JOINT COMMITTEE ON VACCINATION AND IMMUNISATION

Minute of the meeting on 07 June 2017

Coin Street Neighbourhood Centre, Stamford Street, London

Members

Professor Andrew Pollard (Chair)
Dr Andrew Riordan (Deputy Chair)
Prof Judith Breuer
Prof Matt Keeling
Dr Fiona van der Klis
Prof Adam Finn
Prof Anthony Scott
Dr Maggie Wearmouth
Prof Maarten Postma
Dr Peter Elton

Co-opted members

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

Medical Advisor

Prof John Watson (DCMO)

Secretariat

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

Invited Speakers

Richard Pebody (PHE)
Mark Jit (PHE)
Prof. John Watson (DH Deputy CMO)

Invited observers from Devolved Administrations

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

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 (PHE)
Dr Shamez Ladhani (PHE)
Pauline MacDonald (NHSE)
Dr Vanessa Saliba (PHE)
Ruth Howlett-Shipley (MoD)
Joanne White (PHE)
Joanne Yarwood (PHE)
Dr Sema Mandal (PHE)
Dr Peter Grove (DH)
Dr Ian Feavers (NIBSC)
Dr Caroline Trotter (PHE)
Dr Claire Cameron (HPS)

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

2. Apologies had been received from Prof Anthony Harnden, Prof Rob Read and Alison Lawrence.

3. Registered conflicts of interest were provided to the Committee and members were given the opportunity to provide updates.

4. The Chair informed the Committee that the meeting would be the last one for Prof John Watson, and the Chair thanked Prof Watson for all his support to the JCVI during his term as Deputy Chief Medical Officer.

I. Horizon Scanning

5. The Committee thanked all those who contributed information to the annual horizon scanning exercise undertaken by the secretariat. The Committee noted the information provided, and suggested a number of amendments to the forward planning of the Committee's work. JCVI noted, as previously, that members would be interested in reviewing data on new vaccines to prevent GBS disease in the newborn and RSV infection in infants given the burden/severity of these infections, placing these as high priority for consideration for future maternal/childhood programmes.

6. JCVI noted the importance of ongoing work on the development of vaccines for prevention of influenza, a number of nosocomial infections, and antimicrobial resistance. The committee also considered the important work being undertaken to develop vaccines for outbreak pathogens that might threaten global health (e.g. Ebola). The Committee agreed that MenB vaccination should be added to the forward plan given developments regarding a large carriage study, and upcoming MenB vaccines for adolescents. Finally the committee commented on the challenges presented by immunization in older adults, the potential for prevention of invasive bacterial infections including E. coli, and noted upcoming considerations of a new vaccine for shingles in this age group.

II. Minute of the February 2017 meeting

7. The Committee noted correspondence from Glaxo Smith Kline (GSK) regarding the February minute. The Committee considered issues raised regarding wording of the minute in reference to pneumococcal conjugate vaccines. The Committee agreed that the minute as written was accurate, and the issues may have arisen from referral to unpublished data provided by PHE. The Committee agreed that minor changes should be made for clarification, including a citation that the information provided was from PHE and unpublished.

8. The Committee noted a request for clarification regarding the meningococcal section of the minute, with regards to the uncertainty scenarios presented. The Committee noted that the minute described a discussion point on whether the pessimistic scenario modelled was appropriate, and noted comments at the meeting that the most pessimistic scenario was too pessimistic. The Committee agreed that the minute of the February 2017 meeting was an accurate reflection of the discussion, and agreed that the most pessimistic uncertainty scenario was too pessimistic. It was agreed that an average of the outputs from the three less pessimistic uncertainty scenarios would represent a more appropriate uncertainty test.

III. Matters arising

Actions from the last meeting

9. An action from the previous meeting was noted, for data on immunogenicity and persistence for MenACWY vaccine to be reviewed by the Meningococcal Sub-committee Chair following a request from the Travel Sub-committee. The Committee noted that the Meningococcal Sub-committee Chair had reviewed the data, which had been summarised in a paper provided.

10. The Committee agreed with the findings of the paper, that the literature supported boosting after five years. The Committee noted that antibody against MenA disease was the first to wane, and this meant boosting was important for travel, but less important for the routine MenACWY programme in the UK. Given the lack of data on repeat boosting the Committee agreed that boosting every five years would be a sensible approach until data became available.

