N1 component in the LAIV depending on what strain is selected by WHO for the Northern Hemisphere.

VII. HPV sub-committee update

48. The committee received an update from the Chair of the HPV Subcommittee which met on January 18 mainly to consider the issue of the impact and cost effectiveness of extending vaccination to adolescent boys.

49. Prof Marc Brisson of Laval University Quebec presented a meta-analysis of 16 published HPV models which showed that:
    - in the context of high coverage in girls (80%) there is very little additional benefit to be had by vaccinating boys;
    - using the same number of doses for achieving 80% coverage in girls only, would have more impact than using the same number of doses to achieve 40% coverage in girls and boys;
    - vaccinating boys would only give substantial impact when coverage in girls is very low;
    - the advantages in vaccinating boys were that you get a more rapid impact and there is the possibility of achieving eradication, though this also depended on the heterogeneity of sexual behaviour in the population.

50. The findings of the Warwick University model, which were to be published, also showed that extending the programme to vaccinate boys was highly unlikely to be cost effective under the rules of 3.5 % discounting and £20,000 per QALY.

51. The individual based model developed by PHE had been designed in order to deal with a range of issues and questions on immunisation and screening over the next few years. The latest results from PHE model, however, were insufficiently robust to provide additional evidence on whether or not extending vaccination to boys could be cost-effective, as more work was required to generate more robust and precise estimates.

52. The Subcommittee had requested that PHE concentrate on the necessary work to indicate with a higher degree of certainty whether it would be cost-effective or not to extend vaccination to adolescent boys in the context of high coverage in girls, as consistently achieved in UK.

53. Overall the HPV Subcommittee had concluded that the evidence, so far considered, consistently indicated that a programme to vaccinate adolescent boys was unlikely to be cost-effective when coverage in adolescent girls was high.

54. The Committee agreed with the Subcommittee that it would wait to review the results of the PHE model before concluding its advice to the question of whether to recommend extending vaccination to adolescent boys. PHE estimated that the necessary work would take approximately 4 months and the results could be presented to the HPV Subcommittee in early June and the outcome of this reported at the June JCVI meeting.

55. The Committee also agreed that the Warwick University model should undergo independent peer review to meet the standards of JCVI scrutiny and the results of this would also be reported in June.

VIII. Travel sub-committee update

56. The committee received an update from the Chair of the Travel Subcommittee which met on November 23.

<u>Japanese encephalitis</u>

57. Changes had been proposed to the Green Book chapter on Japanese Encephalitis recommending a booster dose10 years after the initial booster dose at 12-24 months for adults aged 18-65 years old who were considered at continued risk.

58. When a primary course plus initial booster was interrupted, the schedule should be resumed (and not restarted), regardless of the delay. A rapid schedule at days 0 and 7 could be considered off-license for children aged 12-18 or adults aged over 65 years of age when there is not sufficient time to give the standard schedule.

59. The Committee also considered that the rapid schedule could also be considered for children less than 12 years, despite there being no data, as 2 doses would be better than one if there was insufficient time for the normal schedule before travel. The Committee agreed there was a need for immunogenicity data on the rapid schedule in young children (JCVI research recommendation).

Influenza

60. The Subcommittee had revisited the issue of influenza vaccination and the Haj in relation to the timing of the Haj which changes year to year, and the availability of the northern or southern hemisphere vaccine for at risk Haj travellers. The sub-committee had concluded that there was very little that could be done regarding vaccine availability other than to ensure and reinforce the message that Haj travellers in risk groups receive the flu vaccine every year as part of the routine influenza programme.

Meningococcal disease

61. The subcommittee had discussed the use of the MenC vaccine for travellers to areas where there were not the benefits of herd protection from an established MenC adolescent programme. The Subcommittee concluded that the best vaccine for travellers would be the MenACWY conjugate vaccine when there was a clear risk i.e. for those travelling to the meningitis belt in Africa or when there were specific outbreaks of meningococcal disease in a particular country.

62. The Subcommittee had noted there was little data on persistence of immunity following MenACWY conjugate vaccination and requested that the Meningococcal subcommittee consider the issue of duration of protection of the MenACWY vaccine and the need for revaccination after 5 years for travellers to at risk areas.

    Action: data on immunogenicity and persistence to be reviewed by meningococcal subcommittee Chair.

63. The sub-committee also considered that it would be important to raise awareness and check vaccination status for at risk groups travelling outside the UK to mass gatherings.

Pneumococcal conjugate vaccine

64. A discussion on the use of PCV13 for those travellers over 65 years of age going to countries where there were not the benefits of herd protection from an established infant programme was deferred.

65. The Committee noted that a new Chair for the Travel sub-committee would need to be identified once the current Chair left the Committee.

IX. Varicella sub-committee update

66. The Committee noted that in 2010 they had not recommended a universal

childhood varicella vaccination programme, as cost-effectiveness modelling indicated that it would not be cost-effective in the recommended two dose schedule. In December 2016 the Varicella subcommittee met to consider evidence on the cost-effectiveness of a one dose childhood varicella vaccination programme. The rationale for considering a one dose strategy was that whilst it was likely to be effective in preventing severe varicella, it would not interrupt transmission and therefore have less of a detrimental impact on immunological boosting ("exogenous boosting") against herpes zoster disease (shingles).