Research Action – Data are required on the need for and timing of booster doses of MenACWY vaccine, after an initial dose and a five year booster.

NITAG session at SAGE

11. The Committee noted that the WHO Strategic Advisory Group of Experts (SAGE) had discussed the strengthening of National Immunisation Technical Advisory Groups (NITAGs) at the April meeting. Substantial work had been undertaken by WHO to establish and strengthen NITAGs globally. The Committee noted that SAGE had commented that NITAGs should have a role in considering the private provision of vaccinations, to ensure consistency outside of national programmes. While the UK had a relatively small private market for vaccinations, compared with other countries, the Committee agreed that consideration should be given to this. The Secretariat agreed to work with the Department of Health on this issue, and the Committee agreed that private providers in the UK should, at least, be providing those vaccines in the national vaccination schedule for the UK.

12. The Committee thanked members of the Committee and the secretariat for the work they had undertaken with WHO in establishing and strengthening NITAGs in a number of countries.

Group B Streptococcal vaccination

13. The Committee noted that the Chair had written to the Department of Health on behalf of the Committee regarding research being commissioned on perinatal antibiotic use, advising that the development of vaccines against GBS disease might reduce this devastating disease in neonates and potentially contribute to reductions in use of antibiotics and further limit the threat of antimicrobial resistance. Following a meeting of academic groups working on GBS with the MHRA to discuss the barriers to development and the potential research gaps. Subsequently, The European Medicines Agency (EMA) had a meeting in May 2017 to discuss the development and pathways to licensure for GBS vaccines, involving industry, academics and public health officials.

14. JCVI acknowledged the important recent well-represented discussions with regulators which had arisen as a result of JCVIs communication with the Department of Health. These meetings had highlighted some important research gaps that should be addressed in the next few years to facilitate assessment of new GBS vaccines in development.

15. In particular, JCVI noted that there was an urgent need for the development of standardised antibody measurement assays which would underpin vaccine development, would be helpful for regulatory assessment and could be used to develop correlates of protection, particularly important in the absence of efficacy data. JCVI also noted that a major effort was needed to establish a serum bank from cord blood that could be used to determine levels of antibody, measured with a new standardised assay, that correlate with protection/susceptibility to GBS disease in the new-born. The need for data on antibody half-life was also discussed as this would allow assessment of levels of antibody needed to protect against late-onset GBS disease.

IV. Influenza Programme Review

16. The Committee noted a presentation from PHE providing an overview of the findings from the 2016/17 influenza season. On the influenza activity in the UK the Committee noted that:

- in the 2016/17 influenza season the predominant subtype was influenza A(H3N2) , with some limited influenza B activity;
- the season started relatively early in December, with the pre-epidemic threshold for influenza-like illness (ILI) GP consultation being breached in week 51 and staying at low intensity levels;
- outbreaks of acute respiratory infection were seen mainly in care homes, with some hospital outbreaks and a small number of school outbreaks;
- lab confirmed hospitalisations rates reached high levels, though the peak rate was lower than the previous season,
- ICU lab confirmed admission rates were lower than the previous season, with the largest numbers of admissions in the over 65 years age group;

- excess mortality reached moderate levels, but was lower than seen in 14/15, and mostly seen in the 65+ age group;
- the 16/17 season's A(H3N2) viruses were difficult to cultivate, with only a small proportion isolated and antigenically characterised; and
- those viruses antigenically analysed were similar to the A/HongKong/4801/2014 Northern Hemisphere 2016/17 A(H3N2) vaccine strain.

17. On vaccine uptake the Committee noted that:

- 70.4% uptake was seen in the over 65 year olds, 48.7% uptake was seen in under 65 year olds in at-risk groups, and 63.4% uptake was seen in healthcare workers;
- for the paediatric programme, uptake was higher this season than last season in all age groups with uptake of 38.9% in all 2 year olds; 41.5% in all 3 year olds; 33.9% in all 4 year olds
- in 2016/17 all children aged 2 to 4 years of age and those in school years 2, 3, and 4 in England were offered LAIV vaccination, in Scotland and Northern Ireland all primary school children were offered vaccine;
- uptake in schools in Northern Ireland was 78%, and 73% in Scotland;
- uptake rates seen in schools programmes were relatively consistent by area in England with uptake of 57.6% in school year 1; 55.4% in school year 2 and 53.3 in school year 3.

18. On the adult influenza vaccination programme, and inactivated vaccines available for use in this age group the Committee noted that:

- in those aged 18-64 years, vaccine effectiveness was modest for all strains, and in those aged 65 years and over vaccine effectiveness was even lower;
- an adjuvanted trivalent influenza vaccine for those aged over 65 years was due to be licensed in the UK later in 2017, and could potentially be used in the programme from the 2018/19 season;
- published studies indicated higher vaccine immunogenicity and effectiveness for the adjuvanted vaccine in comparison with non-adjuvanted vaccines;
- a high dose influenza vaccine for the elderly was not currently available in the UK;

19. On the childhood influenza vaccination programme the Committee noted that:

- in children aged 2-17 years of age vaccine effectiveness for LAIV was good, particularly against influenza B;
- when considering prior vaccination, the highest effectiveness in those aged 2-17 years of age was seen in those vaccinated in both 15/16 and 16/17 compared with those vaccinated in only one of those seasons;

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- in England, when comparing pilot areas (those with full roll out of the primary school programme) to non-pilot areas, lower ILI consultation rates and laboratory confirmed hospitalisation rates were seen in pilot versus non-pilot areas; and
  ICU confirmed admission rates were comparable between pilot and non-pilot areas.

20. On overall impact, the Committee noted that:

- in Scotland and Northern Ireland (where the primary school programme was fully rolled out with good uptake) GP ILI consultation rates did not go above the pre-epidemic threshold at any point during the influenza season;
- in England and Wales (where the primary school programme was not fully rolled out, and with uptake lower than Scotland and Northern Ireland) GP ILI consultation rates went above the pre-epidemic schedule for several weeks in both countries;
- ICU admissions were above the pre-epidemic threshold in Scotland and Wales for a number of weeks, with short periods above the moderate threshold;
- ICU admissions in England were above the moderate threshold for 8 weeks; and
- moderate levels of all cause excess mortality were seen in England for two weeks but not in the other UK countries.

21. The Committee noted a summary of the hypotheses put forward for lower LAIV A(H1N1) effectiveness seen in previous seasons on the United States, the leading hypothesis of which was lower replicative fitness of the A(H1N1) component of the vaccine compared with the other vaccine components. Given this, the company was working on reformulation of the vaccine to improve replicative fitness of the A(H1N1) component. A number of vaccine virus shedding, immunogenicity and effectiveness studies with the 2017/18 formulation were planned in the UK.

22. The Committee agreed that the UK findings continued to support the rationale for the paediatric influenza vaccine programme. An indirect effect was being seen overall, but there was no apparent indirect protection against the most severe cases. However, questions were raised as to whether the analyses were powered to properly assess these outcomes. Comments were made regarding the uncertainties with observational data, and that the effects being seen could be associated with mixing patterns, particularly in younger adults.

23. The Committee considered that the indirect effects indicated by data from Scotland and Northern Ireland could be associated with the numbers of cohorts vaccinated, or the higher uptake being seen in those countries, or both.

24. The Committee noted incremental impact and cost-effectiveness modelling on use of the inactivated quadrivalent influenza vaccine in those aged 65 years and

over. The modelling considered the incremental benefits of the programme in the context of the childhood influenza vaccination programme.

25. The results indicated health benefits from use of quadrivalent vaccine in those aged 65 years and over. However, given that the burden of influenza B was concentrated in younger age groups; the childhood programme used a quadrivalent vaccine; and the well-demonstrated indirect effect of vaccinating children protecting other age groups - the potential impact of a quadrivalent vaccination programme in those aged over 65 years was reduced. Therefore the willingness to pay for the additional B component in the quadrivalent vaccine was relatively small.

26. Given the findings on the incremental benefit of quadrivalent influenza vaccine in those aged 65 and over, the Committee agreed that there was health benefit from using the quadrivalent vaccine in that age group, although the benefit would be limited by the impact of the childhood programme. The Committee agreed that consideration of the wording in the 'Green Book: Immunisation against infectious disease' on quadrivalent vaccines should be considered by correspondence following the meeting.