67. The Chair of the Varicella sub-committee summarised its findings. The Committee noted that:
    - published research on exogenous boosting was reviewed, with data from clinical trials of live zoster vaccine supported the exogenous boosting hypothesis;
    - observational data was mixed as to the extent of any effect, with notable limitations in the data;
    - the sub-committee concluded that the evidence generally supported the hypothesis that varicella vaccination was likely to have an effect on exogenous boosting and therefore could potentially have an effect on zoster rates;
    - data on the extent of that effect was however limited, and was unlikely to become available in the short term;
    - the Australian single dose programme (one dose at 18 months since 2005; catch up for 12-13 year olds) had resulted in a substantial reduction in varicella related consultations, hospitalisations and deaths;
    - there were reports of school outbreaks which could have been due to unvaccinated individuals or breakthrough disease, and a slightly lower than expected vaccine efficacy;
    - two transmission dynamic models were used to investigate the cost-effectiveness of a one dose strategy, incrementally on the existing zoster vaccination programme in the UK;
    - although reducing the number of vaccines given halved the costs, both models predicted that a one dose varicella vaccination strategy was unlikely to be cost-effective;
    - a review of the parameters of the models identified two particular areas where uncertainties could be reduced and which may influence cost-effectiveness outcomes - the probability of boosting given an exposure to varicella and estimates QALY losses associates with disease;
    - further work was planned to reduce these uncertainties, however due to the complexity this was unlikely to become available for some time;

- initial discussion had been made around potential scheduling for a single dose vaccine highlighted issues with available scheduling options; in particular there were concerns that the lowest cost option of a combined MMRV vaccine at 12 months could have a negative impact on MMR coverage.

68. The Committee discussed the balance between avoiding potential zoster increases and managing varicella disease burden. It agreed that a practical approach should be taken to further work on exogenous boosting to ensure that a decision could be made on a varicella vaccination programme. The Committee noted views from members regarding the burden of varicella disease in those with very severe disease or sequelae, and the need to carefully balance definitive evidence on the benefit of vaccination, against the potential for harm in a distinct population.

X. Coverage

69. The Committee received updates on vaccine coverage in England and the Devolved Administrations from representatives from the relevant public health agencies. The Committee noted the information provided.

XI. AOB

70. The Committee noted information on recent outbreaks of hepatitis A disease in men who have sex with men. The Committee firmly supported the response to the outbreaks, noting that any larger programme would need to consider issues associated with funding and the availability of hepatitis A vaccines.

Prof Andrew Pollard (Chair)
Professor Pollard receives no personal payments from the manufacturers of vaccines A study funded by Okairos, initiated prior to his appointment to JCVI, was completed during 2016 He is Director of the Oxford Vaccine Group in the Department of Paediatrics and has current research funding from the Wellcome Trust, The Bill and Melinda Gates Foundation, The Medical Research Council, the World Health Organisation, the National Institute for Health Research, the European Commission, Innovate UK, 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. Other investigators in the Department conduct research funded by vaccine manufacturers and the Department has received unrestricted educational grant funding from Pfizer, GSK and Astra Zeneca for a 3 day course on infection and immunity in children in 2016.
Prof Anthony Harnden (Deputy Chair)
Professor Harnden has no registered conflicts of interest.
Dr Andrew Riordan (Deputy Chair)
Dr Riordan has no registered conflicts of interest.
Dr Peter Baxter
Dr Peter Baxter has no registered conflicts of interest
Prof Judith Breuer
Professor Breuer has no registered conflicts of interest
Dr Peter Elton
Dr Peter Elton has no registered conflicts of interest
Prof Adam Finn
Professor Adam Finn receives no personal payments from the manufacturers of vaccines. The University of Bristol conducts research funded by GSK on meningococcal carriage.
Prof Matt Keeling
Professor Matt Keeling has no registered conflicts of interest.

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
Mrs Anne McGowan
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.
Prof Maarten Postma
Professor Postma has received honoraria from GSK (MenB vaccine), Novartis (non-vaccine), Pfizer (scientific advisory board), AbbVie (non-vaccine). Professor Postma works for the University of Groningen which receives grants from Astrazeneca, Sanofi Pasteur MSD and GSK for work related to influenza vaccines. The University also receives funding from Pfizer and AbbVie for work unrelated to vaccines.
Prof Robert Read
Professor Read receives no payments from the manufacturers of vaccines. The University of Southampton receives CASE studentship awards from Novartis and GSK.
Prof Anthony Scott
Professor Scott receives no payments from the manufacturers of vaccines. Professor Scott is Director of the Vaccine Centre and the Director of the Health Protection Research Unit at the London school of Hygiene and Tropical Medicine, which receives funding from PATH for research into whole cell pneumococcal vaccines. Professor Scott is also a scientific advisor to PATH on whole cell pneumococcal vaccination
Dr Maggie Wearmouth
Dr Wearmouth has no registered conflicts of interest
Dr Lucy Jessop (co-opted member)
Dr Lucy Jessop 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