27. Vaccine effectiveness seen in the elderly for the 2016/17 season in those aged 65 years and over was considered disappointing by the Committee. A trend for lower vaccine effectiveness against H3N2 in the elderly was emerging, which contrasted with higher A(H3N2) effectiveness in younger adults. The Committee agreed that proper consideration should be given to the benefits of the programme in light of the effectiveness being seen in recent H3N2 dominated seasons. The Committee had planned on reviewing the entire programme in 2020, once the paediatric programme had been fully rolled out in primary schools in England. However, the Committee agreed that consideration of the over 65 year olds component of the programme should be brought forward. This was important given the data seen, and that new influenza vaccines, including an adjuvanted vaccine, would be coming onto the UK market.

28. The Committee agreed that they would wish to consider data from a number of years, and would wish greater granularity of effectiveness data by age. The Committee considered that immune senescence could be an important factor in the effectiveness being seen. Timing of vaccination could also be playing a role. Data on incremental benefit and cost-effectiveness would be useful in forming any views on optimisation of the routine over 65 year olds programme, along with use of adjuvanted vaccines. It was noted that this work was underway, and the Committee agreed to consider this at the October 2017 meeting.

29. The Committee considered that the recent findings from the elderly programme meant that a greater focus should be made on rolling out, and improving uptake in the paediatric programme.

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Schizophrenia as a risk group for influenza vaccination

30. The Committee noted a paper by Olfson *et al*[1] on premature mortality in adults with schizophrenia, and a question raised as to whether schizophrenia should be a specified risk group for influenza vaccination. The Committee noted that there were no available data on uptake of vaccine in schizophrenics, and that the 'Green Book' currently advised vaccination for those with certain neurological conditions. Data presented in the paper did not include laboratory confirmed influenza, and it was not possible to compare mortality ratios with those currently used to highlight specific risk groups for a recommendation on vaccine use. Comments were received that schizophrenia could be a proxy for other risk factors, and that data were unavailable on the co-morbidities within that population.

31. The Committee agreed that those with schizophrenia in an existing risk group should be a priority for vaccination, but could not advise adding schizophrenia as a specific risk group. The data presented were hypothesis forming, and further research would need to be presented before any advice could be developed on the issue.

V. HPV vaccination for adolescent boys

32. The Committee received an update from the Chair of the HPV Subcommittee on the outcome of the June 2 Subcommittee meeting which was held by teleconference. The Committee noted that:

- the Subcommittee had discussed the results of the peer review of the Warwick modelling work and the changes made to the PHE modelling work since the January meeting;
- a number of changes to the Warwick modelling work were recommended by the Subcommittee before its publication or potential use for procurement purposes;
- the proposed changes were unlikely to alter the outcome of the main findings;
- there was now more certainty in the results from the PHE model although work would continue in developing the model further for sensitivity analysis and to prepare the work for peer review and publication;
- a model developed by the London School of Hygiene and Tropical Medicine had also been developed (to look at inequalities) and the outputs of this would also be used to look at the cost-effectiveness of extending to boys;
- all the modelling evidence considered to date gave similar findings, in that with high uptake in a girls programme there were relatively small gains in health benefits to be made by vaccinating boys;

[1] Olfson et al (2015) Premature Mortality Among Adults With Schizophrenia in the United States. JAMA Psychiatry 72(12):1172-81

- under standard cost-effectiveness methodology, a boys programme was highly unlikely to be cost effective; and
- the Subcommittee recognised that there were health benefits in vaccinating adolescent boys, but taking the evidence as a whole the Subcommittee could not recommend a gender neutral HPV vaccination programme, as the models showed that it would not be a cost-effective use of public money.

Warwick University - peer review

33. The Committee noted the main comments of the peer review and the response from Warwick University and the feedback received since the Subcommittee meeting in January:
    - to use Scottish data in the model since the study covered the UK and there was good data from Scotland;
    - to include cross protection against HPV 6 and 11 for the bivalent vaccine in the sensitivity analysis;
    - to change the time for the modelled introduction of the boys programme from 2015 to 2017 for the forward simulation of the model since this was now out of date;
    - to give more detail on the cost-effectiveness, including a breakdown of different health conditions to the QALYs and healthcare costs of the different strategies;
    - this would allow the impact of the strategies to be examined on the population, each sex and work out exactly that attributable to herd protection from girls and that attributable from boys vaccination; and
    - to take into account comments received from Natsal researchers on the modelled sexual behaviour using more of the data from the Natsal-3 findings;
34. The Committee agreed with the subcommittee that the uptake modelled in boys should be expected to be more in line with that seen in girls but noted that this would increase the costs relative to the benefits of a boys programme and thereby make a boys programme less cost-effective than when modelled at a lower uptake of 67%.

35. The Committee received a verbal update from Warwick University and noted that reducing the uptake in girls from 90% to 80% did increase the threshold for the willingness to pay price but that the result was still not cost-effective in the uncertainty analysis.

36. The Committee noted that Warwick would be developing the work further to take account of the peer review comments and tease out the detail of the cost-effectiveness results regarding the benefits in vaccinating boys. What was clear however was that the main benefit of vaccinating boys was seen in the additional cervical cancer cases prevented in females, however further work was necessary

to breakdown the benefits in males.

37. Overall the Committee agreed with the Subcommittee that the changes suggested by the peer review were unlikely to affect the outcomes of the modelling which indicated that a boys' programme was highly unlikely to be cost effective when coverage in girls was high. The Committee agreed that before publishing their findings Warwick should take into account the main points highlighted by the reviewers.

PHE model impact and cost-effectiveness assessment

38. The Committee noted that PHE had made the following high priority changes to the model since the last JCVI meeting:

- disease natural history was now modelled using a hybrid approach to allow deterministic progression to rare outcomes;
- model calibration was now based on a Bayesian approach using Sequential Monte Carlo methods with many more iterations;
- much better fits to disease outcomes (except for the rarest outcomes) had now been achieved; and
- screening had been better implemented in the model.

39. The Committee noted that while a better fit had now been achieved to the data there was also now more uncertainty captured which meant there were more outliers at some extremes of the simulations. While the model performed well under the base case scenario (lifetime protection), the results with a 20 year duration of protection were insufficiently robust to give a reliable cost-effectiveness estimate, and more work was required to look at this.

40. The Committee noted that under a girls only vaccination programme, assuming lifetime protection, HPV vaccine types 6/11/18 would be eliminated in females and less than 20% of HPV 16 would remain, meaning there would be little burden left for a boys programme to impact on.

41. The Committee noted that not all cancer outcomes or anogenital warts would be eliminated in MSM under the scenario of a girls-only programme plus a targeted MSM programme. Of the incremental benefit gained by extending vaccination to boys, 30-40% of this would be due to the impact in MSM.

42. The Committee noted that the results of the PHE model indicated that extending vaccination to boys was highly unlikely to be cost effective using the standard economic rules that JCVI followed for assessing cost effectiveness. The Committee noted that the uncertainty analysis showed that a willingness to pay price of less than £5 per dose would only be achieved in a very small proportion of simulations and hence would be regarded as highly unlikely to be cost-effective at that price.

43. The Committee noted that the drop in HPV prevalence was larger than that seen in the previous compartment model, and this was likely due to the IBM capturing

individual sex acts and overlapping partnerships using the data from Natsal 3. This meant that vaccination had a bigger impact and generated stronger herd effects, and therefore was less favourable to gender neutral vaccination than the model which informed the original decision.

44. JCVI and the sub-committee agreed that the parameter values used in the analysis were the most plausible based on the available evidence. The Committee noted that there was still some work to be done to further develop the model, including understanding some of the outliers in the results. In addition the sensitivity analysis for 20 years duration of protection required further simulations in order to provide a robust cost-effectiveness estimate under this assumption.

45. The Committee agreed that the model would also be independently peer reviewed according to the standard process for independent review for JCVI, once the required adjustments had been made.

46. The Committee noted that the model addressed a number of issues raised by stakeholders concerning previously published models, including concurrency, commercial sex work, unprotected sex and a definition of MSM which allowed for single or occasional same-sex partnerships. On the issues of population growth and trends in oropharyngeal cancer rates, PHE considered that there was too much uncertainty in speculating what the future trends might be.

47. On the risk of a fall in uptake in the girls programme due to vaccine hesitancy, the Committee noted that since the introduction of the programme in 2008 there was a history of high uptake. This together with the initial catch-up in the first few years of the programme meant a lot of gains had already been made, which added considerable resilience to the programme in the event of a temporary fall in coverage.

Equality

48. The Committee agreed that equality was an important issue that had been raised by stakeholders as an argument for extending HPV immunisation to adolescent boys. The Committee noted a substantial volume of correspondence from stakeholders and individuals on the matter, and agreed that the correspondence should be taken into account in the consultation on the interim statement. On this issue the Committee considered that:

- JCVI is tasked to provide scientific advice based on the best available evidence and impact and cost-effectiveness modelling, and by design is not equipped to fully consider equality issues in detail;
- JCVI should however show due regard to equality by identifying potential issues for further consideration; and
- DH was equipped to fully consider issues of equality when developing policy based on the advice of JCVI, and it had produced an equality impact assessment on HPV vaccination in 2008.

49. The Committee also considered that the following should also be taken into account by DH when formulating the equality assessment:

- that the scientific evidence indicated that the strong herd effects from the girls programme would provide substantial benefits to males;
- has contributed to a significant decrease in rates of infection with the two main cancer-causing human papillomaviruses in vaccinated and unvaccinated women;
- population level protection from the girls programme has also been observed in males, with a 62% reduction in the rate of first episode genital warts in young men in England since 2009 compared with a 72% decrease in young women;
- the original aim of the programme had been to prevent cervical cancer, but since then the evidence had strengthened on the association of HPV vaccine types with non-cervical cancers which also affected males;
- there were clinical benefits to males which could be achieved by including male vaccination, that would not be achieved from a girls only programme;
- much of the additional health benefit gained from vaccinating boys, and most of the costs saved, would actually be due to the additional cases of cervical and non-cervical cancer prevented in females;
- MSM were disproportionately affected by HPV infection and disease compared to other men and were expected to receive little indirect benefit from the girls programme; and
- the Committee had previously advised a targeted programme for MSM, which was already being piloted and informal feedback suggested that the programme had been well received by both the medical and MSM community.

<u>Data on one dose and mixed schedules</u>

50. The Committee noted ongoing and planned trials of single dose schedules, and had already made a start in considering the potential of this for the HPV programme. The Committee also noted that there was research ongoing on mixed schedules, which it had previously highlighted as a priority. The Committee agreed to review the evidence as it becomes more substantial, and its potential impact on the current programme and the cost-effectiveness of a gender neutral vaccination programme.

<u>Conclusion</u>

51. The Committee recognised that a programme to vaccinate adolescent males would provide those vaccinated with direct protection against HPV infection, and associated disease, and that extension of the existing programme would provide clinical benefit. Modelling also predicted some additional population health benefits from extending the programme to adolescent boys, with most of these benefits being seen in unvaccinated girls and MSM.

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52. The Committee agreed that its remit was to consider the scientific evidence, and that included the cost-effectiveness of changes to the programme. This was important in ensuring its advice reflected the rational use of finite health service resources to maximise the health of the population.

53. The evidence considered, including the PHE model, the Warwick Model, the Brisson meta-analysis, and the original modelling by Jit et al, consistently predicted that extending the HPV programme to adolescent boys would not be a cost-effective use of health service resources. These analyses indicated that with the levels of uptake being seen in the UK, the adolescent girls HPV vaccination programme would have a substantial impact on HPV related disease, not just in the female population, but also indirectly in the male population.

54. While there were aspects of the Warwick University and PHE model still to be addressed, the Committee agreed that the results were sufficiently robust to formulate interim advice.

55. Overall, the additional benefits gained from extending the programme to adolescent boys would be small, relative to the impact of the girls programme, and all the evidence considered consistently indicated that extending the HPV programme to adolescent boys would not be a cost-effective use of health service resources in the UK setting. Taking the evidence as a whole the Committee therefore agreed it was unable to advise extension of the national HPV programme to adolescent boys, according to the cost-effectiveness analyses considered.

56. The Committee recognised arguments made by stakeholders on the issue of equality of access, and agreed to refer this issue to the Department of Health for consideration.

57. The Committee agreed to issue this interim advice for stakeholder consultation to ensure that the most appropriate and up-to-date evidence had been used, and that reasonable assumptions had been made where evidence was limited or unavailable. Once the consultation is completed, the JCVI would develop and publish its final advice.

VI. RSV vaccination

58. It had been noted in previous meetings that there were a number of potential vaccines under development, some of which had reached early trials and some phase III. A number of modelling groups in the UK were looking at the impact and potential cost-effectiveness of RSV vaccination in different scenarios.

59. The Committee noted a paper summarising the work of a number of UK modelling teams, and a presentation from PHE on the progress made on a number of these models. The Committee noted that three different modelling streams were being undertaken including:
    - a static model of maternal immunisation, post-partum passive immunisation and antenatal or infant vaccination;
    - a static model looking at options for immunisation of older adults (manuscript

still in preparation); and
- a dynamic model which covered all scenarios.

60. The Committee noted that work from the static model on maternal/infant immunisation was at an advanced stage, and had already been accepted for publication. There were a number of uncertainties still to be considered in the development of the static model on vaccination of older adults, in particular on the burden of disease. The dynamic model was still in early development and would not be completed until 2019 at the earliest.

61. While the benefits of a maternal vaccination programme and older adult programme could be estimated using a static model, infant immunisation was considered to require dynamic modelling due to the potential for population level protection.

62. When considering maternal and infant immunisation, the key determinant of cost-effectiveness modelling would be the burden of disease in the first year of life. When considering immunisation for older adults, key uncertainties included the burden of disease in older adults, preventable mortality, and whether vaccination would be required each season. Uncertainties for all scenarios included effectiveness, immunogenicity, duration of protection, QALY losses and long term sequelae. It was hoped that work from a European consortium on RSV would provide evidence on the burden of disease, preventable mortality and QALY losses.

63. The Committee considered the importance of protecting premature infants, and agreed that there was a need to consider how premature those at risk were, to inform decisions on when to administer vaccine during pregnancy. It was noted that children were admitted to hospital with RSV up to at least one year of age. Consideration was also given to community transmission, and the role of older siblings in transmission to younger children and infants. It was further considered that it would be important to understand the risk factors for severe RSV disease in all ages.

VII. Coverage

64. The Committee noted the latest data on immunisation coverage across the UK. Considerations were made regarding the continuing trend for lower uptake of shingles vaccine in those eligible.

VIII. Any other business

65. The Committee noted a verbal presentation from PHE on outbreaks of hepatitis A (HAV) which began in July 2016, which had predominantly affected young MSM in England. 545 cases of HAV had been reported since then, of which 308 were confirmed to be due to one of three outbreak strains of genotype 1A or confirmed to have epidemiological links to the MSM population. Cases had also been identified in 15 countries in Europe, in Chile and the US. There had been cases in the general population.

66. The Green Book recommended immunisation of MSM against HAV. In contrast the British Association for Sexual Health and HIV (BASHH) did not recommend universal vaccination, but recommended that MSM with HIV should be vaccinated, and that clinics in large cities such a London should 'offer vaccination when increased rates of infection have been recognised locally'. They also recommend screening for immunity before vaccination.

67. Because of a global shortage of monovalent Hepatitis A vaccine the PHE Incident Management Team (IMT) had made a number of recommendations regarding opportunistic use of vaccine to MSM attending GUM clinics in England. Dose sparing strategies in order to rapidly control spread in London and limiting spread outside of London were also suggested. Advice from PHE indicated that a single dose of Twinrix® or Havrix Junior® in adults would be acceptable as an outbreak control measure. Given that most MSM attending GUM clinics are aged 45 years or under, off label use of low dose preparations was considered likely to provide sufficient short term protection to control the outbreak.

68. The view of the committee was to reinforce the position as stated in the Green Book, and they agreed that the PHE strategy with regard to dose sparing strategies was sensible in the context of the current outbreak and limitations in supply of monovalent vaccine.

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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 Bill and Melinda Gates Foundation, 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 for a three day course from Gilead, MSD, GSK and Astra Zeneca.
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.
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. Professor Finn undertakes unpaid advisory work for Astellas on a klebsiella-pseudomonas vaccine. 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. The University of Bristol conducts research funded by GSK on meningococcal carriage, by Pfizer on pneumococcal carriage and transmission.
Prof Matt Keeling
Professor Matt Keeling has no registered conflicts of interest.

DRAFT

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 SPMSD (health economics) MSD (health economics), and is an advisor to companies with on Rotateq and Rotarix vaccines. Professor Postma works for the University of Groningen which receives grants from SPMSD and GSK for work related to influenza vaccines. Professor Postma attends advisory boards unrelated to vaccines or vaccine industry Professor Postma organized a conference which was financially supported by Pfizer relating to Health Economics.
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

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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

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